Annual Report 2020

Malformation Monitoring Centre Saxony-Anhalt

OTTO VON GUERICKE UNIVERSITÄT MAGDEBURG

SACHSEN-ANHALT
Ministerium für Arbeit, Soziales, Gesundheit und Gleichstellung

Annual Report 2020
of the Federal State of Saxony-Anhalt
about the frequency of congenital malformations and anomalies as well as genetically cause diseases

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Introduction

Dear readers,

the monitoring of malformations in Saxony-Anhalt represents the most important epidemiological basis for the recording of malformations and is an integral part of health reporting in Saxony-Anhalt. We are the only Federal State in Germany which records population-related malformations nationwide. Our thanks therefore goes to all of those who are committed to actively shape this interdisciplinary cooperation within the framework of the prospective recording of malformations.

Currently, there is a widespread discussion among the public regarding the virology of SARS-CoV-2, the geographical distribution and number of cases, transmission, and immunity, including the risk of reinfection. So, it is good that there is enough evidence to prove the safety of a COVID-19 vaccination even in pregnancy. The Standing Commission on Vaccination (STIKO) recommends with update from 17.09.2021 to all still unvaccinated pregnant women from the 2nd trimester and to unvaccinated breastfeeding women to be vaccinated against COVID-19. A transfer of maternal antibodies to the unborn child has been demonstrated in studies. Whether a relevant protection for the newborn can be achieved is not yet clear, according to the STIKO. This area of life will be continued to be monitored and all relevant data will be collected.

Congenital malformations are structural changes of the body, which are present at birth and can affect any part or parts of the body (e.g., heart, brain, foot). They can affect the appearance or function of the body or both. The malformations can be accompanied by mild to severe functional impairment. These can range from changes in the shape and size of organs up to the absence or even the restricted function of organ systems, e.g., gastrointestinal tract in the case of a congenital intestinal obstruction. Congenital malformations are a significant cause of infant mortality, as well as of chronic diseases and disabilities.

Many congenital malformations can already be detected during prenatal ultrasound examination. That is why it is necessary to include all pregnancy outcomes in a prospective registration of malformations. Also, under the aspect of the ongoing challenges of the COVID 19 pandemic, the analysis in the present published report should be viewed. The current epidemiological analysis of the birth cohort 2020 is therefore of particular interest.

In 2020, 773,100 children were live births nationwide, and in our state, 16,113 live births and 73 stillbirths were registered. The number of births decreased slightly compared to the previous year. In 608 cases, the pregnancy was affected by at least one major birth defect, which corresponds to a proportion of 3.8 percent, similar to the previous year.

Congenital malformations which are diagnosed prenatally or postnatally, confront parents with different challenges than they expected with the birth of a healthy baby. It is then helpful to have professional support from midwives, nurses and doctors who can assist parents. The society as a whole should also become more open in order not to complicate the decision to have a child with a malformation - not only in the first years, but overall.
I would like all children to have the same opportunities in life, and not just on paper. To achieve this, we must be prepared to create the best possible conditions.

I would like to thank all those who dedicate their professional or private lives to support children and their families who are affected by malformations.

Your sincerely

Petra Grimm-Benne

Federal Minister of Labor, Social Affairs, Health and Equality of the State of Saxony-Anhalt

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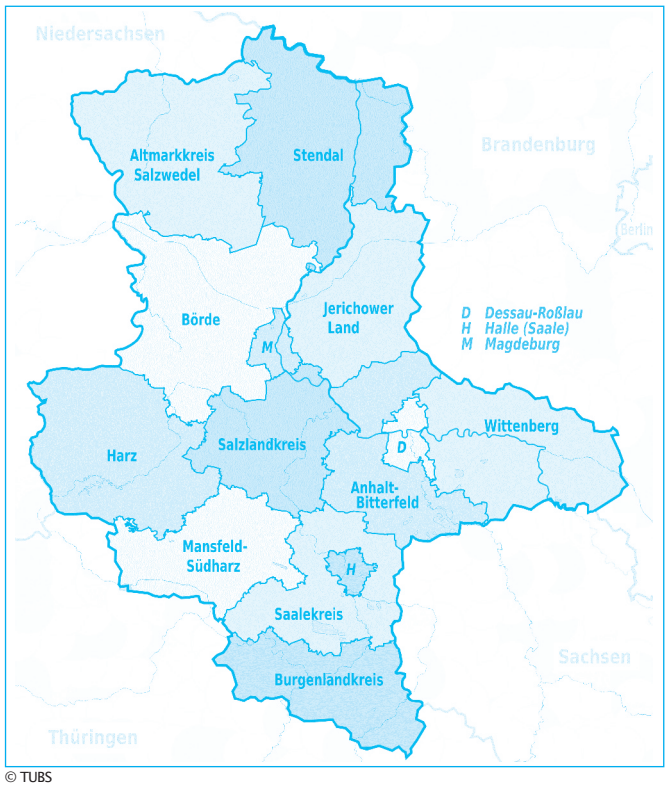
Abbreviations

AABR	automated auditory brainstem response (Hirnstammaudiometrie)
ASD	atrial septal defect t
ATC	anatomical-Therapeutic-Chemical classification
AVSD	atrioventricular septal defect
blt.	bilateral
BMI	Body-Mass-Index
BP	basis prevalence
CI	confidence interval
CNS	central nervous system
dB	decibel
DIV	double inlet ventricle
DORV	double outlet right ventricle
DUP	dilated uropathy
ENT	ears, nose, throat
EUROCAT	European Surveillance of Congenital Anomalies
FAS	fetal alcohol syndrome
FASD	fetal alcohol spectrum disorder r
G-BA	Federal Joint Committee (Gemeinsamer Bundesausschuss)
ICBDSR	International Clearinghouse for Birth Defects Surveillance and Research
ICSI	intracytoplasmic sperm injection
IUGR	intrauterine growth restriction
LB	live births
MCA	multiple congenital anomalies
NHS	newborn hearing screening
NIPT	non-invasive prenatal test (cell-free DNA analysis)
NT	nuchal translucency
o. (n.) s.	not otherwise specified
OR	odds ratio
P	prevalence
PDA	persistent ductus arteriosus
PFO	persistent foramen ovale
SA	spontaneous abortion
SB	standard deviation
SG	stillbirths
TEOAE	transistoric evoked otoacoustic emission
TOP	termination of pregnancy
UTS	urinary tract system
VSD	ventricular septal defect
WOG	weeks of gestation

1 Births and fetuses 2020 in the registration region

Districts / major cities	Live births*	Stillbirths*	Live births and stillbirths in total*	*Spontaneous abortions (>16. SSW)#*	*Terminations of pregnancy#*
Altmarkkreis Salzwedel	564	2	566	-	*2*
Anhalt-Bitterfeld	1,043	4	1,047	-	*2*
Börde	1,258	4	1,262	*3*	*11*
Burgenlandkreis	1,216	6	1,222	-	*1*
Dessau-Roßlau	514	1	515	-	-
Halle	2,188	9	2,197	-	*9*
Harz	1,432	5	1,437	-	*12*
Jerichower Land	643	5	648	-	-
Magdeburg	2,132	10	2,142	*2*	*12*
Mansfeld-Südharz	830	5	835	-	*3*
Saalekreis	1,336	8	1,344	-	*3*
Salzlandkreis	1,292	5	1,297	*3*	*3*
Stendal	810	4	814	*4*	*8*
Wittenberg	855	5	860	-	-
Landkreis in Sachsen-Anhalt o.n.A.	-	-	-	*4*	-
Sachsen-Anhalt	**16,113**	**73**	**16,186**	*16*	*66*

* Source: © Statistical office Saxony-Anhalt, Halle (Saale), 2021
\# Data of the Monitoring of malformation registration Saxony-Anhalt



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2 Participating institutions of the region 2020

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

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

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

- Dipl. Heilpädagogin Schlote, Glindenberg/Magdeburg
- Dr. Perlitz, Fachärztin für Frauenheilkunde und Geburtshilfe, Haldensleben
- Krankenhaus St. Elisabeth und St. Barbara Halle, Pränatale Ultraschalldiagnostik: CA Dr. Seeger, OÄ Dr. Radusch
- Zentrum für Pränatale Medizin Halle: S. Rieße, N. Manthey
- Dr. Altus, Dr. Ababei, Fachärztinnen für Humangenetik, Magdeburg
- Dr. Jaekel, Fachärztin für Kinderchirurgie, Magdeburg
- Dr. Karstedt, Facharzt für Kinder- und Jugendmedizin, Kinderkardiologie, Magdeburg
- Dr. Karsten, Facharzt für Frauenheilkunde und Geburtshilfe, Magdeburg
- Klinikum Magdeburg, Pränatale Ultraschalldiagnostik: OÄ Dr. Schleef
- Universitätsklinkum Magdeburg A.ö.R., Institut für Humangenetik
- Universitätsklinkum Magdeburg A.ö.R., Universitätsfrauenklinik, Pränatale Ultraschalldiagnostik: OÄ Dr. Gerloff
- Universitätsklinkum Magdeburg A.ö.R., Institut für Klinische Chemie, Screeninglabor
- Trackingstelle 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, Pränatale Ultraschalldiagnostik: CA Dr. Müller
- Dr. Achtzehn, Dr. Adams, Dr. Blaschke, Fachärzte für Kinder- und Jugendmedizin, Wanzleben
- Harzklinikum Dorothea Christiane Erxleben Klinikum Wernigerode, Pränatale Ultraschalldiagnostik: OÄ Dr. Schulze

2.3 Pathological-anatomical institutes (ordered by location))

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

3. Malformation registration in Saxony-Anhalt

3.1 General information

Our **thanks** for the continued interdisciplinary cooperation **to you as sender** should be placed at the beginning of the current annual report (data evaluation birth cohort 2020).
In the second year of the SARS-CoV-2 pandemic, we were able to continue population-based malformation registration in Saxony-Anhalt despite other special challenges. Even and especially under the special conditions of the pandemic, monitoring is necessary. This nationwide recording of malformations would not have been possible without the continuous support of the Ministry of Labor, Social Affairs, Health and Equality of Saxony-Anhalt. We are pleased that the successful cooperation under Ms Karen Müller has continued. Furthermore, we are happy about the continued good cooperation in department 23 under the new management of Dr. med. A. Henze. Our special thanks for the good cooperation is dedicated to Dr. H. Willer as the outgoing head of unit and Mr. M. Schiener for the continuous collaboration.

„Developmental congenital hearing disorders" is our special topic in the current annual report. For this purpose, data war evaluated from the newborn hearing screening tracking in Saxony-Anhalt since the introduction of the NHS in Germany in 2009. The health policy significance of congenital malformations and the advantages of implementing a universal screening program can be demonstrated clearly by the example of congenital permanent hearing loss.

COVID-19 disease will enter its fourth wave in Germany in November 2021. To date, staff and resources have been sufficiently available to provide all prenatal care procedures in a timely manner. There are only single published cases indicating vertical COVID-19 transmission (transmission to the fetus), although the risk of such transmission in fetal interventions may then theoretically be increased. For more information, please refer to chapter 14.2. It is still too early to be certain that fetuses, which are infected during the vulnerable first trimester, will not be harmed.
The European network EUROCAT and the WHO-associated ICBDSR network are focusing on the prevalence trajectories under the pandemic.
With the data from Saxony-Anhalt, the malformation monitoring has represented Germany since 1993 at the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), a WHO-associated institution of 42 malformation registries from 38 countries around the world (www.icbdsr.com).
Furthermore, we have been a member since 1992 of the population-based malformation register EUROCAT (**https://eu-rd-platform.jrc.ec.europa.eu/eurocat**).

We would also like to thank the Medical Faculty of Otto von Guericke University Magdeburg for its constant cooperation and involvement in the Saxony-Anhalt malformation monitoring project. We are pleased that this support has continued quite productively under Prof. Dr. med. H.-J. Heinze, Medical Director, and Dr. K. Stachel, Commercial Director, in 2020. We would like to express our special thanks our continued work with the Dean, Prof. Dr. rer. nat. D. C. Dieterich.

3.2 Registration and analysis

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

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

The expected date of delivery is used as basis for analysing the termination of pregnancy, e.g. 2020 is considered the year of birth although some terminations of pregnancy after prenatal diagnostics took place at the end of 2019. 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 Land Statistical Office in Halle for the previous year. The percentages and prevalences shown are rounded values.

All data transmitted to the Monitoring of Congenital Malformations is medically controlled upon receipt and the diagnoses are encoded according to ICD-10 and according to a further extension (Adaptation of the Royal College of Paediatrics and Child Health). Details about the intake of medication during pregnancy are registered by using the internationally recommended ATC codes.

The total number of infants with major malformations as well as the geographical distribution of appearance in the big cities and districts is outlined in chapter 6 and 7. Infants with only minor malformations or rather norm variations are not evaluated separately since this data is only collected incompletely in the end and not target of permanent observation.

Chapter 9 outlines the most frequent single diagnoses of major malformations registered from 2008 to 2020.

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 2020 in comparison to the last 12 years (2008-2019). Here, **a total number of 207,948 births** forms basis for the **basis prevalence** calculation **2008 to 2019**.

The graphical presentation of the annual prevalences allows to identify frequent appearances and gives a good overview about rarely appearing indicator births defects. The exact calculation of confidence levels is based on the binominal distribution with a confidence probability of 95%. To discover a certain trend, the percentage change of an indicator malformation prevalence is illustrated as well during the publishing time of the Annual Report (Chapter 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. For the 2020 birth cohort, 1,822 records were newly recorded, corresponding to about 11% of all children and fetuses in Saxony-Anhalt. Since the last annual report was published, the number of children/fetuses reported has risen from 1,738 to 1,787 due to subsequent reports for 2019.

The malformation monitoring received 2,029 reports for the birth year 2020, including 442 from outpatient facilities. For 11.4 % of the children/fetuses, we received information from different facilities. To confirm or reject a suspected malformation or to classify multiple malformations more precisely, this redundancy is essential and very welcome.

Our special thanks is dedicated to the AMEOS Klinikum Schönebeck. In terms of births per clinic, this clinic continuously sends the most reporting forms. The reporting rate by the University Hospital Magdeburg and the St. Marienstift Hospital is above the average, as well. However, in 2020, we received no malformation reports from the AMEOS Klinikum Aschersleben. From the HELIOS Clinic Jerichower Land in Burg and the SRH Klinikum Naumburg, which had not reported in 2019, information was sent to us in 2020 about three, respectively one child. Highly appreciated are the reports from the outpatient facilities, such as from the Center for Prenatal Medicine Halle, Dr. Karstedt (specialist in pediatric and adolescent medicine,
pediatric cardiologist), Dr. Karsten (specialist in gynecology and obstetrics) and Dr. Welger (specialist for gynecology and obstetrics).

High data quality is achieved through complete information on the reporting sheets and detailed descriptions of diagnoses. They are a precondition for the correct entry of information into the database and have an impact on the quality of the statistics. Thanks to the excellent cooperation of the respondents, the data quality was again very good in 2020: Important information was submitted almost in full in 2020: Gender at 98.4 %, age of mother at 99.1 % and district at 99.6 %. Birth weight was not reported 71 times, but of these only 16 were born alive. The head circumference, which is relevant for the assessment of a microcephaly, was not given for 24.7 % of the children.

We ask all senders to continue to report all malformations, to indicate all accompanying malformations and to describe them as completely as possible. In the year of birth 2020, a total of 98 indicator malformations were diagnosed prenatally at 83 births. 6 times there was no postnatal finding that could be assigned. If this is missing, the prenatally findings are not included into the analysis of the indicator malformations (Chapter 10).

We receive two thirds of malformation registrations and indications of control cases by means of the **„green documentation sheets“**, which we provide free of charge to the reporting institutions. Documentation sheets may be ordered at any time by phone **+49 391-6714174** or e-mail to **monz@med.ovgu.de**. Additionally, it is also possible to report on so-called „**white documentation sheets“**. This form serves to register a minimum data set. The indication of the above-mentioned information and possible risk factors like intake of medication or family histories and an exact description of the malformation and corresponding symptoms are important here.
Both documentation sheets are also available for download on our homepage **www.angeborene-fehlbildungen.com.** It is possible to complete them manually or to enter the data directly into the PDF file, print it out and send it back to us. Mostly, we receive the reports by mail on our documentation form sheets. In many institutions fax reports have become the preferred method of transmission. Our **fax number** is: **+49 391-6714176**. We will be at your disposal for answering any further questions about the reporting procedure and congenital malformations in general.

5 Sex Ratio

Sex ratio of all live births and stillbirths of Saxony-Ahalt according to the information of the Statistcal Office

male	8314 live births and stillbirths
female	7872 live births and stillbirths
total	16,186 live births and stillbirths

Sex ratio m : f = 1.06

The Statistical Office of Saxony-Anhalt indicated a number of 16,113 live births in 2020. During the last four years (2016: 18,092), the number of live births in Saxony-Anhalt has been declining in contrast to the number of stillborn children. Whereas 66 stillbirths were registered in 2008, a number of 73 was reported in 2020, after a maximum value was registered in the previous year (2019: 99).

This is also the case in 2020 (m : f =1.06). In the reporting period (2008- 2019: m : f = 1.05) the minimum value of the ratio of m : f was 1.03 and the maximum value was 1.07. When regarding the stillbirths separately, the sex ratio ranged between 0.73 and 2.37. For 2020, a gynecotropy (2020: m : f = 0.87) can be observed.

Major malformations affected 608 children/fetuses in 2020 (live births and stillbirths, terminations of pregnancy and spontaneous abortions from 16 weeks gestation). For children/fetuses with major malformations, an androtropy (2020: m : f = 1.37) could be observed.

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

male	340 births
female	249births
indeterminate	1birth
unknown	18 births
total	608 births

sex ratio m : w = 1,37

Among the 198 children/fetuses with only minor malformations which were reported to the malformation monitoring for the birth cohort 2020, a boyishness can be observed (m : f = 1.32). Almost always, the ratio of boys to girls is greater than one, even for exclusively small malformations.

Sex ratio of all births with only minor malformations and anomalies

männlich	112 births
weiblich	85 births
unbekannt	1 birth
gesamt	198 births

sex ratio m : w = 1,32

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

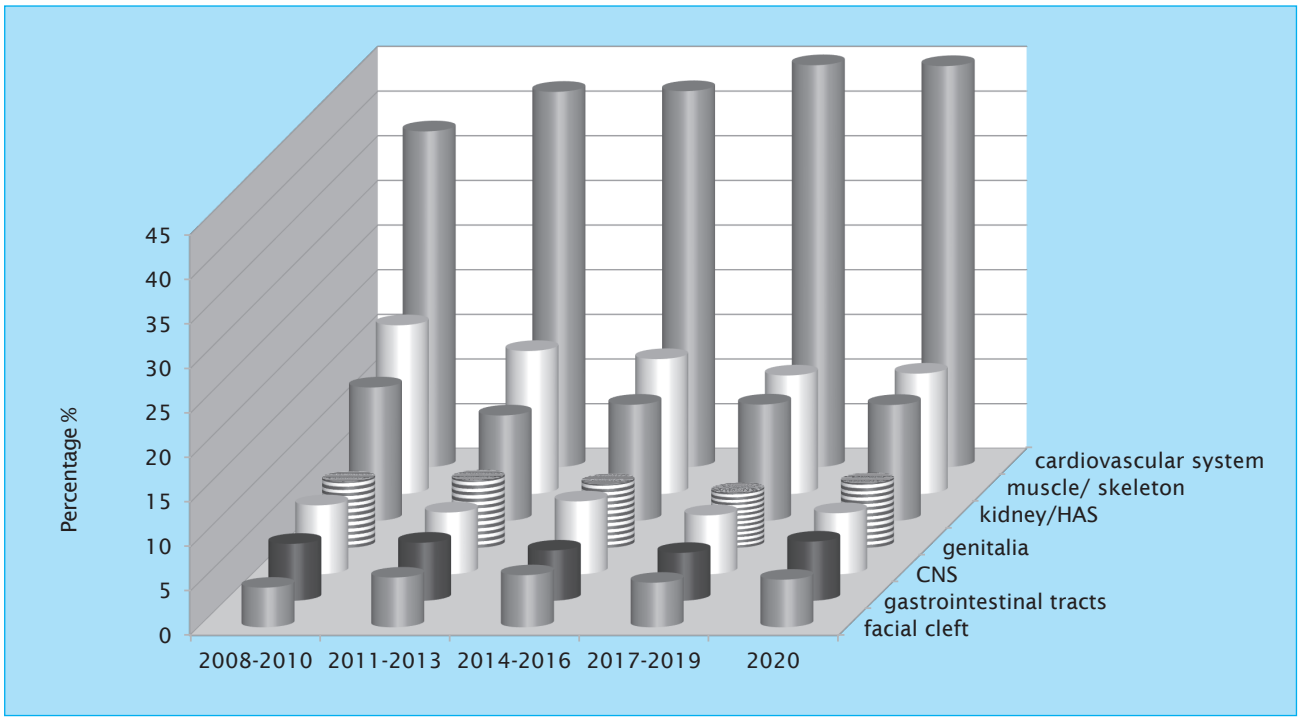


Fig. 5: Organ system involvement in major malformations (grouped)

608 children/fetuses were reported to have major malformations in Saxony-Anhalt in 2020. The diagram above (Fig. 5) shows for seven selected organ systems the proportion of children/fetuses that are affected by a malformation in these organ systems during the reporting period.

More than 40% of all children/fetuses with major malformations (2020: 253) have malformations of more than one organ system. As a result, it is possible that children/ fetuses are counted more than once. The values of the year 2020 are shown separately, those of the previous years, starting with the year 2008, are grouped into four 3-year sections.

Malformations of the cardiovascular system group always occur most frequently. On average, 42.14 % (2008-2019) of all children/fetuses who suffer from a major malformation have a cardiac malformation. An increasing trend can be observed during the last 12 years (2020: 44.90 %). This development matches to the evaluation of the most frequent individual malformations (table page 22).

The musculoskeletal system is the organ system with the second highest incidence of malformations (2008-2019: 15.77 % of all children/fetuses with major malformations). Although the share in 2020 was with 13.49% slightly higher than in the last year (2019: 13.10%), a decrease in the proportion can be observed over the years of the reporting period.

The proportion of children/fetuses with kidney and urinary tract malformations (2020: 12.99%) fluctuates during the years (2008-2019: minimum 9.44%; maximum 16.82%), but a trend does not emerge. On average, the proportion lies at 13.21 % (2008- 2019).

Hypospadias represents by far the largest proportion of genital malformations. Epispadias, ectopia testis, and female genital malformations generally occur less frequently. The prevalence of hypospadias is within the expected range in 2020 (Chapter 10.20). Thus, the proportion of children/ fetuses with malformations of the genital system reaches a common value (2008-2019: 7.04 %) when regarding them as part of all malformed children/fetuses (7.24 %).

CNS malformations were found in 6.91% of all children/ fetuses with major malformations.
This proportion is slightly lower than the usual proportion (2008-2019: 7,41 %). Overall, CNS malformations were observed at 28.23 per 10,000 children/fetuses (2008-2019). The neural tube defect malformations (Chapter 10.1) form with 9.28 per 10,000 children/fetuses (2008-2019) approximately one-third.

In 2020, the proportion of children/fetuses with malformations of the intestinal tract ranges in the middle field with 6.74%. Over the reporting period, the proportion ranges between a minimum value of 4.59% (2015) and 7.29% (2011).

Facial clefts include the cleft palate (one-third) and cleft lip and palate (about two-thirds). In 2020, the proportion of children/fetuses with facial clefts (5.43%) as part of all children/fetuses with major malformations corresponded approximately to the mean proportion of the years 2008-2019 (5.30%).

Most frequent single diagnosis 2019 (only major malformations)

	ICD-10	Diagnosis	Children/foetuses2020		Children/foetuses 2008-2019	
			Number	Prevalence /10,000*	Prevalence /10,000	Confidence interval (CI 95%)
1.	Q21.1	Atrial septal defect (without PFO)	131	80.9	70.1	66.5 - 73.8
2.	Q21.0	Ventricular septal defect	82	50.7	46.8	43.9 - 49.9
3.	Q62.3	Dilated uropathy grade II-IV/ ureterocele	43	26.6	24.4	22.3 - 26.6
4.	Q90.	Down`s syndrome (trisomy 21)	40	24.7	19.3	17.4 - 21.3
	Q54.	Hypospadias	40	24.7	23.9	21.8 - 26.0
5.	H90.	Conductive and sensorineural hearing loss	35	21.6	23.0	21.0 - 25.2
6.	Q69.	Polydactyly (pre- and postaxial)	29	17.9	12.1	10.6 - 13.7
7.	Q37.	Cleft palate with cleft lip	20	12.4	10.3	9.0 - 11.8
8.	Q62.1	Stenosis and atresia of ureter	16	9.9	9.1	7.8 - 10.5
9.	Q66.0	Pes equinovarus congenitus (clubfoot)	15	9.3	15.1	13.5 - 16.9
10.	Q61.4	Renal dysplasia	14	8.6	6.0	5.0 - 7.2
11.	Q25.1	Aortic coarctation	13	8.0	5.8	4.8 - 7.0
12.	Q62.2	Congenital megaureter	12	7.4	8.1	6.9 - 9.4
	Q40.0	Hypoplasia/agenesis of the corpus callosum	12	7.4	5.0	4.1 - 6.1
13.	Q21.2	Defects of the atrial and ventricular septum (AVSD/ASD I)	10	6.2	5.3	4.3 - 6.4
14.	Q63.0	accessory kidney / duplex kidney	9	5.6	8.1	6.9 - 9.4
	Q22.1	pulmonary valve stenosis	9	5.6	7.0	5.9 - 8.3
	Q65.0-2	Subluxation of the hip joint (one sided/both sided/ without indication of side)	9	5.6	2.5	1.9 - 3.3
	Q25.4	right running aortic arch	9	5.6	3.1	2.4 - 4.0
	Q05.	Spina bifida	9	5.6	5.4	4.5 - 6.5
	Q91.0-3	Edwards syndrome (trisomy 18)	9	5.6	4.4	3.6 - 5.4
15.	Q25.0	Open ductus botalli (PDA), haemodynamically effective	8	4.9	10.4	9.0 - 11.9
	Q03.	Congenital Hydrocephalus (without neural tube defects)	8	4.9	5.5	4.5 - 6.6
16.	Q65.3-5	Subluxation of the hip joint (one sided/both sided/ without indication of side)	7	4.3	9.1	7.9 - 10.5
	Q23.0	Aortic valve stenosis/atresia	7	4.3	2.6	2.0 - 3.4

* in reference to 16,186 births
** in reference to 207,948 births

The table on the opposite page presents the most frequently observed major individual malformations in Saxony-Anhalt. The list is sorted according to the current prevalence in 2020, with reference to a population of 16,186 births. For this purpose, the basis prevalence is listed together with the confidence interval (2008-2019: 207,948 births).

Eight cardiac malformations appeared among the 25 major malformations that occupy the top 16 spots in the ranking of malformations in 2020. The heart is the most frequently affected organ system by malformations. The atrial septal defect (2008-2019: 70.1 per 10,000 births) has always been by far the most common congenital heart defect. Malformations of the heart were reported more frequently and in greater detail, especially in the last few years of the reporting period. Therefore, this year's calculated prevalence of five cardiac malformations, atrial septal defect (2020: 80.9 per 10,000 births), ventricular septal defect (2020: 50.7 per 10,000 births; 2008-2019: 46.8 per 10,000 births), aortic coarctation (2020: 8.0 per 10,000 births; 2008-2019: 5.8 per 10,000 births), right trending aortic arch (2020: 5.6 per 10,000 births; 2008-2019: 3.1 per 10,000 births) and aortic valve stenosis/ atresia (2020: 4.3 per 10,000 births; 2008-2019: 2.6 per 10,000 births) each exceeded the corresponding basis prevalence. The defect of the atrial and ventricular septum (2020: 6.2 per 10,000 births) showed a prevalence in the range of the basis prevalence. Only the two cardiac malformations pulmonary valve stenosis (2020: 5.6 per 10,000 births; 2008-2019: 7.0 per 10,000 births) and the hemodynamically effective PDA (2020: 4.9 per 10,000 births; 2008-2019: 10.4 per 10,000 births) were diagnosed less frequently than usual in 2020.

As frequently, it also happenes in 2020, that the atrial septal defect and ventricular septal defect are followed by the dilated uropathy II-IV. grade/ ureterocele. In this year, we have a value close to the upper confidence limit with 26.6 per 10,000 births, however, it lies still within the range of basis prevalence.

Down`s syndrome, which is the most common chromosomal disorder, occupies the fourth place in the ranking. It occurred in 2020 (24.7 per 10,000 births) more frequently than usual (2008- 2019: 19.3 per 10,000 births). Only in two years of the reporting period (2013, 2018), it was diagnosed even more often. With the same prevalence (2020: 24.7 per 10,000 births) in the current year, hypospadias appeared inconspicuously within the range of the confidence interval.

From 2007, the newborn hearing screening with tracking of congenital hearing disorders took place in Saxony-Anhalt. The prevalence of congenital hearing loss increased due to significantly better detection and reporting from the mid-single digits to 23.0 per 10,000 births in 2008-2019. Until then, hearing disorders were often not noticed until after neonatal age. This year's prevalence lies with 21.6 per 10,000 births within the range of basis prevalence.

The sixth place in the frequency list 2020 is occupied by polydactyly with 17.9 per 10,000 births. It was observed more often than expected in 2020 (2008-2019: 12.1 per 10,000 births).

Polydactyly includes both postaxial polydactyly (2020: 12.4 per 10,000 births; 2008-2019: 9.5 per 10,000 births) as well as the less frequent indicator malformation preaxial polydactyly
(2020: 5.6 per 10,000 births; 2008-2019: 3.2 per 10,000 births; Chapter 10.27). For both, a value far above the respective basis prevalence was calculated in 2020. This year's prevalence of postaxial polydactyly represents a maximum in the reporting period.

The cleft lip and palate (2020: 12.4 per 10,000 births; 2008-2019: 10.3 per 10,000 births) is located on the seventh place in 2020. It forms together with cleft lip the indicator malformation cleft lip and palate (Chapter 10.14). In 2020, the incidence of cleft lip and palate was slightly higher than normal, which is reflected in the current annual prevalence of this indicator malformation.

Among the top 16 places of the frequency list of 2020, four malformations of the urinary tract system can be found. For atresia and stenosis of the ureter in eighth place (9.9 per 10,000 births) and the megaureter in 12th place (7.4 per 10,000 births) the calculated prevalence was within the confidence interval of the basis prevalence. However, renal dysplasia (2020: 8.6 per 10,000 births; 2008-2019: 6.0 per 10,000 births) occurred in greater numbers than expected. Accessory kidney (2020: 5.6 per 10,000 births), on the other hand, was found less frequently than usual.

With only 15 cases in 2020, clubfoot (9.3 per 10,000 births) was seen unusually infrequently (2008-2019: 15.1 per 10,000 births). During the reporting period it was only seen less frequently in 2013 with a minimal value (7.1 per 10,000 births).

For hypoplasia/agenesis of the corpus callosum, the prevalence of 2020 was seen above normal (7.4 per 10,000 births; 2008-2019: 5.0 per 10,000 births). However, prevalences fluctuated widely during the reporting period. Minimally, 2.9 per 10,000 births were reported (2018) and a maximum of 8.1 per 10,000 births (2009) was observed.

The most common single malformations in 2020 include two malformations, which differ only in their severity. The dislocation of the hip joint (7.4 per 10,000 births; 2008-2019: 5.0 per 10,000 births) was reported more frequently than in previous years and subluxation of the hip joint (4.3 per 10,000 births; 2008-2019: 9.1 per 10,000 births) was reported significantly less.

Edwards syndrome, another chromosomal aberration on the upper ranks, was seen slightly more frequently in the current year than it might have been expected (2020: 5.6 per 10,000 births; 2008-2019: 4.4 per 10,000 births).

Eight of the malformations which form part of the most frequent single malformations had a prevalence in 2020, which was within the range of the corresponding basis prevalence of 2008-2019. In addition to the above-mentioned malformations, two additional malformations of the CNS can be added, the spina bifida and congenital hydrocephaly.

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

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

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

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

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

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

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

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

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

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

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

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

17. Oesophageal atresia/stenosis:
a congenital malformation characterized by absence of continuity or narrowing of the esophagus, with or without

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

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

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

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

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

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

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

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

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

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

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

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

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

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

31. Gastroschisis:
a congenital malformation characterized by visceral herniation through a right side abdominal wall defect to an intact umbilical cord and not covered by a membrane. 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 (Karoytype 47,XXY). Anomalies of the gonosomes in a male phenotype also include structural anomalies of the gonosomes or a gonosome mosaic.

Note:

The prevalences we calculated in the following chapters are population-based. The value indicates the number of births with malformations born in a certain population with reference to the total number of births in this population.
Since the birth cohort 2000, the coverage area of the malformation monitoring includes the entire Federal State of Saxony-Anhalt. The prevalence calculations starting with the birth cohort 2000 are based on live and stillbirths of mothers who have their place of residence in Saxony-Anhalt during pregnancy and at the time of birth. Between 1980 and 1993, the coverage area grew to include the former district of Magdeburg. After the district reform in 1993, it comprised 13 (1994/1995), 14 (1996/1997), 15 (1998) and 16 (1999) of 21 districts in Saxony-Anhalt. The calculation of the basic prevalences (2008 to 2019) is based on a total number of 207,948 births.

The analysis of the 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.

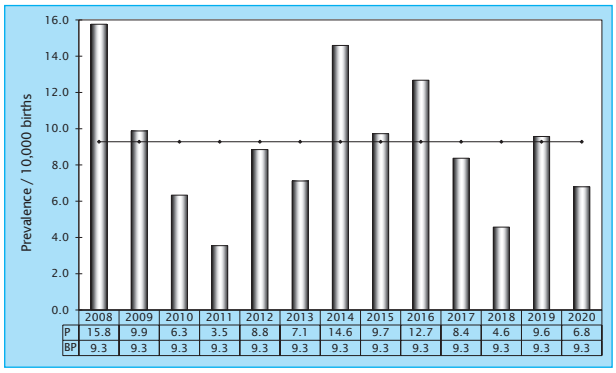
The in chapter 10 indicated comparison prevalences which correspond to the basis prevalences of Saxony-Anhalt are based on data of the years 2008-2019 of the 36 Full-Member-Register of European Surveillance of Congenital Anomalies (EUROCAT) from 18 different European countries. The calculation of the EUROCAT prevalence is based on a total number of 8,486,123 births (source: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data_en).

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

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	11	6.80	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	9.28	8.02 - 10.69	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	10.20	9.99 - 10.42	

Neural tube defects are neural closure defects, which are subdivided into anencephaly, spina bifida and encephalocele. The majority of those affected by a neural tube defect shows a spina bifida.
Nine spina bifida, two anencephalies and no encephalocele were observed in Saxony-Anhalt in 2020. The current **prevalence** for neural tube defects lies with **6.8 per 10,000** births below the confidence interval of the basis prevalence (2008-2019: 9.3 per 10,000 births). During the reporting period, the lowest value was observed in 2011 with a prevalence of 3.5 per 10,000 births.

The confidence interval of the basis prevalence of Saxony-Anhalt covers, with slightly wider limits, the confidence interval of the European prevalence given by EUROCAT (10.2 per 10,000 births). Accordingly, the annual prevalence of Saxony-Anhalt, compared to that of EUROCAT can be rated as rather low.



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	15.8	9.9	6.3	3.5	8.8	7.1	14.6	9.7	12.7	8.4	4.6	9.6	6.8
BP	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3	9.3

Fig. 6: Development of prevalence/10,000 births with neural tube defects in Saxony-Anhalt since 2008

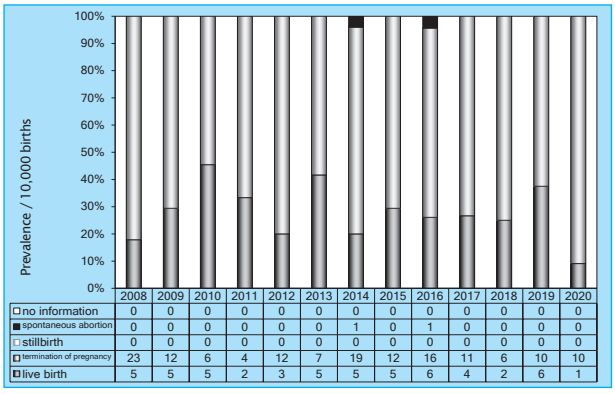
Note

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

additional information:

pregnancy outcome	1 x live birth 10 x termination of pregnancy
sex	3 x male 4 x female 4 x no indication
number of isolated malformations/MCA	5 x MCA 6 x isolated

Only one child with a neural tube defect was born alive in 2020. 10 times the pregnancy was terminated (2019: 90.9 %, 2008-2019: 72.5 % of children/fetuses with neural tube defect).



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
no information	0	0	0	0	0	0	0	0	0	0	0	0	0
spontaneous abortion	0	0	0	0	0	0	1	0	1	0	0	0	0
stillbirth	0	0	0	0	0	0	0	0	0	0	0	0	0
termination of pregnancy	23	12	6	4	12	7	19	12	16	11	6	10	10
live birth	5	5	5	2	3	5	5	5	6	4	2	6	1

Abb. 7: Anteil der Schwangerschaftsausgänge bei Neuralrohrdefekten in Sachsen-Anhalt seit 2008

In 2020, one neural tube defect per 1,471 births was registered in Saxony-Anhalt.

Neural tube defects are probably the most investigated congenital malformation within scientific studies. Already in 1995, several German specialist societies published their recommendation regarding primary prevention of folic acid sensitive neural tube defects. A periconceptional intake of 0.4 mg folic acid was recommended to women at child-bearing age. On the other hand, insufficient realisation of this recommendation is urged by recent studies as in case of unplanned pregnancy (first consultation of gynaecologist not before 5 to 7 WOGs) and by risk groups with low socio-economic status or migrants. An own sample confirmed this insufficient implementation [1].

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

10.2 Anencephaly (Q00.)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	2	1.24	↓
	Berichtszeitraum 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	2.55	1.91 - 3.33	
EUROCAT (Full members)	Period 2009-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	4.05	3.91 - 4.18	

Anencephaly was reported in Saxony-Anhalt only twice in 2020. With a **prevalence 1.2 per 10,000 births**, the prevalence for 2020 is below the basis prevalence (2008-2019: 2.5 per 10,000 births). The double number of cases would have been expected.

When comparing the prevalences for Saxony-Anhalt, for 2020 as well as for the reporting period, with the prevalence provided by EUROCAT of the European registers for 2008-2019 (4.0 per 10,000 births), our prevalence is far below. Valencia in Spain (2008-2019: 2.5 per 10,000 births) has a similarly low prevalence as Saxony-Anhalt. Five of 36 registries report
prevalences of more than 6.0 per 10,000 births.

Both fetuses with anencephaly were stillbirths. One pregnancy was terminated in the 12th and one in the 17th week of gestation, respectively, one week after the diagnosis was made during ultrasound screening

additional information:

pregnancy outcome	2 x termination of pregnancy
Geschlecht	1 x female 1 x no indication
Anzahl isolierter Fehlbildungen/MCA	1 x MCA 1 x isolated

Malformation combinations (MCA) or superordinated syndromes detected:

- Omphalocele, cleft palate, Cantrell pentalogy, ectopia cordis, absent sternum

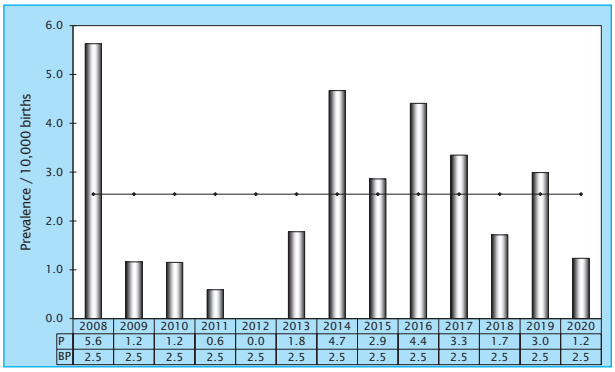


Fig. 8: Development of prevalence/10,000 births with anencephaly in Saxony-Anhalt since 2008

I In 2020, one anencephaly per 8,093 births was registered in Saxony-Anhalt.

10.3 Spina bifida (Q05.)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	9	5.56	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	5.43	4.48 - 6.53	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	4.96	4.81 - 5.11	

This year's **prevalence** for spina bifida (2020: **5.6 per 10,000 births**) lies, similar to last year, inconspicuously within the range of the baseline prevalence (2008-2019: 5.4 per 10,000 births). In Saxony-Anhalt, nine children/ fetuses suffered from spina bifida in 2020.

The basis prevalence of Saxony-Anhalt shows a slightly higher value compared to the prevalence reported by EUROCAT for the years 2008-2019. The annual prevalence Saxony-Anhalt is within the normal range of the prevalence, but because of the narrower European confidence interval, it ranges slightly above it.

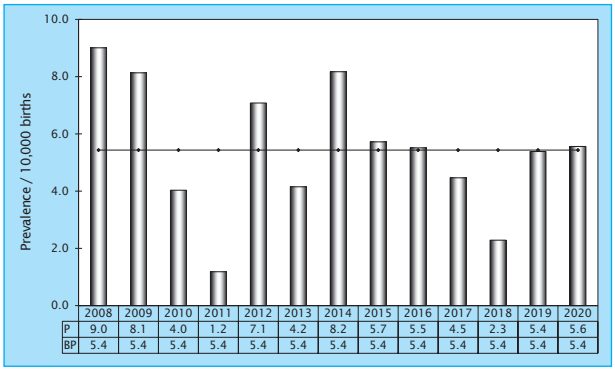
additional information:

pregnancy outcome	1 x live birth 8 x termination of pregnancy
sex	3 x male 3 x female 3 x no indication
number of isolated malformations/ MCA	4 x MCA 5 x isoliert

In eight fetuses, prenatal ultrasonography revealed one cervical, three lumbar, and three lumbosacral spina bifida between the 19th and 22nd week of gestation. Four fetuses of these were affected by other severe malformations. All eight pregnancies
were terminated between the 20th and 25th WOG. One live-born child was diagnosed with a sacral lipomyelomeningocele, which was not detected prenatally.

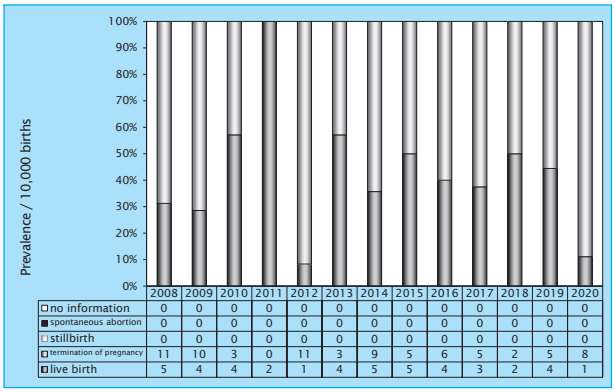
Malformation combinations (MCA) or superordinated syndromes detected:

- Tetrasomy 9p syndrome with: Potter sequence, cleft lip and cleft palate on the left, craniofacial dysmorphia, low-set ears, wide nasal bridge
- caudal regression syndrome with: sacral lipomyelomeningocele, rectal atresia with vestibular fistula, vagina and uterus duplex, DUP II. degree right and III. degree on the left, neurogenic bladder, kinky heel foot right, nevus flammeus
- Agyration of the cerebrum
- Hemivertebra with scoliosis



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	9.0	8.1	4.0	1.2	7.1	4.2	8.2	5.7	5.5	4.5	2.3	5.4	5.6
BP	5.4	5.4	5.4	5.4	5.4	5.4	5.4	5.4	5.4	5.4	5.4	5.4	5.4

Fig. 9: Development of prevalence/10,000 births with spina bifida in Saxony-Anhalt since 2008



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
no information	0	0	0	0	0	0	0	0	0	0	0	0	0
spontaneous abortion	0	0	0	0	0	0	0	0	0	0	0	0	0
stillbirth	0	0	0	0	0	0	0	0	0	0	0	0	0
termination of pregnancy	11	10	3	0	11	3	9	5	6	5	2	5	8
live birth	5	4	4	2	1	4	5	5	4	3	2	4	1

Fig. 10: Pregnancy outcomes of spina bifida in Saxony-Anhalt since 2008

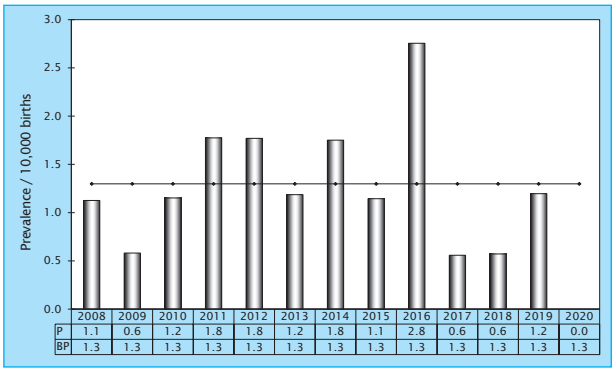
In 2020, one spina bifida per 1,798 births was registered in Saxony-Anhalt.

10.4 Encephalocele (Q01.)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	0	0.0	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	1.30	0.86 - 1.89	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	1.19	1.12 - 1.27	

With a basis **prevalence** of **1.3 per 10,000 births** (2008-2019) in Saxony-Anhalt, the indicator malformation encephalocele is one of the rare malformations. A maximum of five cases per year (2016) were observed in the reporting period. In 2020, this malformation was not diagnosed at all.

EUROCAT gives an overall prevalence for encephalocele of 1.2 per 10,000 births (2008-2019). The prevalence interval of the basis prevalence of Saxony-Anhalt is broader and exceeds the interval of the European malformation registries due to smaller numbers, but the value of the prevalences is similarly high



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	1.1	0.6	1.2	1.8	1.8	1.2	1.8	1.1	2.8	0.6	0.6	1.2	0.0
BP	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3

Fig.11: Development of prevalence/10,000 births with encephalocele in Saxony-Anhalt since 2008

In 2020, no encephalocele was registered in Saxony-Anhalt.

10.5 Microcephaly (Q02.)

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	3	1.85	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	3.85	3.05 - 4.79	
EUROCAT (Full members)	Period 2009-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.69	2.58 - 2.80	

In the year 2020, three children were born in Saxony-Anhalt who developed a microcephaly. Already at birth, the head circumference of one child deviated from normal by -2.3 SD and in another child by -3.1 SD. In one small-for-date child, the microcephaly developed during the course of the child's life and was diagnosed at an age of nine months. The diagnosis of microcephaly is always made by assessing the measured circumference depending on gestational age and maturity. The malformation monitoring uses for this purpose the data available from the INTERGROWTH-21st project study about the internationally valid percentile curves. During the first year of life the diagnosis becomes definitive with the non-development of the brain and skull.

The **prevalence** of 2020 lies with a value of **1.9 per 10,000** births in the third year far below the basis prevalence calculated for Saxony-Anhalt (2008-2019: 3.8 per 10,000 births). During the years 2012 to 2017, prevalence values between 4.2 and 6.5 per 10,000 births were observed. The change in prevalence over the reporting period is classified as nonlinear due to increasing values at the beginning of the reporting period and decreasing values during the recent years (Chapter 10.38).

The tolerance range calculated by EUROCAT Europe-wide of the prevalence of the years 2008-2019 (2.7 per 10,000 births) is below the confidence interval of the basis prevalence from Saxony-Anhalt. This year's prevalence of Saxony-Anhalt lies also below the confidence interval of the overall prevalence of the European malformation centers.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- cleft lip with cleft palate bilateral
- partial chromosome 6 deletion with: reduced intelligence, strabismus

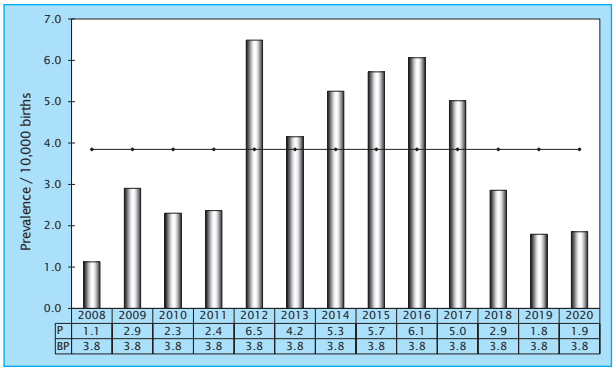


Fig. 12: Development of prevalence/10,000 births with microcephaly in Saxony-Anhalt in 2008

In 2020, one microcephaly per 5,395 births was registered in Saxony-Anhalt.

10.6 Congenitale Hydrocephaly (Q03.)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	8	4.94	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	5.48	4.52 - 6.59	
EUROCAT (Full members)	Zeitraum 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	5.45	5.30 - 5.61	

In 2020, eight congenital hydrocephalies were reported to the monitoring of congenital malformations. Hydrocephalies that occur as a result of a neural tube defect or after hemorrhage or infection are not included.

This year's **prevalence** of **4.9 per 10,000 births** lies in the lower range of the basis prevalence of Saxony-Anhalt (2008-2019: 5.5 per 10,000 births). Compared with the European prevalence provided by EUROCAT (2008-2019: 5.5 per 10,000 births), this year's prevalence in Saxony-Anhalt is slightly below, but both confidence intervals are at the same level. The confidence interval of the basis prevalence of Saxony-Anhalt has due to the smaller population included into the study a wider variation range than the confidence interval of the European prevalence.

additional information:

pregnancy outcome	6 x live births 1 x live birth, deceased after 7 days of life 1 x termination of pregnancy
sex	5 x male 3 x female
number od isolated malformations/MCA	4 x MCA 4 x isolated

Three times, chromosomal defects caused the congenital hydrocephaly. In one case with Patau syndrome, the pregnancy was terminated. One child with Edwards syndrome and other severe malformations in addition to the hydrocephaly, died.

Malformation combinations (MCA) or superordinated syndromes detected:

- Down`s syndrome with: PFO at preterm infant
- Patau's syndrome with: discordant ventriculoarterial junction, median cleft palate, bilateral renal dysplasia, bilateral accessory 6th finger
- Edwards syndrome with: Corpus callosum agenesis,
- ASD II, riding aorta, VSD, hypertelorism, microstomia, low-set ears, craniofacial dysmorphia, overlapping fingers, sandal gaps,
- sacral dimples
- Corpus calloum agenesis

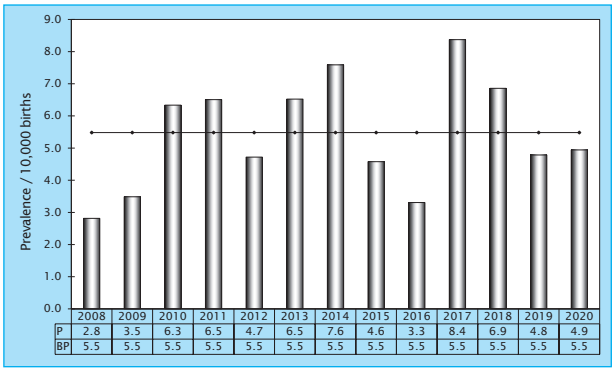


Fig. 13: Development of prevalence/10,000 births with congenital hydrocephalus in Saxony-Anhalt since 2008

In 2020, one neural tube defect per 2,023 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	1	0.62	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	1.64	1.13 - 2.28	
EUROCAT (Full members)	Period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	1.61	1.53 - 1.70	

The indicator malformation arhinencephaly/holoprosencephaly is a very rare malformation with a basis prevalence of 1.6 per 10,000 births (2008-2019). In the year 2020, only one fetus in Saxony-Anhalt **(prevalence 2020: 0.6 per 10,000 births)** showed a holoprosencephaly, as a symptom of Patau syndrome. This results in a prevalence for 2020 that is significantly below the basis prevalence, for the second year in a row. However, this is not surprising due to the small numbers. In the years 2008 and 2014, the malformation was not detected at all in Saxony-Anhalt and in 2010 it was reported in eight children/fetuses (maximum). The trend analysis shows for arhinencephaly/holoprosencephaly with inconspicuous linear
proportion a strong nonlinear proportion, therefore the trend is evaluated as nonlinear.

When comparing the prevalence rates reported by EUROCAT for the years 2008-2019 (1.6 per 10,000 births) with the annual prevalence of Saxony-Anhalt, it is to find far below. The confidence interval of the basis prevalence of Saxony-Anhalt lies with the interval of the average prevalence of the European registries but spans a larger safety range due to smaller numbers.

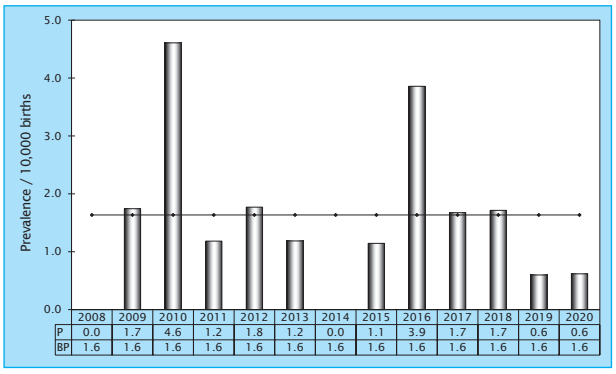
additional information:

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

Holoprosencephaly is a developmental disorder of the forebrain and face. It was detected at the affected fetus in the 20th week of gestation by prenatal sonography. The abruptio took place in the 22nd WOG

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: median facial cleft, cardiac malformation, partial disjunction of the pulmonary vein



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	0.0	1.7	4.6	1.2	1.8	1.2	0.0	1.1	3.9	1.7	1.7	0.6	0.6
BP	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6

Fig. 14: Development of prevalence/10,000 births with arhinencephalie/holoprosencephalie in Saxony-Anhalt since 2008

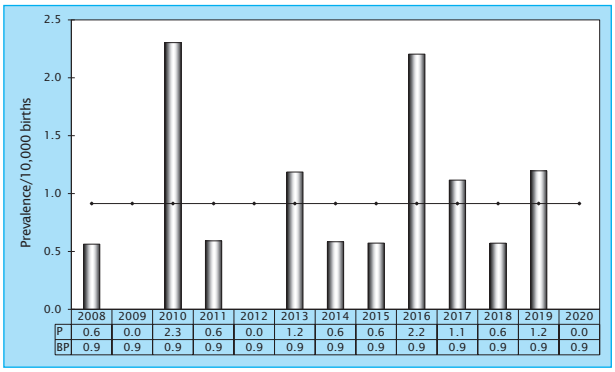
In 2020, one arhinencephaly/holoprosencephaly per 16,186 births was registered in Saxony-Anhalt.

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

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	0	0.0	↓
	iBerichtszeitraum 2008-2019		
	Basisprävalenz/ 10.000 Geburten	Konfidenzintervall (KI 95%)	
	0.91	0.55 - 1.43	
EUROCAT (Full members)	Zeitraum 2008-2019		
	Basisprävalenz/ 10.000 Geburten	Konfidenzintervall (KI 95%)	
	0.93	0.87 - 1.00	

The indicator malformation anophthalmia/microphthalmia belongs with a basis prevalence of 0.9 per 10,000 births (2008-2019) in Saxony-Anhalt, to the rarely appearing malformations. On average, one or two cases may occur in Saxony-Anhalt per year. As in the current year (2020), the malformation is not detected at all (2009 and 2012).

EUROCAT gives an overall prevalence of anophthalmia/microphthalmia of 0.9 per 10,000 births (2008-2019). The basis prevalence of Saxony-Anhalt corresponds to the overall prevalence of the European registries. The prevalence interval is, however, due to the much smaller population of Saxony-Anhalt broader and overlaps the interval of the European malformation registries.



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	0.6	0.0	2.3	0.6	0.0	1.2	0.6	0.6	2.2	1.1	0.6	1.2	0.0
BP	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9

Fig 15: Development of prevalence/10,000 births with anophthalmos/microphthalmos in Saxony-Anhalt since 2008

In 2020, no anophthalmos/microphthalmos was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	3	1.85	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	2.98	2.29 - 3.82	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

The indicator malformation microtia/anotia occurred only three times in 2020 in Saxony-Anhalt. This results in a current annual **prevalence** (**1.9 per 10,000 births**) which is significantly lower than the basis prevalence of 3.0 per 10,000 births (2008-2019). The increasing trend of 12.9%, which was evident for the period 2006-2019 in the last annual report did not continue this year.

In 2007, the newborn hearing screening and tracking started in Saxony-Anhalt. Since the indicator malformation microtia/annotia is often associated with a hearing disorder it is possible that the positive development of the reporting quality through the newborn hearing screening also led to an increased number of registered cases of the indicator malformation microtia/annotia.

EUROCAT does not provide prevalence data for the indicator malformation microtia/ anotia. For the much rarer anotia, EUROCAT gives a prevalence of 0.26 per 10,000 births (2008-2019; CI 0.23-0.30). The prevalence of Saxony-Anhalt for anotia is 0.63 per 10,000 births (2008-2019; CI 0.33-1.07). In 2020, no anotia was registered in Saxony-Anhalt.

additional information:

pregnancy outcome	3 x live births
sex	3 x male
number od isolated malformations/MCA	3 x MCA

Three microtia were seen in Saxony-Anhalt in 2020. Of these, one showed up on the right and two on the left. A bilateral microtia did not occur.

Detected malformation combinations (MCA) or superordinate syndromes:

- Conductive disorder with absent auditory canal left, VSD, hemodynamically effective PDA and PFO at mature infant, right ventricular myocardial hypertrophy, preauricular appendage on the right
- 2 x unilateral conductive disorder with atresia of the osseous auditory canal (1 x right, 1 x left)

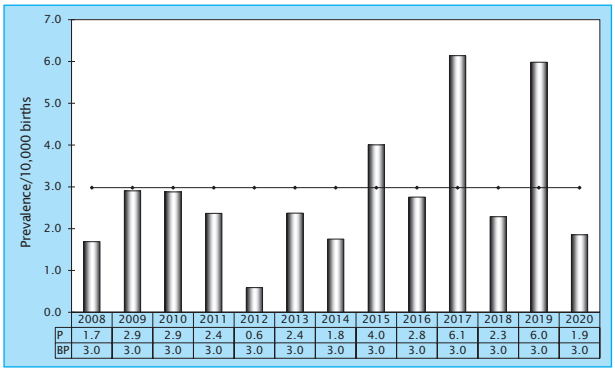


Fig. 16: Development of prevalence/10,000 births with microtia/ anotia in Saxony-Anhalt since 2008

In 2020, one microtia/anotia per 5,395 births was registered in Saxony-Anhalt.

10.10 Tetralogy of Fallot (Q21.3)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	4	2.47	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	3.51	2.75 - 4.41	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	3.67	3.54 - 3.80	

If pulmonary stenosis, VSD, riding aorta, and right ventricular hypertrophy are diagnosed together at one child, this is called tetralogy of Fallot. For the 2020 birth cohort this complex cardiac malformation was reported only in four children/fetuses in Saxony-Anhalt (**prevalence 2.5 per 10,000 births**). The annual prevalence lies far below the lower limit of the confidence interval of the basis prevalence (2008-2019: 3.5 per 10,000 births).

The confidence interval of the overall prevalence of the European malformation registries (2008-2019) ranges in total on a similar level but is narrower than the confidence interval of the basis prevalence Saxony-Anhalt. For this reason, the prevalence of 2020 of Saxony-Anhalt is therefore low compared to the overall European prevalence

additional information

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

The pregnancy was terminated in one case of a fet with tetralogy of Fallot and other cardiac malformations at 32 weeks gestation. In two of the three live births, the malformation was already detected prenatally during an ultrasound examination.

Malformation combinations (MCA) or superordinated syndromes detected:

- Rectal atresia with fistula, ASD II, aortic valve insufficiency
- persistent left superior vena cava, ASD
- Deletion in NOTCH1 gene

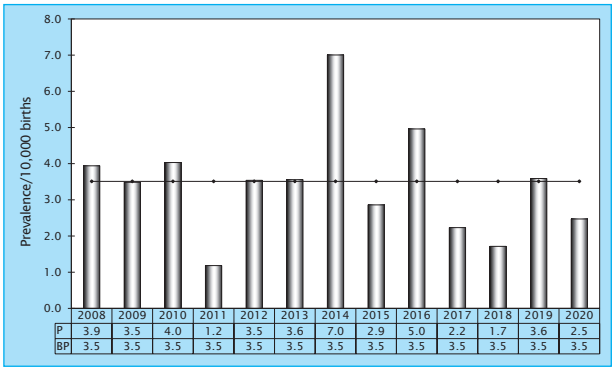


Fig. 17: Development of prevalence/10,000 births with Tetralogy of Fallot (Q21.3) in Saxony-Anhalt since 2008

In 2020, one Tetralogy of Fallot per 4,047 births was registered in Saxony-Anhalt..

10.11 Transposition of great vessels - TGA (Q20.1/Q20.3)

Saxony-Anhalt	Jahr 2020		
	Number	Prevalen-ce/10,000 births	Comparison to basis prevalence
	7	4.32	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	4.62	3.74 - 5.64	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	3.59	3.47 - 3.72	

The transposition of the great arteries (TGA) is one of the most complex cardiac malformations. It exists when the vessels leaving the heart are interchanged. Seven children/fetuses were affected in Saxony-Anhalt in 2020. This year's **prevalence** of **4.3 per 10,000** births lies inconspicuously in the range of the basis prevalence of Saxony-Anhalt (2008-2019: 4.6 per 10,000 births).

Compared with the prevalence of the EUROCAT registers (2008-2019: 3.6 per 10,000 births), the Saxony-Anhalt basis prevalence, as well as the current annual prevalence (2020), is to be regarded as high. The prevalences are only comparable to a limited extent, since the calculation of the prevalence of EUROCAT does not include the Double Outlet Ventricle (DORV).

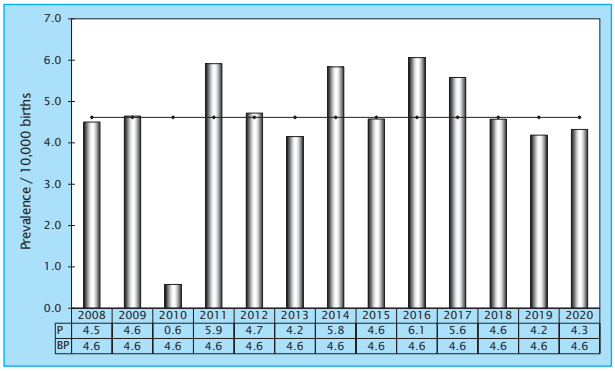
additional information:

pregnancy outcome	6 x live births 1 x termination of pregnancy
sex	4 x male 3 x female
number of isolated malformations/MCA	7 x MCA

One pregnancy was terminated after confirmation of a Patau-syndrome. Besides the complex cardiac malformation TGA, all live births showed other cardiac malformations and were for the most part operated in the German Heart Center in Leipzig. Two live births showed the rare DORV, which belongs to TGA.

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: Hydrocephaly, median cleft palate, bilateral renal dysplasia, bilateral accessory 6th finger
- Taussig-Bing syndrome with: VSD, preductal aortic coarctation, hypoplasia of the aorta, total subdiaphragmatic misjunction of the pulmonary veins, persistent left superior vena cava, accessory right nipple, retarded maturity of the hip and sandal gap bilateral
- Preductal aortic coarctation, VSD, ASD II, coronary aneurysm, hypoplasia of the aorta
- 2 x VSD, PFO at full term infant (1 x with pulmonary valve stenosis)
- VSD
- ASD II



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	4.5	4.6	0.6	5.9	4.7	4.2	5.8	4.6	6.1	5.6	4.6	4.2	4.3
BP	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6

Fig. 18: : Development of prevalence/10,000 births with transposition of great vessels in Saxony-Anhalt since 2008

In 2020, one transposition of great vessels per 2,312 births was registered in Saxony-Anhalt..

10.12 Hypoplastic left heart syndrome (Q23.4)

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	5	3.09	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	2.89	2.20 - 3.71	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.78	2.67 - 2.89	

The indicator malformation hypoplastic left heart syndrome is one of the most severe cardiac malformations. Children without medical and surgical care usually die neonatally. The **prevalence** determined for 2020 of **3.1 per 10,000 births**, lies after a maximum in the previous year (2019: 5.4 per 10,000 births) again in the middle range of the basis prevalence (2008-2019: 2.9 per 10,000 births).

The baseline prevalence of Saxony-Anhalt for the years 2008-2019 and the European prevalence provided by EUROCAT (2008-2019: 2.7 per 10,000 births) are similar high, whereas the Saxony-Anhalt confidence interval has a much wider range. The 2020 annual prevalence lies therefore above the upper confidence limit of the European prevalence.

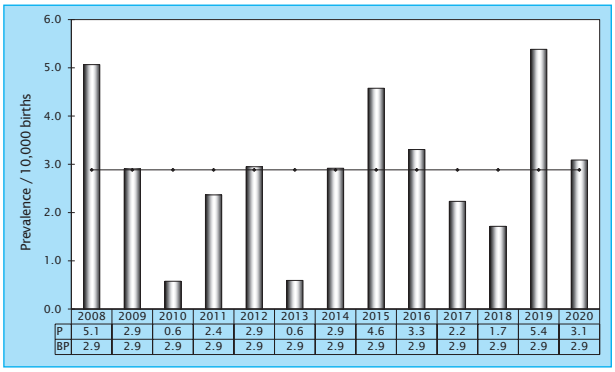
additional information:

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

The hypoplastic left heart syndrome was not detected prenatally at two live births. One child who had already been transferred to a heart center prenatally died after one week of life. One pregnancy was terminated after detection of the hypoplastic left heart syndrome during prenatal ultrasound screening.

Malformation combinations (MCA) or superordinated syndromes detected:

- postductal aortic coarctation, corrected transposition of the great vessels, stenosis of the pulmonary artery at full term infant
- VSD
- malformation of the coronary vessels



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	5.1	2.9	0.6	2.4	2.9	0.6	2.9	4.6	3.3	2.2	1.7	5.4	3.1
BP	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9

Fig. 19: Development of prevalence/10,000 births with hypoplastic left heart syndrome in Saxony-Anhalt since 2008

In 2020, one child with a hypoplastic left heart syndrome per 1,857 births was registered in Saxony-Anhalt..

10.13 Coarctation of aorta (Q25.1)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	14	8.65	↑
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	5.82	4.83 - 6.95	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	3.97	3.84 - 4.11	

14 births with a haemodynamically relevant coarctation of aorta were registered in 2020. The resulting **annual prevalence** of **8.6 per 10,000 births** lies clearly below the basis prevalence of 5.8 per 10,000 births (2008-2019). In 2008, the basis prevalence was exceeded even more significantly with a maximum value (9.6 per 10,000 births).

A comparison with the EUROCAT prevalence for 2008-2019 (4.0 per 10,000 births) suggests a prevalence value for Saxony-Anhalt, which lies far above the European average for 2020 as well as for the whole reporting period. In only three European registries, even higher prevalence values were determined for the period of 2008-2019.

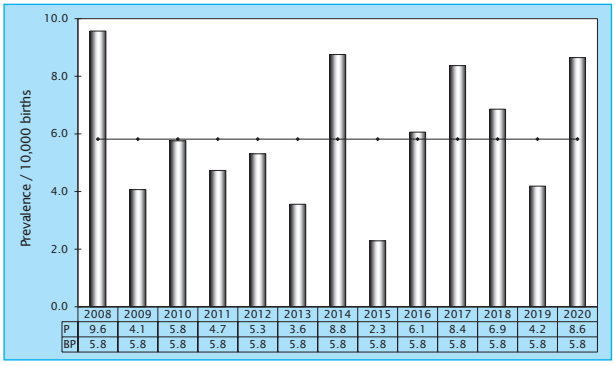
additional information:

pregnancy outcome	13 x live births 1 x termination of pregnancy
sex	4 x male 10 x female
number of isolated malformations/MCA	12 x MCA 2 x isolated

Coarctation of aorta is often found postnatally as it is difficult to detect on prenatal ultrasound screening and occurs together with other cardiac malformations. Only three times, the diagnosis could be made prenatally. Another three times, other severe or multiple cardiac malformations were diagnosed prenatally. One pregnancy, in which the fetus was affected by a Shone complex, was terminated.

Malformation combinations (MCA) or superordinated syndromes detected

- Hypoplastic left heart syndrome, corrected transposition of the great vessels, stenosis of the pulmonary artery at full term infant
- Taussig-Bing syndrome with: VSD, discordant atrioventricular
- junction, hypoplasia of the aorta, total subdiaphragmatic misjunction of the pulmonary veins, persistent left superior vena cava, accessory right mammilla, retarded maturity of the hip
- and sandal gap bilateral
- Dextro-transposition and hypoplasia of the aorta, VSD, ASD II, coronary aneurysm
- CATCH 22 with: VSD, persistent left vena cava superior
- median cleft palate, VSD, aortic valve stenosis, PFO in full term infant, double left kidney
- VSD, ASD in full term infant, persistent left vena cava superior, right diaphragmatic herniation
- bicuspid aortic valve, VSD, ASD II
- bicuspid aortic valve, hypoplasia of the aorta
- 2 x VSD
- 2 x PFO in full term infant (1 x with tricuspid regurgitation 1st degree)



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	9.6	4.1	5.8	4.7	5.3	3.6	8.8	2.3	6.1	8.4	6.9	4.2	8.6
BP	5.8	5.8	5.8	5.8	5.8	5.8	5.8	5.8	5.8	5.8	5.8	5.8	5.8

Fig. 20: Development of prevalence/10,000 births with coarctation of aorta in Saxony-Anhalt since 2008

In 2020, one coarctation of aorta per 1,156 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	24	14.83	↗
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	13.13	11.62 - 14.78	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	8.63	8.44 - 8.83	

Cleft lip and cleft lip and palate are defined as cleft formations of the upper lip with or without cleft of the alveolar ridge or the hard palate. Cleft lip and palate, as the most frequent one, was observed in Saxony-Anhalt in 2020 16 times, a cleft upper lip and a cleft lip and jaw 4 times each. In total, 24 children/ fetuses had a cleft lip and cleft lip and palate.

The determined **prevalence** for Saxony-Anhalt for 2020 of **14.8 per 10,000 births** is slightly higher than the calculated basis prevalence (2008-2019: 13.1 per 10,000 births).
The basis prevalence of cleft lip and cleft palate for Saxony-Anhalt significantly exceeds the prevalence value given by EUROCAT. Thereby, the lower confidence limit of the basis prevalence of Saxony-Anhalt lies still above the European confidence interval.
For many years, Saxony-Anhalt has shown a high prevalence of cleft lip and cleft lip and palate in the upper third of the European registers. The maximum value for the period 2008 to 2019 was obtained from the Bulgarian register Pleven (13.6 per 10,000 births).

additional information

pregnancy outcome	20 x live births 1 x spontaneous abortion 3 x termination of pregnancy
sex	14 x male 9 x female 1 x no indication
number of isolated malformations/MCA	11 x MCA 13 x isolated

Once the cleft lip and palate occurred as a concomitant malformation of an Edwards syndrome. This pregnancy ended spontaneously at 16 weeks of gestation. In about two-thirds of live births the cleft formation occurred isolated.

Predominantly (17 x), the cleft lip and cleft lip with cleft palate occurred unilateral (6 x left, 9 x right, 2 x unilateral n.o.s.). Normally the left-sided form is seen more frequently: between 2008 and 2019, more than twice as many left-sided (112) than right-sided (52) cases were observed. 6 times bilateral cleft lip and cleft lip and palate were reported in 2020 and once no indication of sidedness was given.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: bilateral lateral neck cysts
- Tetrasomy 9p syndrome with: Potter sequence, cervical spina bifida with hydrocephaly, craniofacial dysmorphia, low-set ears, wide nasal bridge
- Bland-White-Garland syndrome with: vascular ring of the great arteries, supravalvular pulmonary artery stenosis and PFO at preterm infant, left foot with rudimentary rays (II / III) and syndactyly in the left foot type I
- Deletion at chromosome 11
- Popliteal pterygium syndrome with: conduction disorder bilateral, hypoplastic labia bilateral
- Omphalocele, diaphragmatic hernia, dextrocardia, VSD,
- pulmonary valve stenosis
- omphalocele, VSD, wrist flexion deformity
- Microcephaly (<2SD)
- arachnoid cyst
- Sound conduction disorder bilateral
- PFO in full term infant, retarded hip maturity bilateral

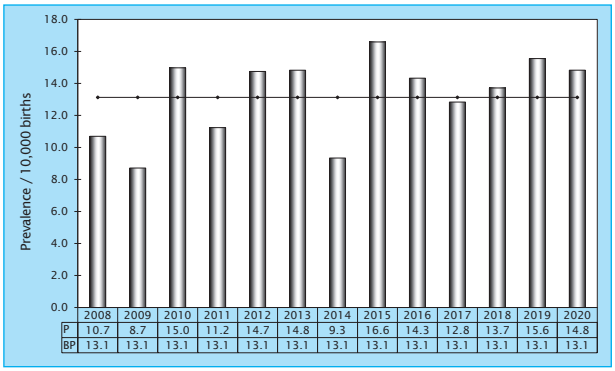


Fig. 21: Development of prevalence/10,000 births with cleft lip with or without cleft palate in Saxony-Anhalt since 2008

In 2020, one child with cleft lip with or without cleft palate per 674 births was registered in Saxony-Anhalt.

10.15 Gaumenspalte (Q35.1/Q35.3/Q35.5/Q35.9)

Saxony-Anhalt	Jahr 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	8	4.94	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	6.88	5.80 - 8.10	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	5.83	5.67 - 6.00	

The indicator malformation cleft palate only includes cleft palate without lip involvement. Cleft palate occurred 8 times in Saxony-Anhalt in 2020, the cases were predominantly (5 x) described as median. The resulting annual **prevalence** of **4.9 per 10,000 births** is clearly below the confidence interval of the basis prevalence of Saxony-Anhalt (2008-2019: 6.9 per 10,000 births). A minimum value was recorded in the reporting period in 2010 with 4.6 per 10,000 births.
The basis prevalence of Saxony-Anhalt for cleft palate is higher than the average European prevalence provided by EUROCAT (2008-2019: 5.8 per 10,000 births). Thereby the confidence intervals overlap somewhat. The current annual prevalence of Saxony-Anhalt is also lower than the lower confidence limit of the European prevalence.

additional information:

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

All three terminations of pregnancy, in which malformations were diagnosed between the 16th and 19th week of gestation, had in addition to the indicator malformation cleft palate additional malformations of other organ systems. One child was diagnosed with bilateral hearing loss.

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: hydrocephaly, discordant ventriculoarterial junction, bilateral renal dysplasia, bilateral accessory 6th finger
- anencephaly, omphalocele, Cantrell pentalogy, ectopia cordis, absent sternum
- preductal aortic coarctation, VSD, aortic valve stenosis, PFO at full term infant, double left kidney
- AEC syndrome with: bilateral synechia of the eyelids, wide nasal root
- bilateral combined conduction and sensory disturbance, bilateral retarded hip maturity
- hypertrophy of the bladder wall, DUP, mandibular retrognathia

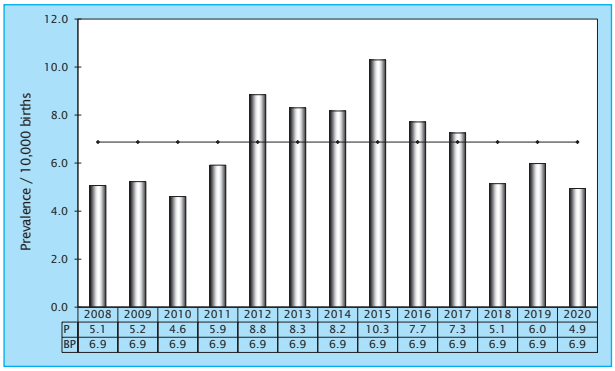


Fig. 22: Development of prevalence/10,000 births with cleft palate in Saxony-Anhalt since 2008

In 2020, one child with cleft palate per 2,023 births was registered in Saxony-Anhalt.

10.16 Choanal atresia (Q30.0)

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	5	3.09	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	2.60	1.95 - 3.39	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	0.93	0.86 - 1.00	

In 2020, five children with choanal atresia or choanal stenosis requiring a therapy were born in Saxony-Anhalt. This results in a current **prevalence** of Saxony-Anhalt **(2020: 3.1 per 10,000 births)** which is in the upper normal range of the years 2008-2019 (2.6 per 10,000 births). Even with one choanal atresia more or one less, the annual prevalence would no longer be within the normal range. In the first half of the reporting period, the annual prevalences seem to increase and to decrease in the second half. A trend analysis (chapter 10.38) reveals a significant nonlinear component. Therefore, the prevalence development of the indicator malformation is classified as a nonlinear change.

Measured by the European prevalence rate determined by EUROCAT (2008-2019: 0.9 per 10,000 births), both the basis prevalence as well as the annual prevalence of Saxony-Anhalt can be considered as extraordinarily high. Most other registries indicated prevalences below 2.0 per 10,000 births.

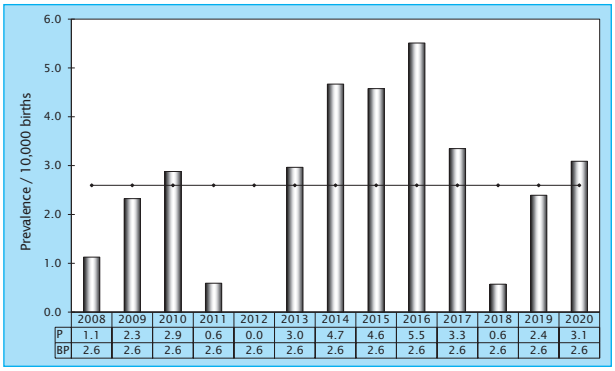
In two children, who died after one month and half a year, respectively, the malformation was found to be part of an Edwards syndrome. The malformation occurred three times bilaterally and twice on the right side.

additional information:

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

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: Corpus callosum hypoplasia, DUP II. grade and right ureteral outlet stenosis, bilateral inguinal hernia at preterm infant, septum pellucidum anomalies, low-set ears
- Edwards syndrome with: VSD, ASD II, bilateral postaxial accessory finger, flat feet, bilateral laterally sloping eyelid axes
- bilateral hydrothorax, bilateral undescended testicles at full term infant, low-set ears, macrocephaly



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	1.1	2.3	2.9	0.6	0.0	3.0	4.7	4.6	5.5	3.3	0.6	2.4	3.1
BP	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6	2.6

Fig. 23: Development of prevalence/10,000 births with choanal atresia in Saxony-Anhalt since 2008

In 2020, one child with a choanal atresia per 3,237 births was registered in Saxony-Anhalt.

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

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	4	2.47	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	2.79	2.12 - 3.61	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.65	2.54 - 2.76	

Four cases of oesophageal atresia/stenosis/fistula were registered in Saxony-Anhalt in 2020. The calculated **prevalence** of 2020 **(2.5 per 10,000 births)** lies in the middle of the confidence interval of the basis prevalence (2008-2019: 2.8 per 10,000 births). During the reporting period, the prevalence of the indicator malformation esophageal atresia/ stenosis/ fistula ranged between a minimum of 0.6 per 10,000 births (2013) and a maximum of 4.7 per 10,000 births (2012).

Due to the smaller numbers, the confidence interval of the basis prevalence of Saxony-Anhalt includes the interval limits of the total prevalence of the European registries given by EUROCAT (2008-2019: 2.6 per 10,000 births). The current prevalence value of Saxony-Anhalt of 2020 also fits to the European overall prevalence.

additional information

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

Two children suffered from atresia of the oesophagus with fistula between the trachea and the lower oesophageal pouch (type Vogt III b). For two other children no information was provided regarding the severity of the malformation. In two further cases, a polyhydramnios was detected during pregnancy, but the indicator malformation was not discovered.

Malformation combinations (MCA) or superordinated syndromes detected:

- VATCERL association with: anal atresia, duodenal atresia, gallbladder agenesis, VSD, ASD II, DUP III. degree and ureteral outlet stenosis on the right, pancreas annulare, plexus cyst on the right side, clinodactyly of the 5th finger on the left side
- Hydrothorax bilateral, iris coloboma right
- VSD, foot deformity right, elapsed philtrum

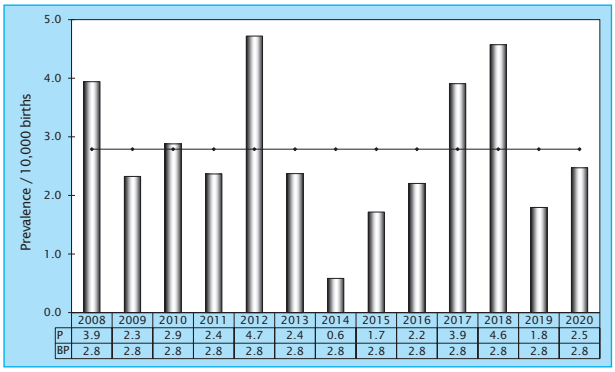


Fig. 24: Development of prevalence/10,000 births with oesophageal atresia/stenosis/fistula in Saxony-Anhalt since 2008

In 2020, one child with oesophageal atresia/-stenosis/-fistula per 4,047 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	4	2.47	↗
	Reporting period 2008-2019		
	Basisprävalenz/ 10.000 Geburten	Konfidenzintervall (KI 95%)	
	1.73	1.21 - 2.40	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	0.94	0.88 - 1.01	

The indicator malformation small intestinal atresia/stenosis belongs with a basis prevalence of 1.7 per 10,000 births (2008-2019) to the rare appearing malformations. In 2020 it was diagnosed 4 times in Saxony-Anhalt. With a **prevalence** of **2.5 per 10,000 births**, it was seen slightly more often than expected. During the years of the reporting period the numbers ranged between the minimum value zero (2014) and a maximum value of seven (2012).

The confidence interval of the basis prevalence of Saxony-Anhalt lies above the interval of the European registers (2008-2019: 0.9 per 10,000 births). Thus, the current prevalence of Saxony-Anhalt is also above the total prevalence of EUROCAT. However, the Saxony-Anhalt basis prevalence does not reach the maximum value (2008-2019: 1.8 per 10,000 births) from the Pleven registry (Bulgaria).

additional information

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

In three cases the ileum was affected, twice an atresia and once a stenosis was present. One child suffered from jejunal atresia.

Malformation combinations (MCA) or superordinated syndromes detected:

- -Gastroschisis, cholestasis
- -Athyreosis

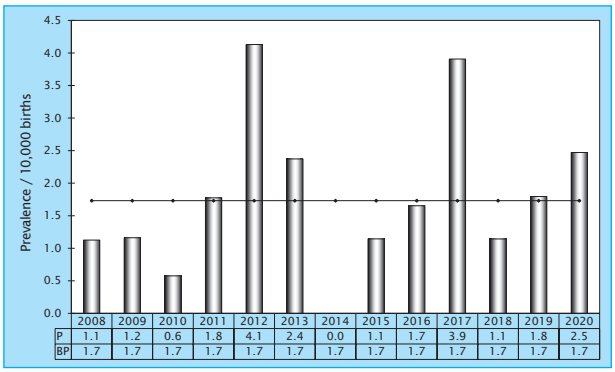


Fig. 25: Development of prevalence/10.000 births with small intestinal atresia/stenosis in Saxony-Anhalt since 2008

In 2020, one child with small intestinal atresia/stenosis per 4,047 births was registered in Saxony-Anhalt.

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

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	9	5.56	↗
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	4.33	3.48 - 5.32	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	3.35	3.23 - 3.48	

A slightly higher **annual prevalence (2020: 5.6 per 10,000 births)** was observed in 2020 for the indicator malformation rectal and anal atresia/stenosis in comparison to the basis prevalence (2008-2019: 4.3 per 10,000 births). However, there are still indications, similar to the previous year, that the significant downward trend for the period 2007-2020 with a percentage change of -17.53 % (CI -23.78% to -7.60%) (Chapter 10.38) continues.

During the years 2007 to 2010, rectal and anal atresia/ stenosis occurred much more frequently than in any year since the beginning of malformation recording in 1980. Since a peak in 2008 with the extreme value of 8.4 per 10,000 births, the prevalence has always been below the upper limit of the confidence interval. This year's prevalence value is the highest since then.

The 2020 annual prevalence of Saxony-Anhalt exceeds the European prevalence provided by EUROCAT (2008-2019: 3.4 per 10,000 births), as the confidence interval of the basis prevalence lies above the overall prevalence of the European registries (2008-2019). The basis prevalence of Saxony-Anhalt, however, does not reach the maximum value of the EUROCAT register of Styria (Austria), which indicated a value of 5.6 per 10,000 births (2008-2019).

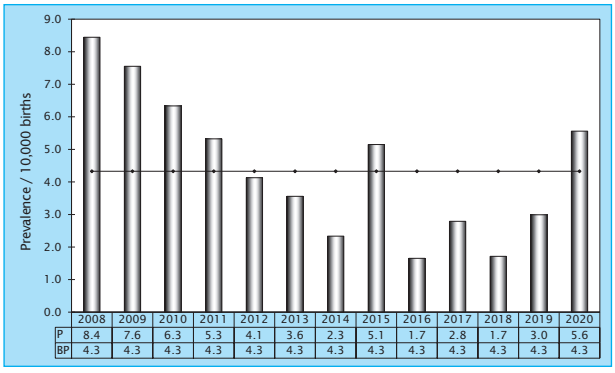
additional information:

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

As of birth year 2020, anal atresia with fistula occurred 5 times, once without fistula and three times rectal atresia with fistula. Often, rectal and anal atresia/stenosis can only be diagnosed neonatally because it is difficult to detect during prenatal ultrasound screening. However, currently anal atresia without fistula and rectal atresia with vestibular fistula were detected prenatally. One child of the nine live births with rectal and anal atresia/stenosis died with caudal regression syndrome on the first day of life and another died with VACTERL association postoperatively.

Malformation combinations (MCA) or superordinated syndromes detected:

- caudal regression syndrome with: agenesis of the left kidney, polycystic right kidney, urethral atresia, indeterminate sex, pulmonary hypoplasia, bilateral hip joint dislocation and pes calcaneovarus congenitus
- caudal regression syndrome with: sacral lipomyelomeningocele, vagina and uterus duplex, DUP right II degree and left III degree, neurogenic bladder, kinked heel on the right, nevus flammeus
- VATCERL association with: atresia of the oesophagus (Vogt III b), duodenal atresia, gallbladder agenesis, VSD, ASD II, DUP III. degree and ureteral outlet stenosis
- right, pancreas annulare, plexus cyst right, clinodactyly of the 5th finger on the left
- VACTERL-association with: partial misjunction of the pulmonary veins, VSD, stenosis of the pulmonary artery at preterm infant, accessory thumb, pulmonary sequestration on the right side, bronchopulmonary isomerism, hemivertebra with scoliosis
- tetralogy of Fallot, ASD II, aortic valve insufficiency
- duodenal atresia, tracheal stenosis, cardiac malformation
- glandular hypospadias, Meckel's diverticulum, DUP I. grade right, hydrocele and plexus cyst left



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	8.4	7.6	6.3	5.3	4.1	3.6	2.3	5.1	1.7	2.8	1.7	3.0	5.6
BP	4.3	4.3	4.3	4.3	4.3	4.3	4.3	4.3	4.3	4.3	4.3	4.3	4.3

Fig. 26: Development of prevalence/10,000 births with anorectal atresia/-stenosis in Saxony-Anhalt since 2008

In 2020, one anorectal atresia/ stenosis per 1,798 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Vergleich zur Basisprävalenz
	40	24.71	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	23.85	21.80 - 26.05	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	17.92	17.64 - 18.21	

Hypospadias is the most frequent malformation among the indicator malformations. The current **prevalence (24.7 per 10,000 births)** lies with 40 affected children within the normal range of the basis prevalence (2008-2019: 23.9 per 10,000 births). Even when regarding only the boys in the calculation, the current annual prevalence (2020: 48.1 per 10,000 boys) lies within the tolerance range of the corresponding basis prevalence (2008-2019: 46.4 per 10,000 boys; CI 42.4-50.7).

Seven boys (4.3 per 10,000 births) with hypospadias were suffering from a severe form of hypospadias, mostly penile hypospadias in 2020. A glandular form was described 31 times and twice a hypospadias coronaria was registered. Often the mild forms become apparent only during the first year of life and are not recorded by the malformation monitoring any more.

The European-wide confidence interval determined by EUROCAT of the prevalence of the years 2008-2019 (17.9 per 10,000 births) is far below the confidence interval of the basis prevalence of Saxony-Anhalt. The highest value among the EUROCAT registries was reported by Wales (UK) (2008-2019: 31.4 per 10,000 births).

additional information:

pregnancy outcome	40 x live births
sex	40 x male
number of isolated malformations/MCA	6 x MCA 34 x isolated

In 2020, all boys who showed hypospadias were live births. All, except four children, were born as full-term infants.

Malformation combinations (MCA) or superordinated syndromes detected:

- Anal atresia, Meckel's diverticulum, DUP I. degree right, hydrocele and plexus cyst on the left side
- volvulus, athyreosis, double sided hernia inguinalis at preterm infants
- VSD, ASD at full term infant
- PFO at full term infant
- accessory right thumb
- clubfeet

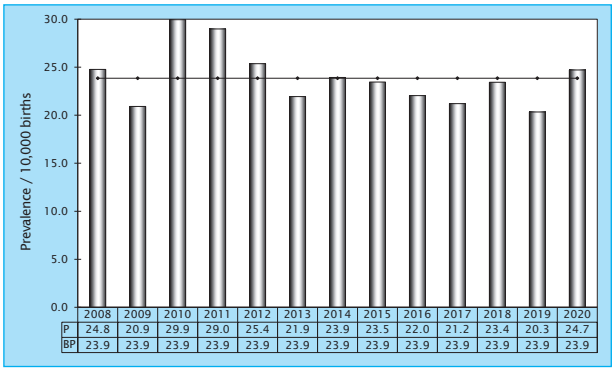


Fig. 27: Development of prevalence/10,000 births with hypospadias in Saxony-Anhalt since 2008

In 2020, one hypospadias per 405 births (208 boys) was registered in Saxony-Anhalt.

10.21 Epispadias (Q64.0)

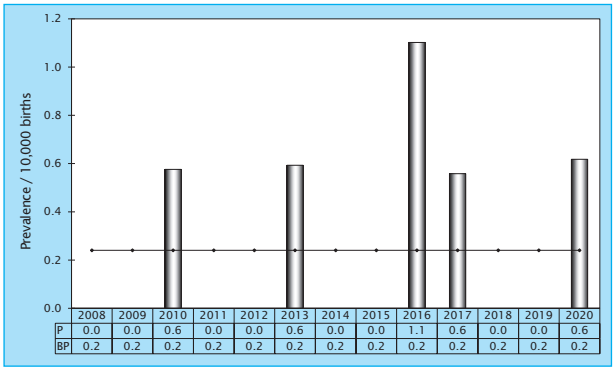
Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	1	0.62	↗
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	0.24	0.08 - 0.56	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

Epispadias is the least frequently diagnosed indicator malformation. In most years it was not diagnosed at all and in five years of the reporting period (2008- 2019) it was diagnosed in no more than two children. In 2020 it occurred once. The resulting **prevalence** of **0.6 per 10,000** births is slightly higher than the upper confidence limit of the basis prevalence (2008-2019: 0.2 per 10,000 births), which would be far exceeded with two cases.
Calculated for boys only (born alive and stillborn), the result is a basis prevalence for epispadias of 0.60 per 10,000 boys (2008-2019).

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

additional information

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



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	0.0	0.0	0.6	0.0	0.0	0.6	0.0	0.0	1.1	0.6	0.0	0.0	0.6
BP	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2

Fig. 28: Development of prevalence/10,000 births with epispadias in Saxony-Anhalt since 2008

In 2020, one epispadias per 16.186 births (8.314 boys) was registered in Saxony-Anhalt.

10.22 Indeterminate sex (Q56.)

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	1	0.62	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	0.63	0.33 - 1.07	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	0.58	0.53 - 0.64	

With a basis **prevalence of 0.6 per 10,000** births (2008-2019), the indicator malformation of indifferent sex occurs only occasionally. In Saxony-Anhalt, only one or two cases are registered per year. In the last two years, no case was registered at all. In the year 2020, this malformation was also found in only one child (prevalence 0.6 per 10,000 births), who died due to other serious malformations on the first day of life.

EUROCAT gives an overall prevalence for indifferent sex of 0.6 per 10,000 births (2008-2019). The prevalence interval of the basis prevalence of Saxony-Anhalt is broader and spans due to the smaller numbers that of the European malformation registers, but the prevalence value is similar.

additional information:

pregnancy outcome	1 x live birth, deceased until 7 days of life
sex	1 x indifferent
number od isolated malformations/MCA	1 x MCA

Malformation combinations (MCA) or superordinated syndromes detected:

- caudales Regressionssyndrom mit: Analatresie, Agenesie der linken Niere, polyzystischer rechter Niere, Urethralatresie, Lungenhypoplasie, bds. Hüftgelenksluxation und Pes calcaneovarus congenitus

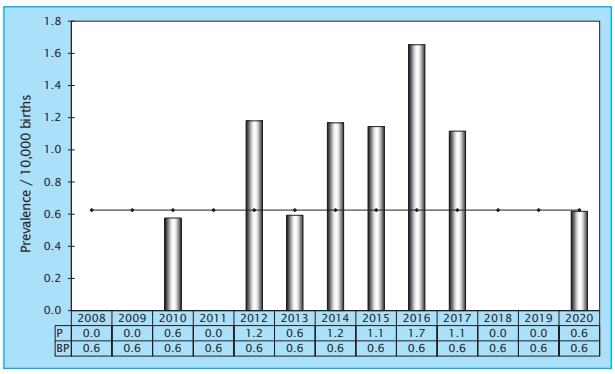


Fig. 29: Development of prevalence/10,000 births with indeterminate sex in Saxony-Anhalt since 2008

In 2020, one indeterminate sex per 16,186 births was registered in Saxony-Anhalt.

10.23 Potter sequence (Q60.6)

	Jahr 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	4	2.47	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	2.89	2.20 - 3.71	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	1.27	1.20 - 1.35	

The indicator malformation Potter sequence was diagnosed four times in 2020. This results in a **prevalence** of **2.5 per 10,000 births**, which is similar to the basis prevalence of 2008-2019 (2.9 per 10,000 births). In the recent year (2019), the annual prevalence reached a minimum value during the reporting period of 1.2 per 10,000 births and in 2016 a maximum value of 5.0 per 10,000 births. This range of variation results from the small numbers.

The confidence intervals of the overall prevalence of the European registers (1.3 per 10,000 births) and the basis prevalence of Saxony-Anhalt do not overlap. Saxony-Anhalt shows a higher prevalence, which can be found in the upper third of the prevalences of other EUROCAT centres. Compared with the total European prevalence, the annual prevalence of Saxony-Anhalt for 2020 lies clearly above.

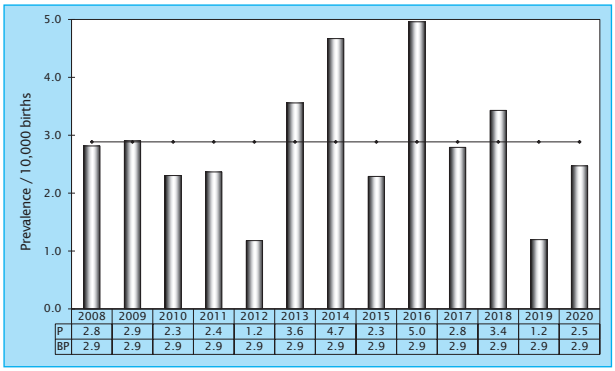
additional information:

pregnancy outcome	1 x live birth, deceased until 7 days of life 3 x termination of pregnancy
sex	3 x male 1 x female
number of isolated malformations/MCA	4 x MCA

A live-born twin child, who died after one day, suffered from a missing kidney, the other kidney was hypoplastic and non-functional. One fet was affected by bilateral renal agenesis. Two fetuses showed bilateral non-functional polycystic kidneys. As a consequence of the Potter sequence, two fetuses had a pulmonary hypoplasia and one fetus showed clubfeet. In all four children/ fetuses, the Potter sequence and other malformations were diagnosed during prenatal ultrasound screening between the 18th and 20th week of gestation. Information about maternal medication intake is not available to the malformation monitoring.

Malformation combinations (MCA) or superordinated syndromes detected:

- Tetrasomy 9p syndrome with: cervical spina bifida with hydrocephaly, cleft lip and palate left side, craniofacial dysmorphia, low-set ears, wide nasal root
- plagiocephaly, malformation of a large vein, low-seated ears, flat eyelid axes
- cardiac malformation
- urinary bladder agenesis



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	2.8	2.9	2.3	2.4	1.2	3.6	4.7	2.3	5.0	2.8	3.4	1.2	2.5
BP	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.9

Fig. 30: Development of prevalence/10,000 births with Potter sequence in Saxony-Anhalt since 2008

In 2020, one Potter sequence per 4,047 births was registered in Saxony-Anhalt.

NOTE

What are ACE inhibitors and what is Sartan fetopathie?

The group of pharmaceuticals „sartans“ were developed from ACE inhibitors. Mainly used in the antihypertensive therapy, they have a teratogenic effect in case of maternal intake during second and third trimenon of pregnancy. The suspected pathomechanism of both substances results in a reduced perfusion of the foetal organs, in particular of the kidneys. That means both substances interrupt the renin-angiotensin system at different points. The result of such a fetal damage is an intrauterine oliguria. Since amniotic fluid production depends from the second trimenon 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).

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

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	5	3.09	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	6.16	5.14 - 7.32	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

This year's **prevalence** for unilateral renal agenesis (2020: **3.1 per 10,000 births**) shows an average prevalence of 6.2 per 10,000 births (2008-2019) and is to be considered as very low. Only in 2016, the prevalence was even lower (2.2 per 10,000 births). As of birth year 2020, only five children with a unilateral missing kidney were registered in Saxony-Anhalt.

During the reporting period, unilateral renal agenesis showed high prevalence rates in the years until 2012 above or within the confidence interval (e.g., 2008: 9.6 and 2012: 9.4 per 10,000 births). Since 2013, the prevalence has always been in or below the confidence interval of the basis prevalence. A trend analysis from 2007-2020 (Chapter 10.38) shows a decrease in annual prevalences. The trend is marked with a percentage change of -8.34 % (CI -15.34% to -0.03%) as slightly significant. The development remains to be observed.

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

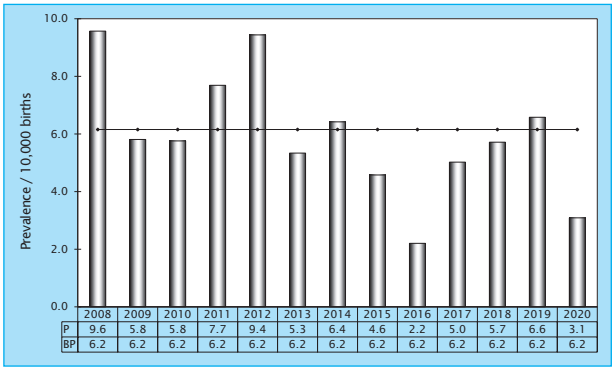
additional information:

pregnancy outcome	4 x live births 1 x live birth, deceased until 7 days of life
sex	4 x male 1 x indeterminate
number of isolated malformations/MCA	1 x MCA 4 x isolated

Children/fetuses with unilateral renal agenesis showed that the left kidney was missing more frequently than the right kidney (2008-2019: left 60,5 %). In 2020, the left predominance was confirmed as well. Four times the left kidney was missing, only once the right kidney. Four of the children with unilateral renal agenesis had no other malformations. One child with unilateral renal agenesis which occurred in the context of a caudal regression syndrome died on the first day of life.

Malformation combinations (MCA) or superordinated syndromes detected:

- caudal regression syndrome with: anal atresia, polycystic right kidney, urethral atresia, undetermined sex, pulmonary sex, pulmonary hypoplasia, bds. dislocation of the hip and pes calcaneovarus congenitus



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	9.6	5.8	5.8	7.7	9.4	5.3	6.4	4.6	2.2	5.0	5.7	6.6	3.1
BP	6.2	6.2	6.2	6.2	6.2	6.2	6.2	6.2	6.2	6.2	6.2	6.2	6.2

Fig. 31: Development of prevalence/10,000 births with unilateral renal agenesis in Saxony-Anhalt since 2008

In 2020, one renal agenesis, unilateral per 3,237 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	15	9.27	↑
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	6.88	5.80 - 8.10	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

Cystic kidneys can have very different causes. They are potentially associated with a loss of function of the affected kidney. According to a low prevalence for cystic kidneys in 2019 (4.8 per 10,000 births), the **prevalence** in 2020 is again very high with 15 affected children/fetuses in Saxony-Anhalt and a value of **9.3 per 10,000** births. The maximum value of the reporting period of 11.5 per 10,000 births in 2010 was not reached again, but the prevalence of 2020 lies significantly above the basis prevalence calculated for 2008-2019 with a value of 6.9 per 10,000 births.

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

additional information:

pregnancy outcome	13 x live births 1 x live birth, deceased until 7 days of life 1 x termination of pregnancy
sex	3 x male 11 x female 1 x indeterminate
/MCA	7 x MCA 8 x isolated

A bilateral cystic kidney degeneration occurred twice in 2020. In one child, the mother was also affected by bilateral cystic kidneys. In 13 live births the finding was unilateral, 6 times on the left side and 7 times on the right side. One child with caudal regression syndrome showed other severe malformations such as agenesis of the other kidney. It died on the first day of life..

Malformation combinations (MCA) or superordinated syndromes detected:

- Patau syndrome with: hydrocephaly, discordant ventriculoarterial junction, median cleft palate, bilateral kidney dysplasia, bilateral accessory 6th finger
- caudal regression syndrome with: anal atresia, agenesis of the left kidney, urethral atresia, indeterminate gender sex, lung hypoplasia, bilateral dislocation of the hip joint and pes calcaneovarus congenitus
- ASD II, retarded hip maturity bilateral
- Hemodynamically effective PDA in full term infant, plexus cyst
- bilateral sound sensation disturbance
- Polydactyly and membranous syndactyly of the left foot
- Hymenal atresia

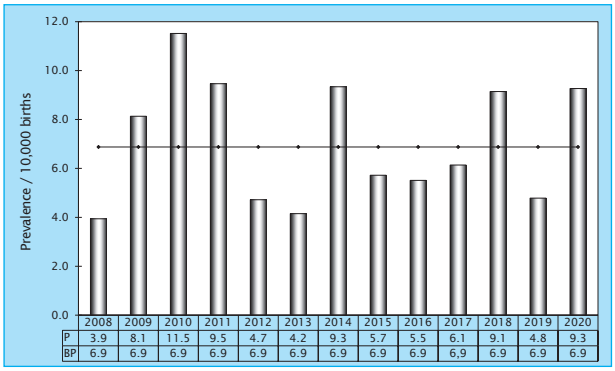


Fig. 32: Development of prevalence/10,000 births with cystic kidneys in Saxony-Anhalt since 2008

In 2020, one child with cystic kidney per 1,079 births was registered in Saxony-Anhalt.

10.26 Bladder Exstrophy (Q64.1)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	0	0.0	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	0.34	0.13 - 0.69	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

The indicator malformation exstrophy of the urinary bladder belongs to the extremely rare occurring malformations. Only seven cases were registered in Saxony-Anhalt during 2008 to 2019. This results in a very low basis prevalence of 0.3 per 10,000 births (2008-2019). In 2020, urinary bladder exstrophy was not detected at all, similar to 2019 and to the other five years of the reporting period.

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

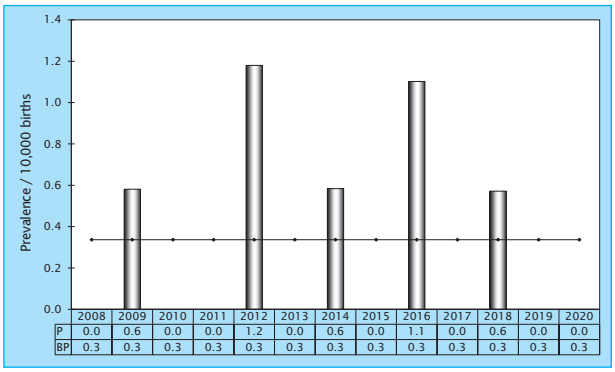


Fig. 33: Development of prevalence/10,000 births with bladder exstrophy in Saxony-Anhalt since 2008

In 2020, no birth with a bladder exstrophy was registered in Saxony-Anhalt.

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

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	9	5.56	↑
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	3.22	2.50 - 4.09	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

With nine affected children in 2020, we registered a significantly higher annual **prevalence** of **5.6 per 10,000** births in comparison to the basis prevalence (2008-2019: 3.2 per 10,000 births) for the indicator malformation preaxial polydactyly. Nevertheless, as in the previous year, a significant decreasing trend over the years 2007-2020 with a percentage change of -17.33% (CI -24.46% to -6.39%) (Chapter 10.38) can be observed. This is also illustrated in Figure 34: After very high annual prevalence values of over 5.0 per 10,000 births in 2008-2010, other years with prevalence values within the confidence interval and from 2016 to 2019 well below the lower confidence limit of the basis prevalence followed. The linear portion of the trend is decreasing.

Comparative EUROCAT data for preaxial polydactyly is not available.

additional information:

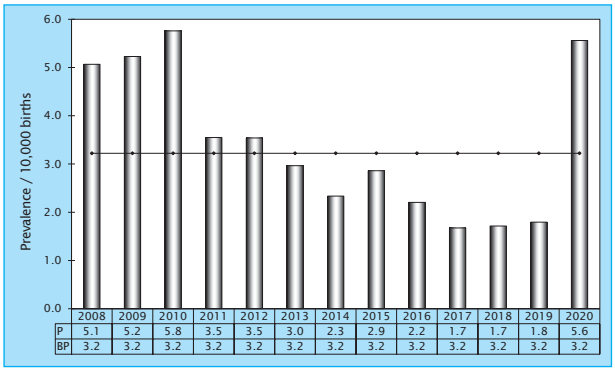
pregnancy outcome	8 x live births 1 x live birth, deceased after 7 days of life
sex	5 x male 4 x female
number of isolated malformations/MCA	3 x MCA 6 x isolated

The indicator malformation preaxial polydactyly is characterized by additional thumbs or big toes. Only about one third of all polydactyles are pronounced preaxially, about two thirds postaxially. For all polydactyles, the **prevalence** for 2020 lies at **17.9 per 10,000 births**. This prevalence lies significantly above the normal range (2008-2019: 12.1 per 10,000 births) (Chapter 9). Also postaxial polydactyles (2020: 12.4 per 10,000 births) occurred more frequently than usual (2008-2019: 9.0 per 10,000 births).

Seven children showed an accessory thumb in 2020 (2 x right, 4 x left, 1 x side was not indicated) and two children showed an additional big toe.

Malformation combinations (MCA) or superordinated syndromes detected:

- VACTERL association with: Rectal atresia with vestibular fistula, partial misjunction of the pulmonary veins, VSD, stenosis of the pulmonary artery in premature, right lung sequestration, bronchopulmonary isomerism, hemivertebrae with scoliosis
- glandular hypospadias
- PFO at full term infant, retarded hip maturity bilateral



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	5.1	5.2	5.8	3.5	3.5	3.0	2.3	2.9	2.2	1.7	1.7	1.8	5.6
BP	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2

Fig. 34: Development of prevalence/10,000 births with preaxial polydactyly in Saxony-Anhalt since 2008

In 2020, one preaxial polydactyly per 1,798 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	9	5.56	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	8.13	6.95 - 9.45	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	5.23	5.08 - 5.38	

With a **prevalence** of **5.6 per 10,000 births**, the 2020 annual prevalence of the indicator malformation limb reduction defect clearly falls below the confidence interval of the basis prevalence (2008-2019: 8.1 per 10,000 births). In the previous year (2019), we registered a minimum value of 4.7 per 10,000 births. During the reporting period, the highest rate of reduction malformation of the extremities was observed in 2012. Since then, the prevalence values have been decreasing.This is reflected in the trend calculation over the period from 2007-2020 (Chapter 10.38), with a significant downward trend and a percentage change of -7.66% (CI -13.66% to -0.63%).

Compared to the average prevalence of EUROCAT (2008-2019: 5.2 per 10,000 births), the basis prevalence of Saxony-Anhalt is far above the normal range of the values of the European registries. The annual prevalence of Saxony-Anhalt is in between and therefore above the upper confidence limit of the European prevalence. The basis prevalence of Saxony-Anhalt does not reach the maximum value of the Auverge registry (France) of 9.4 per 10,000 births (2008-2019).

additional information:

pregnancy outcome	6 x live births 3 x termination of pregnancy
sex	6 x male 2 x female 1 x no indication
number of isolated malformations/MCA	6 x MCA 3 x isolated

The indicator malformation limb reduction defect was observed in 2020 4 times in the upper extremities and 5 times in the lower extremities. The right side was affected twice, the left side 4 times and twice both sides.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards syndrome with: VSD, persistent left superior vena cava, left clubfoot, gallbladder atresia, septum pellucidum anomalies
- Bland-White-Garland syndrome with: Vascular ring of the great arteries, supravalvular pulmonary artery stenosis and PFO at preterm infants, cleft lip and palate on the left foot, syndactyly type I of the left foot
- OPHN1 syndrome with: cardiac malformation
- hemivertebra with scoliosis, hexadactyly on the right foot
- Volvulus, bilateral sensorineural disorder, membranous syndactyly of the toes (Digit III / IV) right foot, cholestasis
- Pulmonary valve stenosis, syndactyly (Digit I / II and III / IV on the right foot and digit II / III on the left foot), plexus cyst, PFO at preterm infant

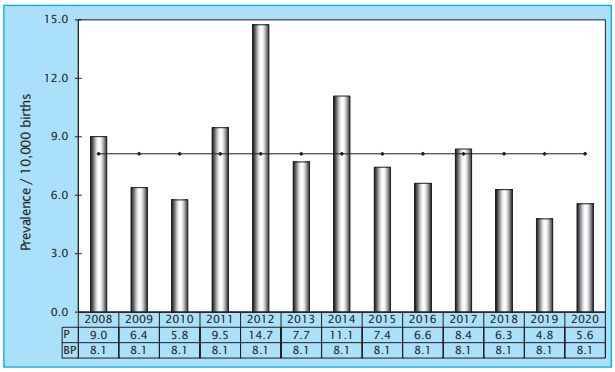


Fig. 35: Development of prevalence/10,000 births with limb reduction defects in Saxony-Anhalt since 2008

In 2020, one limb reduction defect per 1,798 births was registered in Saxony-Anhalt.

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

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	7	4.32	↑
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	2.55	1.91 - 3.33	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.98	2.86 - 3.10	

With a high **prevalence** value of **4.3 per 10,000** births, the annual prevalence 2020 exceeds again the basis prevalence of diaphragmatic hernias in Saxony-Anhalt (2008-2019: 2.6 per 10,000 births) significantly, after a low value in the previous year. As of birth year 2020, seven children/fetuses were diagnosed with diaphragmatic hernia. The number of cases in Saxony-Anhalt ranged from a minimum of two (2016) and the maximum of eight cases (2008, 2018) during the reporting period.

The confidence interval of the basis prevalence of Saxony-Anhalt spans a larger safety range than the interval of the average prevalence of the European registries (3.0 per 10,000 births). The basis prevalence can be found in the lower third of all prevalence values of the European malformation registers. This year's prevalence value of Saxony-Anhalt is also higher than the European comparative values.

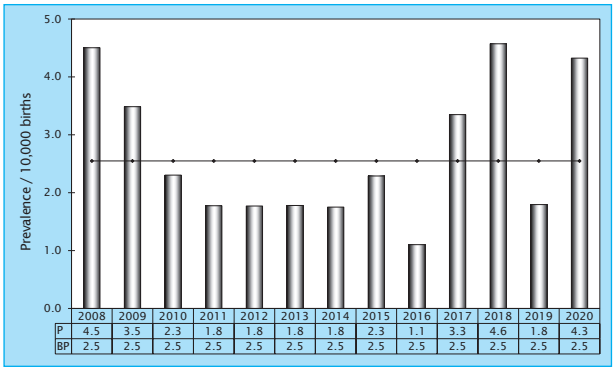
additional information:

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

Four of the seven diaphragmatic hernias occurred left sided in 2020, one on the right side, and of two children/fetuses who had an abdominal wall defect, the sidedness of the diaphragmatic hernia was not reported. Diaphragmatic hernias develop between 8 and 10 weeks of gestation. In two cases, the malformation was not noticed until the 28th or 29th week of gestation.

Malformation combinations (MCA) or superordinated syndromes detected:

- Omphalocele, cleft lip and palate on the right, dextrocardia, VSD, pulmonary valve stenosis
- gastroschisis, azygos continuation of the inferior vena cava
- ASD II, mechanical ileus due to marked adhesions, hernia inguinalis in a preterm infant on the left side
- cardiac malformation



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	4.5	3.5	2.3	1.8	1.8	1.8	1.8	2.3	1.1	3.3	4.6	1.8	4.3
BP	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5

Fig. 36: Development of prevalence/10,000 births with diaphragmatic hernia in Saxony-Anhalt since 2008

In 2020, one diaphragmatic hernia per 2,312 births was registered in Saxony-Anhalt.

10.30 Omphalocele (Q79.2)

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	5	3.09	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	3.32	2.58 - 4.20	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	3.54	3.41 - 3.66	

Five cases of omphalocele were registered in Saxony-Anhalt in 2020. The resulting **prevalence** determined from this number **(2020: 3.1 per 10,000 births)** lies within the confidence interval of the basis prevalence of Saxony-Anhalt (2008-2019: 3.3 per 10,000 births).

The confidence interval of the basis prevalence of Saxony-Anhalt coincides with that of the prevalence of the EUROCAT registries (2008-2019: 3.5 per 10,000 births). Thereby it is wider than the interval of the European overall prevalence because of the smaller numbers. The annual prevalence 2020 of Saxony-Anhalt is lower than the European average.

additional information:

pregnancy outcome	1 x live birth 4 x termination of pregnancy
sex	2 x male 2 x female 1 x no indication
number of isolated malformations/MCA	5 x MCA

The indicator malformation omphalocele is an abdominal wall defect. If the physiological umbilical hernia does not regress before the 10th week of gestation, an omphalocele develops. Often the children/fetuses, like the affected infants in 2020, suffer from additional malformations of other organ systems. Cardiac malformations and cleft lip, jaw or palate were reproted three times. In one live birth, only the intestine was involved. A chromosomal aberration was the cause of the omphalocele in one case.

Malformation combinations (MCA) or superordinated syndromes detected:

- Edwards Syndrome
- Anencephaly, cleft palate, Cantrell pentalogy, ectopia cordis, absent sternum
- Diaphragmatic hernia, right cleft lip and palate, dextrocardia, VSD, pulmonary valve stenosis
- Cleft lip and palate, VSD, wrist flexion deformity
- Mesenterium ileocolicum commune, intestinal malrotation

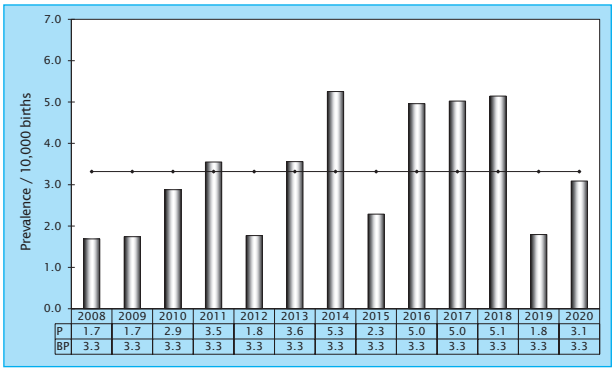


Fig. 37: Development of prevalence/10,000 births with omphalocele in Saxony-Anhalt since 2008

In 2020, one omphalocele per 5,572 births was registered in Saxony-Anhalt.

10.31 Gastroschisis (Q79.3)

Saxony-Anhalt t	Jahr 2020		
	Saxony-Anhalt	Prevalence/10,000 births	Comparison to basis prevalence
	6	3.71	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	3.65	2.88 - 4.57	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.71	2.60 - 2.82	

With six concerned children/fetuses, this year's **prevalence (2020: 3.7 per 10,000 births)** corresponds to the basis prevalence of Saxony-Anhalt (2008-2019: 3.7 per 10,000 births). It shows up in the middle range of the confidence interval.

The confidence interval of the basis prevalence of Saxony-Anhalt is above the overall prevalence of the European registers of malformations (2008-2019: 2.7 per 10,000 births). The Saxony-Anhalt basis prevalence is in the upper third of the prevalences of all EUROCAT-centers. Compared to the European prevalence, the annual prevalence of Saxony-Anhalt for 2020 lies clearly above.

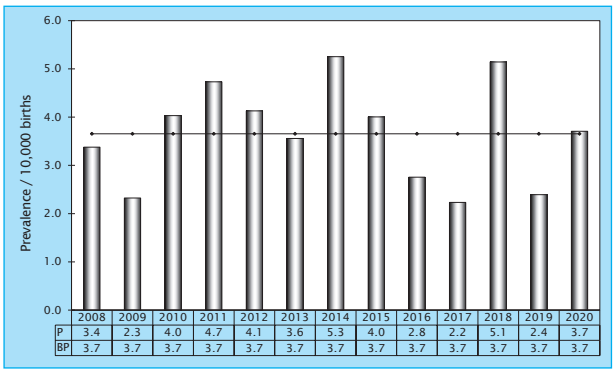
additional information:

pregnancy outcome	4 x live births 1 x live birth, deceased after 7 days of life 1 x termination of pregnancy
sex	3 x male 2 x female 1 x no indication
number of isolated malforamtions/MCA	4 x MCA 2 x isolated

The gastroschisis was known prenatally in all children/fetuses. In case of a fetus with caudal regression syndrome the malformations were already discovered in the 12th week of gestation and the pregnancy was terminated early. All other children were delivered by caesarean section between the 29th or 37th week of gestation and operated on the first day of life in a university hospital.

Malformation combinations (MCA) or superordinated syndromes detected:

- caudal regression syndrome with: agenesis of the Os sacrum
- Jejunum atresia with lack of fixation to posterior abdominal wall, cholestasis
- diaphragmatic hernia, azygos-continuation of the vena cava
- inferior
- DUP of III degree on the right side, PFO at full term infant



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
P	3.4	2.3	4.0	4.7	4.1	3.6	5.3	4.0	2.8	2.2	5.1	2.4	3.7
BP	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7

Fig. 38: Development of prevalence/10,000 births with gastroschisis in Saxony-Anhalt since 2008

In 2020, one gastroschisis per 2,698 births was registered in Saxony-Anhalt.

10.32 Prune-Belly syndrome (Q79.4)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	0	0.0	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	0.82	0.48 - 1.31	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

The indicator malformation prune-belly sequence occurs rarely and therefore does not occur at all in Saxony-Anhalt in some years it. No cases were registered in four of the 13 years of the reporting period, including the years 2019 and 2020. Except for a one-time case of five affected children/ fetuses in 2011, the prune-belly sequence has never been found more frequently than twice a year. The basis prevalence (2008-2019) lies at 0.8 per 10,000 births

EUROCAT does not provide an overall European prevalence for comparison.

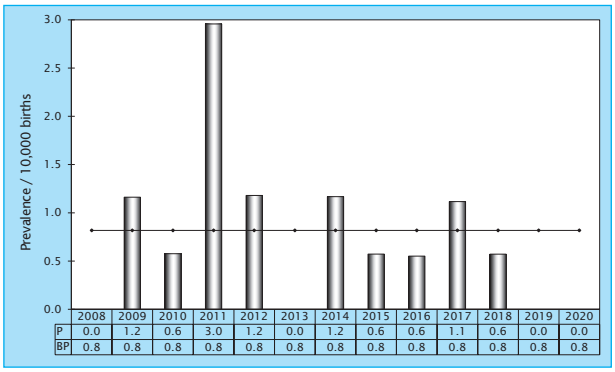


Fig. 39: Development of the prevalence/10,000 births with Prune belly syndrome in Saxony-Anhalt since 2008

In 2020, no Prune-Belly-syndrome was registered in Saxony-Anhalt.

10.33 Down`s Syndrome - Trisomy 21 (Q90.)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	40	24.71	↑
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	19.28	17.44 - 21.27	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	24.32	23.99 - 24.65	

With 40 registered cases in 2020, the **annual prevalence** of **24.7 per 10,000** births lies clearly above the upper confidence limit of the basis prevalence of 19.3 per 10,000 births (2008-2019). However, it does not reach the maximum value of 2018 (25.7 per 10,000 births). Thus, the Down`s syndrome is the most common chromosomal aberration. The prevalence of live births (2008-2019: 8.1 per 10,000 births) does no longer meet the European criterion of a rare disease of <5.0 per 10,000 births.

The basis prevalence of Saxony-Anhalt is below the European prevalence determined by EUROCAT of 24.3 per 10,000 births (2008-2019) and lies in the lower quarter of the prevalence values of all European registries. The reason for this is the lower average maternal age in Saxony-Anhalt at birth compared to the EU average (2013-2019: 29.3 years vs. 30.8 years*). The risk of the child/fetus to develop a Down`s syndrome correlates with the maternal age. The high prevalence for Saxony-Anhalt in 2020 lies even higher than the European baseline prevalence.

additional information:

pregnancy outcome	20 x live births 20 x termination of pregnancy
sex	19 x male 16 x female 5 x no indication
number of isolated malformations/MCA	17 x MCA 23 x isolated

In 20 cases the pregnancy was terminated after confirmation of the prenatal diagnosis of Down`s syndrome with Ø 14.2 WOG (Ø 15.7 WOG, median 16.0 WOG). The earliest termination took place in the 13th WOG and the latest in the 19th WOG.

Malformation combinations (MCA) or superordinated syndromes detected:

- Hydrocephaly, PFO at preterm infant
- - AVSD, ASD II, cataracta congenita right, corpus callosum hypoplasia
- - AVSD, teratoma
- - AVSD, brachycephaly
- AVSD, small ears, umbilical hernia
- 3 x AVSD
- VSD, multiple ASD
- VSD, PFO at full term infant, non-hemodynamically effective PDA at full term infant, hepatomegaly, bicuspid aortic
- bicuspid aortic valve, PFO at full term infant, stenosis of the pulmonary artery, DUP I. grade left
- ASD II
- pulmonary valve stenosis
- PFO at full term infant
- bilateral acoustic sensation disorder
- clubfeet, auricular appendage on the left side
- Brachycephaly, lateral neck cyst

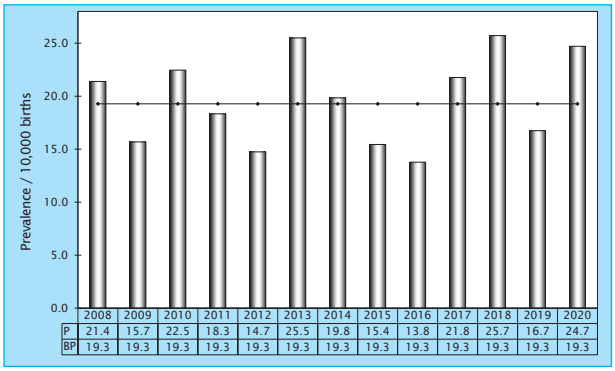


Fig. 40: Development of prevalence/10,000 births with Down`s syndrome in Saxony-Anhalt since 2008

I In 2020, one Down`s syndrome per 405 births was registered in Saxony-Anhalt.

* Source: https://ec.europa.eu/eurostat/databrowser/view/demo_fordagec/default/table?lang=de
last update: 28.06.2021 23:00

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

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	2	1.24	↔
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	1.20	0.78 - 1.77	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.23	2.13 - 2.33	

A Patau syndrome (trisomy 13), which is the third most common trisomy, was detected prenatally in two fetuses in Saxony-Anhalt in 2020. The resulting **annual prevalence (1.2 per 10,000 births)** corresponds to the normal range of the basis prevalence of Saxony-Anhalt (2008-2019: 1.2 per 10,000 births).

A Europe-wide comparison shows that the confidence interval of the Saxony-Anhalt basis prevalence for Patau syndrome is below the confidence interval of the total prevalence given by EUROCAT (2008-2019: 2.2 per 10,000 births). The basis prevalence of Saxony-Anhalt is in the lower quarter of the prevalence determined for the EUROCAT centers. There is evidence, that the development of Patau syndrome, just lik Down's syndrome and Edwards syndrome, is associated with the maternal age. Both mothers of the affected fetuses were over 40 years old.

additional information:

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

Prenatal ultrasound showed that both fetuses had severe malformations which are typical for Patau syndrome. The chromosomal findings were available once after a NIPT and once after an amniocentesis.

Malformation combinations (MCA) or superordinated syndromes detected:

- Hydrocephaly, TGA, median cleft palate, bilateral renal dysplasia, bilateral accessory 6th finger
- Holoprosencephaly, median facial cleft, cardiac malformation, partial misjunction of the pulmonary veins

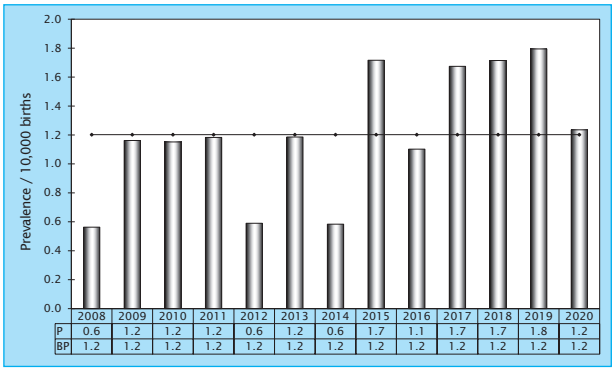


Fig. 41: Development of prevalence/10,000 births with a Patau syndrome in Saxony-Anhalt since 2008

In 2020, one Patau syndrome (trisomy 13) per 8,093 births was registered in Saxony-Anhalt.

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

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	9	5.56	↗
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	4.42	3.57 - 5.43	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	5.98	5.82 - 6.15	

Edward's syndrome occurs when the chromosome 18 in the chromosome set of the affected children/fetuses is missing. In Saxony-Anhalt, the defect was diagnosed 9 times in 2020. This results in a **prevalence** of **5.6 per 10,000 births** for Saxony-Anhalt, which lies slightly above the confidence interval of the basis prevalence (2008-2019: 4.4 per 10,000 births).

The confidence interval of the basis prevalence of Saxony-Anhalt and that of the European overall prevalence reported by EUROCAT (2008-2019: 3.5 per 10,000 births) do not overlap. The basis prevalence of Saxony-Anhalt is even lower. It can be found in the lower third of the average prevalence of the European registers. The risk of developing an Edwards syndrome depends on the maternal age at conception. The difference of the lower average maternal age in Saxony-Anhalt in contrast to the average maternal age in the EU, is reflected in the unequal prevalence levels.

additional information:

pregnancy outcome	1 x live birth 2 x live births, deceased after 7 days of life 1 x spontaneous abortion 5 x termination of pregnancy
sex	3 x male 5 x female 1 x no indication
number of isolated malformations/MCA	7 x MCA 2 x isolated

The finding was known prenatally in case of a live birth by amniocentesis. The diagnosis was verified postnatally as mosaic. In two further children there were no prenatal findings of a chromosomal aberration.

Malformation combinations (MCA) or superordinated syndromes detected:

- Choanal stenosis bilateral, corpus callosum hypoplasia, DUP II. grade and ureteral outlet stenosis on the right side, bilateral inguinal hernia at preterm infant, septum pellucidum anomalies
- choanal stenosis right, VSD, ASD II, bilateral postaxial accessory finger, flat feet, bilateral laterally sloping eyelid axes
- Hydrocephaly, corpus callosum agenesis, ASD II, riding aorta, VSD, sacral dimple
- bilateral cleft lip and palate and lateral neck cysts
- omphalocele
- VSD, persistent left superior vena cava, clubbed hands, clubfoot left, gallbladder atresia, Septum pellucidum anomalies
- Corpus callosum agenesis, AVSD

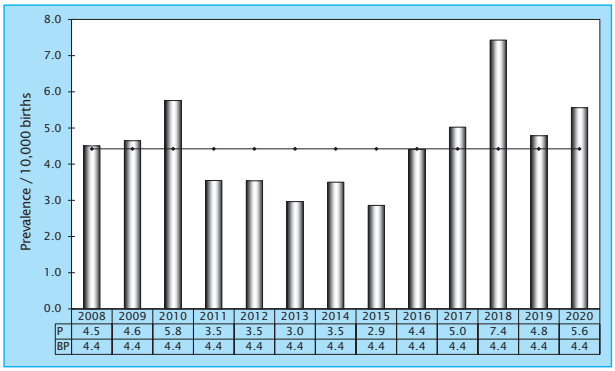


Fig. 42: Development of prevalence/10,000 births with Edwards syndrome in Saxony-Anhalt since 2008

In 2020, one Edwards syndrome per 1,798 births was registered in Saxony-Anhalt.

10.36 Turner Syndrome (Q96.)

Saxony-Anhalt	Year 2020		
	Number	Prevalence/10,000 births	Comparison to basis prevalence
	2	1.24	↓
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	2.12	1.54 - 2.84	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	2.52	2.41 - 2.63	

The indicator malformation Turner syndrome is rare and yet the most common form of gonadal dysgenesis. In the reporting period it was diagnosed a maximum of 7 times per year (2012, 2016) in Saxony-Anhalt. In 2020, Turner syndrome was found only in two children. In one girl, a hydrops fetalis led to her stillbirth.

The current **prevalence** of Turner syndrome **(2020: 1.2 per 10,000 births)** is significantly lower than the normal range of the basis prevalence of Saxony-Anhalt (2008-2019: 2.1 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 (2008-2019: 2.5 per 10,000 births).
The annual prevalence of Saxony-Anhalt lies also below the European overall prevalence. A goodthird of European malformation registries report for confidence interval of the European prevalence (2008- 2019: 2.5 per 10,000 births). The annual prevalence in Saxony-Anhalt is below the European of the European overall prevalence. A good third of the European malformation registries report an even lower baseline prevalence for Turner syndrome than Saxony-Anhalt. It is known that not all Turner syndromes are recognized at birth. The diagnosis is predominantly made with the absence of menstrual bleeding in puberty.

additional information:

pregnancy outcome	1 x live birth 1 x stillbirth
sex	2 x female
number of isolated malformations/MCA	2 x isolated

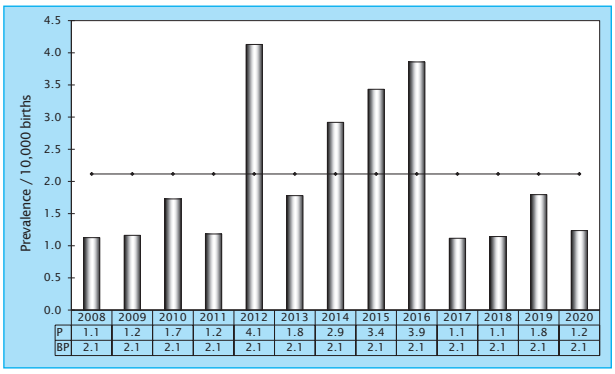


Fig. 43: Development of prevalence/10,000 births with Turner syndrome in Saxony-Anhalt since 2008

In 2020, one Turner syndrome per 8,093 births was registered in Saxony-Anhalt.

10.37 Klinefelter syndrome/male gonosome anomalies (Q98.)

	Year 2020		
Saxony-Anhalt	Number	Prevalence/10,000 births	Comparison to basis prevalence
	1	0.62	↘
	Reporting period 2008-2019		
	Basis prevalence / 10,000 births	Confidence interval (CI 95 %)	
	1.11	0.70 - 1.66	
EUROCAT (Full members)	Period 2008-2019		
	Prevalence/10,000 births	Confidence interval (CI 95 %)	
	no information	no information	

As in the previous year, only one boy was diagnosed with a gonosomal anomaly in 2020. The indicator malformation Klinefelter syndrome/male gonosome anomalies is a very rarely appearing indicator malformation. In Saxony-Anhalt, a maximum of four cases are counted per year. In some years, the malformation is not diagnosed at all, as it was the case for the last time in 2015.

In 2020, the current **prevalence** lies at **0.6 per 10,000 births**. The annual prevalence is slightly below the basis prevalence determined for the reporting period (2008-2019: 1.1 per 10,000 births).

The prevalence for the rare Klinefelter syndrome (Q98.0-Q98.4) shows a value of 0.9 per 10,000 births for Saxony-Anhalt in the reporting period 2008-2019.

EUROCAT gives a slightly lower prevalence for Klinefelter syndrome of 0.7 per 10,000 births (2008-2019).

additional information:

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

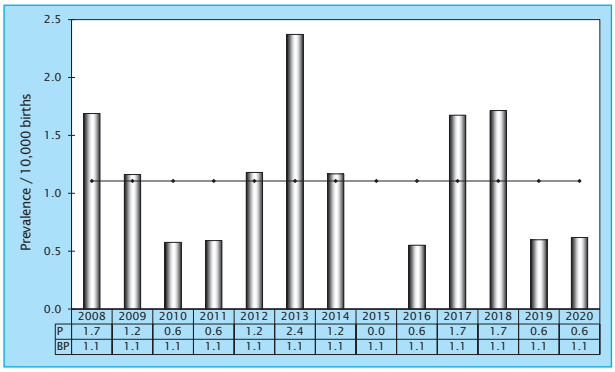


Fig. 44: Development of prevalence/10,000 births with Klinefelter syndrome/male gonosome anomalies in Saxony-Anhalt since 2008

In 2020, one Klinefelter syndrome/male gonosome anomalies per 16.186 births was registered in Saxony-Anhalt.

10.38 Trend analysis of indicator malformations

The monitoring of malformations has the task to identify clusters or trends in the occurrence of malformations. Each of the previous chapters 10.1 to 10.37 of the annual report deals with one of the indicator malformations (chapter 10.0) that are clearly described by the ICBDSR (International Clearinghouse for Birth Defects Surveillance and Research) and internationally used. It is reported how far the currently observed frequency of the malformation can be classified temporally and spatially. Chapter 10.38 is dedicated to the frequency development of all indicator malformations over the **years 2007 to 2020**.

28 cases showed two or more, and a maximum of five indicator malformations. A total of 266 indicator malformations were registered.180 children with indicator malformations (78.3 %) were live births in 2020, ten of them died in the first year of life. Between 2008 and 2019 the proportion of live births was Ø 74.0%. Indicator malformations were registered in 2020 only at one stillbirth and at one spontaneous abortion after 16 weeks of gestation (together 0.9%). The proportion of cases in which pregnancy was terminated after prenatal diagnosis, was lower in 2020 (20.9%) compared to the whole reporting period (2008-2019: 23.5%).

1.42% of all children/fetuses in Saxony-Anhalt had one of the 37 indicator malformations. Therefore, the current prevalence can be found in the middle range of the basis prevalence (2008-2019: 1.43 %, CI 1.38-1.49).

The aim of the following trend analysis is to detect long-term trends in the occurrence of malformations. The current report analyses therefore in the following the strength and orientation of the changes of indicator malformations within a time period of 2007-2020.

The trend estimation has been an integral part of the annual report for the recent 10 years. Condition for the trend analysis is that we expect each malformation to appear at least five times or that we registered at least two cases of the corresponding malformation. If in each case up to the annual report 2018, values from individual years are considered, the initial requirement is not met for about one third of the indicator malformations, depending on the frequency. In order to be able to carry out the test for changes even in the case of indicator malformations with a lower frequency, 2-year intervals are formed and tested for the first time in this report.

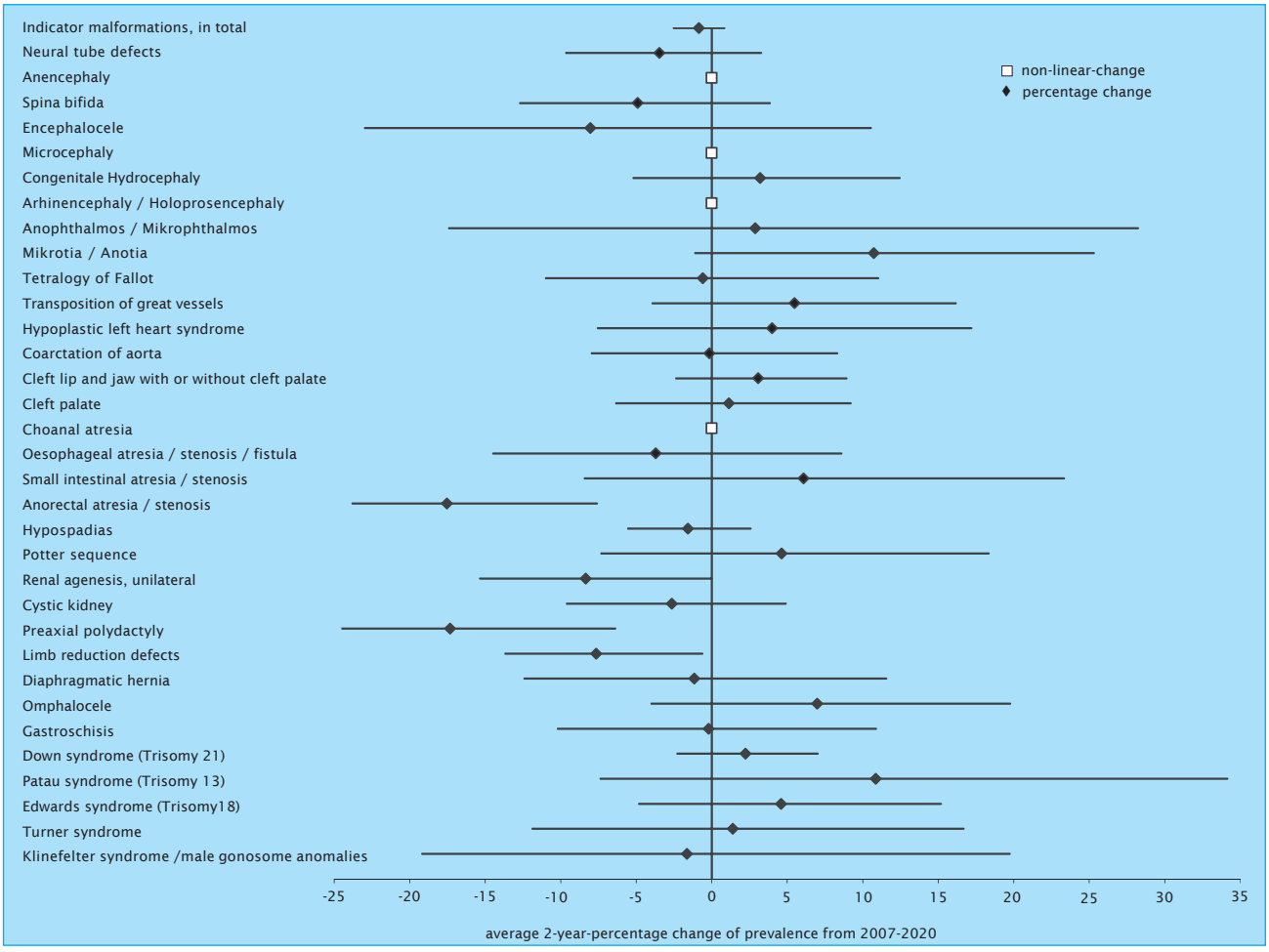


Fig. 45: Trend analysis 2007 to 2020 with average percentage change of two-year prevalence (95% CI)

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 anencephaly, microcephaly, arhinencephaly/ holoprosencephaly and choanal atresia.

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** cannot be observed 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, unilateral renal agenesis, preaxial polydactyly and limb reduction malformations.

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	-0.86	-2.51 to 0.83
Neural tube defects	-3.45	-9.64 to 3.28
Spina bifida	-4.90	-12.69 to 3.85
Encephalocele	-8.04	-22.97 to 10.55
Congenital hydrocephaly	3.20	-5.19 to 12.45
Anopthalmia / Micropthalmia	2.88	-17.39 to 28.23
Microtia / Anotia	10.73	-1.09 to 25.31
Tetralogy of Fallot	-0.59	-10.98 to 11.03
Transposition of great vessels	5.50	-3.91 to 16.17
Left heart hypoplasia	4.01	-7.54 to 17.19
Coarctation of aorta	-0.15	-7.94 to 8.31
Cleft lip with or without cleft palate	3.09	-2.35 to 8.93
Cleft palate	1.13	-6.33 to 9.21
Oesophageal atresia/stenosis/fistula	-3.70	-14.46 to 8.58
Small intestinal atresia	6.09	-8.41 to 23.33
Anorectal atresia/stenosis	-17.53	-23.78 to -7.6
Hypospadias	-1.57	-5.53 to 2.58
Potter sequence	4.63	-7.31 to 18.34
Renal agenesis, unilateral	-8.34	-15.34 to -0.03
Cystic kidney	-2.65	-9.59 to 4.9
Preaxial polydactyly	-17.33	-24.46 to -6.39
Limb reduction defects	-7.66	-13.66 to -0.63
Diaphragmatic hernia	-1.15	-12.4 to 11.56
Omphalocele	6.99	-3.98 to 19.77
Gastroschisis	-0.21	-10.18 to 10.87
Down‘s-Syndrome (Trisomy 21)	2.24	-2.27 to 7.02
Patau Syndrome (Trisomy 13)	10.87	-7.36 to 34.15
Edwards Syndrome (Trisomy 18)	4.60	-4.8 to 15.17
Turner Syndrome	1.39	-11.87 to 16.68
Klinefelter Syndrome / male gonosome anomalies	-1.64	-19.17 to 19.73

13 Summary

The present Annual Report 2020 of the Federal State of Saxony-Anhalt about the incidence of congenital malformations and anomalies as well as genetically caused diseases gives an overview about frequencies and development of malformations on basis of the nationwide data submitted to the malformation monitoring. With the help of the official birth figures of the Statistical Office of Saxony-Anhalt data of the years 2008-2020 were statistically evaluated and presented. For the determined prevalences of the indicator malformations, European prevalences of EUROCAT are listed. Saxony-Anhalt is the only state in Germany that currently holds up-to-date data about malformations.

With **16,113 live births in 2020** fewer children were born in Saxony-Anhalt than at any time since the mid-1990s, than at any time since the mid-1990s, and fewer than the average for the period under review (2008-2019: 17.258,2). According to the Federal Statistical Office (Destatis), 773,144 children were born alive in Germany in 2020, slightly fewer than in 2018 (778.090). Only 2.1 % of all newborns in Germany came from Saxony-Anhalt in 2020.

In 2020, **73 children were stillbirths** in Saxony-Anhalt, according to the Statistical Office. During the reporting period (2008-2019) this results in a ratio of one stillbirth to 244 live births and accordingly in the year 2020 in one stillbirth to 221 live births.

The evaluations for the annual report are based on a total number of **16,186 births in 2020** (Chapter 2). In addition to data about live and stillbirths, data of **66 medically induced terminations** of pregnancy and 1**6 spontaneous abortions** from the 16th week of gestation were included in the analysis.

Major malformations were found in **608 infants/fetuses** (3.76% of births) in 2020. The malformation rate in 2020 is in the lower range of the basis prevalence (2008-2019: 3.81%, CI 3.73 to 3.89%). 544 infants with major malformations were live births. Of these, 16 children died in the first year of life (2,9 %). In 6 cases (10.2% of children/ fetuses with major malformations) the pregnancy was terminated (Chapter 6). I

The most frequent single diagnoses in 2020, as in every previous year, are the two cardiac malformation VSD and ASD. The ASD was diagnosed in 0.81% and the VSD in 0.51% of all births. Dilated uropathy II.-IV.˚/ureterocele occurred in 0.26 % of all births within the expected range. Down`s syndrome, significantly more frequent than expected, and hypospadias, in the usual frequency (0.25% of all births each), follow in the frequency ranking (Chapter 9).

230 children/fetuses were affected by one of the 37 clearly defined indicator malformations (Chapter 10). A higher **annual prevalence** than the corresponding basis prevalence (2008-2019) was seen for aortic isthmus stenosis, cystic kidneys, preaxial polydactyly, diaphragmatic hernia, and Down`s syndrome. A lower annual prevalence was seen in neural tube defect, anencephaly, encephalocele, microcephaly, arhincephaly/holoprosencephaly, anophthalmia/ microphthalmia, microtia/anotia, tetralogy of Fallot, cleft palate, unilateral renal agenesis, exstrophy of the urinary bladder, limb reduction malformations, prune-belly sequence, and Turner syndrome.

In 2020, the malformation monitoring registered **62 terminations of pregnancy** of fetuses with malformations. On average, these pregnancies were terminated prematurely at 18.6 weeks of gestation. Depending on the malformation, the pregnancy progressed differently at the time of the abortion. The earliest pregnancies were terminated in the presence of a chromosomal aberration (54.8%) with an average of 17.5 weeks gestation. In fetuses with multiple anomalies and other malformations (29.0%), abortion was performed at 19.3 WOG and in fetuses with CNS malformation (16.1%) the termination was performed latest with Ø 20.7 WOG (Chapter 12).

Malformations that are complex or not limited to one organ system are organ system are presented in Chapter 11. As of birth year 2020, 33 children/fetuses showed **genetic/co-conditional diseases or microdeletions**. 12 children/fetuses were affected by a **sequence, association, or a complex**. In 14 children an **embryopathy or fetopathy** war diagnosed and in 2 children an infection was present. A **chromosomal aberration** was diagnosed in 59 children/fetuses, of which the majority (40 children/fetuses) were diagnosed as Down`s syndrome.

Developmental relevant congenital hearing disorders are the main topic of chapter 14.1. Risk factors for hearing loss in children and its importance for language acquisition are presented, as well as information on the neonatal hearing screening process and results. The topic of chapter 14.2. is the risks of COVID-19 infection during pregnancy and the value of COVID-19 vaccination.

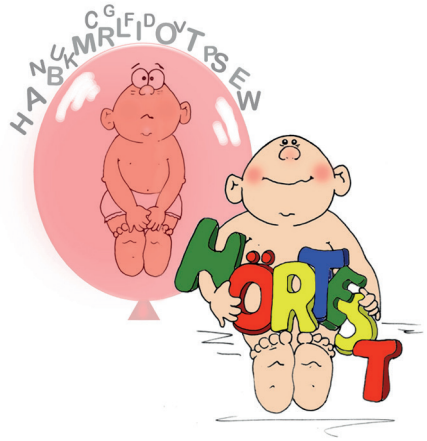
The malformation monitoring received **2,029 reports** (chapter 4) about 1,822 children/ fetuses in 2020. Among them were 608 children/fetuses with at least one major malformation and further on 198 children/fetuses with minor malformations or anomalies. In addition, the data of children without malformations is important as well, as risks can only be scientifically assessed in comparison (case-control study design) with these data.

With the help of many colleagues from different medical institutions who have been reporting congenital malformations for many years, a solid database has been created which also served as basis for the 2020 annual report. We would therefore like to express our sincere thanks to all our „senders“, in the confidence that we will continue to work successfully together, and we look forward to go ahead with our interdisciplinary cooperation!

14. Focus theme

14.1 Developmental congenital hearing disorders

Newborn hearing screening



Permanent childhood hearing loss refers to a hearing impairment during childhood that is not only temporarily caused by factors such as middle ear infections. It can be congenital or acquired, and the child may be affected unilaterally or bilaterally.
The definition of hearing loss and hearing deficit may vary in different classification systems, but hearing losses (HV) are generally categorized as

- mild (25-40 dB),
- moderate (41-70 dB),
- severe (71-95 dB) und
- profound (≥95 dB).

Deafness is the term reserved for profound hearing loss. Thresholds are expressed in decibels (dB) on a hearing level scale (dB hearing loss).

Permanent infantile hearing loss affects all aspects of language acquisition, since the child's ability to extract information from the oral language models of his environment is impaired. Studies have repeatedly shown the negative effects on language and reading development. Children who are born with hearing loss are particularly susceptible to impaired and delayed speech development, as they experience an auditory deprivation [1] during a „sensitive phase" of language acquisition in the first months of life. [1].

Significant permanent hearing loss is a common congenital disorder and may lead to delayed speech development, difficulties in behaviour and psychosocial interactions, and poor academic performance. In contrast, early detection of hearing loss in infancy can help to initiate intervention that can lead to language acquisition (or improvement of language, cognitive, behavioural and educational abilities) [2]. The decline in language learning ability and efficiency with increasing age, which is characteristic of the sensitive period, is underpinned by changes at the neuronal level: the lack of adequate auditory input during the early sensitive period has direct effects on the neuronal pathways in the brain that also support language acquisition, whereas the absence of auditory stimuli later in life does not have these effects [1]. In addition, the structural and functional changes in the brain, resulting from early language deprivation can be reversed to some extent if an intervention in form of electrical stimulation of the auditory pathway, such as a cochlear implant, is applied early enough in life. The effect is lost later, which results from a higher degree of plasticity in the brain during the first period of life [3]. This highlights the need for early intervention in children with congenital permanent hearing loss [4].

Universal newborn hearing screening (NHS) is a strategy to detect congenital deafness and hearing loss. Over the past two decades screening of newborns for hearing loss has become a care standard in many countries around the world. The consensus goal worldwide is to screen children with all types and degrees of hearing loss, both bilateral and unilateral, and to identify the age at diagnosis for early hearing amplification, to improve language skills and literacy development and, in turn, to maximize intellectual abilities.
Since January 01, 2009, universal newborn hearing screening has also been offered nationwide in Germany according to the decision of the Joint Federal Committee (G-BA) (amendment to the Children's Guideline of 19.06.2008). Every newborn has the right to participate in a hearing screening as part of the universal newborn hearing screening program (NHS). As with any screening program, the justification for the program depends on a precise case definition. The primary purpose of the G-BA guideline-based on NHS is primarily intended to detect bilateral permanent hearing impairment from a hearing loss of ≥35 dB. Such hearing disorders should be diagnosed by the end of the 3rd month of life and an appropriate therapy should be initiated by the end of the 6th month of life [5]. To achieve this time window certain tracking measures are necessary (= follow-up) of the findings that need to be checked.
The hearing loss threshold of ≥35 dB was chosen because there is strong evidence from studies that losses of this magnitude or more are associated with clinically significant impairments in speech development and the resulting limitations. Hearing screening is performed bilaterally with either transitory evoked otoacoustic emissions (TEOAE) or with automated auditory brainstem response (AABR). Abnormal TEOAE findings should always be monitored with AABR. Children at risk for congenital hearing disorders should generally be examined with AABR [5]. Details of the newborn hearing screening tracking in Saxony-Anhalt for the 2020 birth cohort are presented in chapter 16 of this report.
Studies on the long-term development of mildly to moderately hearing-impaired children conclude that even for children with unilateral hearing loss, delayed development (especially in reference to language development) and problems at school are likely [6]. Therefore, examination of both ears is mandatory. Even though hearing loss may be delayed or acquired, the congenital hearing loss, detectable in the NHS, is the focus. Among possible causes are congenital infections (cytomegalovirus = CMV), genetic cause, including syndromic and non-syndromic causes, and trauma.
Hearing rehabilitation for children with permanent congenital hearing impairment may include the use of hea-

ring aids, cochlear implants, bone-anchored devices, or the use of assistive devices such as frequency modulating systems.

Hearing loss in the neonatal period may appear as transient or permanent conductive hearing loss, permanent sensorineural, auditory neuropathy and can be classified as mixed defects.

- A **conductive hearing loss (SLSH)** is caused by a problem in the outer or middle ear, that interferes with the conduction of sound to the inner ear. It can occur at any location from the outer ear (pinna, external auditory canal) to the stapes footplate and the oval window. In children beyond infancy, conductive hearing loss is usually transient (e.g., otitis media with effusion).
- **Sensorineural hearing loss (SNHL)** is a hearing loss, that results from congenital structural disorders, diseases or functional disorders that affect the inner ear (e.g., the cochlea) and/or the auditory nerve (cranial nerve VIII).
- In **auditory neuropathy spectrum disorder (ANSD)** (also called auditory neuropathy, neural synchronization disorder) the cochlea can detect sound, but the signals are not transmitted properly from the inner ear to the brain. ANSD is characterized by normal otoacoustic emissions, which indicate normal function of the outer hair cells. However, the responses of the auditory brainstem are disturbed, which indicates to a disturbance of the inner hair cells of the cochlea or the cochlear branch of cranial nerve VIII.
- The term combined hearing loss refers to a combination of **conductive hearing loss (SLSH)** and **sensorineural hearing loss (SNHL)**.

Overall, permanent childhood hearing loss is the result of overlapping factors such as genetic predisposition, intrauterine environmental influences, perinatal and postnatal factors. The worldwide studies indicate that the prevalence of moderate and severe bilateral hearing loss (>40 dB) in healthy newborns is 1 to 3 per 1,000 live births and 2 to 4 per 100 live births in a high-risk population (infants in intensive care unit) [2]. This data confirms that hearing impairment is one of the most common potentially disabling conditions in infancy and one of the most common congenital anomalies (see also chapter 9).

Risk factors for sensorineural hearing loss or auditory neuropathy in infancy

Acquired prenatal factors	perinatal infections (CMV, syphilis, toxoplasmosis, rubella, HIV, Zika virus)
	maternal diabetes
	prenatal drugs (antimalarials, aminoglycosides, isotretinoin)
	maternal drug use
	lack of prenatal care
	craniofacial anomalies
Acquired postnatal factors	very low birth weight (<1,500 g)
	perinatal asphyxia
	severe hyperbilirubinemia (requiring exchange transfusion)
	low Apgar score (<4 after one minute or <6 after five minutes)
	mechanical ventilation >5 days
	meningitis (bacterial, fungal)
	ototoxic drugs (aminoglycosides1, diuretics)
	extracorporeal membrane oxygenation (ECMO)
	persistent pulmonary hypertension (PPHN)
	hypothyroidism (SD hypofunction)
Genetic disorder	autosomal recessive (e.g. mutations in the GJB2 gene)
	autosomal dominant (e.g. Waardenburg syndrome)
	X-linked (e.g. X-linked congenital sensorineural hearing loss)
	Mitochondrial (e.g. Kearns-Sayre syndrome)

Table modified according to [7] [8].
[1] Certain genetic predispositions appear to increase the risk of aminoglycoside-induced hearing loss in infants.

Prenatal causes of hearing loss include congenital infections and genetic and non-genetic congenital malformations. Cytomegalovirus, which is found worldwide in approximately 0.2-2.5% of all newborns worldwide, is considered the main cause of infantile non-genetic hearing loss. Both symptomatic and non-symptomatic congenital cytomegalovirus infections can lead to hearing loss which is usually progressive and may be noticed even after the newborn period. In this case, the hearing loss is usually sensorineural [2, 9].

Technical implementation

The most frequently used techniques worldwide and successfully applied methods in the German NHS are: AABR and TOAE. Both the TOAE and AABR techniques allow non-invasive recordings of physiological activity underlying normal hearing function, and both are easy to perform in neonates and infants. They are validated by numerous professional organizations as reliable and objective screening methods. TOAE screening is highly sensitive (between 85 and 100% sensitivity in studies) and reasonably specific (between 91 and 95% specificity).

The problem with the exclusive use of the TOAE test is the high referral rate to audiological centers. The guidelines published by the G-BA in Germany require that a good NHS program should have a referral rate of no more than 4%. According to studies, the main reason for false-positive TOAE tests are transient disturbances in the external auditory canal (e.g., collapse of the auditory canal and presence of debris) and in the middle ear (e.g., presence of amniotic fluid and mucus) as well as a high ambient noise level. These problems usually resolve within the first hours or days of life. Because the screening protocol enables more than one TOAE test, more newborns will pass the test and the referral rate may be lower.
Another reason for the high referral rates are lower frequencies (1-4 kHz) used in some TOAE tests. Sounds of different frequencies are transmitted differently in the middle ear. The presence of amniotic fluid and mesenchyme in the middle ear in the first days of life reduces the volume of the middle ear airspace and increases its stiffness, which impairs the transmission of lower frequency sounds. During the examination of higher frequencies (2-4 or 2-5 kHz), the rates of referral are lower, as they are not affected as strong due to the presence of fluid and debris [2].

However, since the TOAEs are generated during the procedure within the cochlea, TOAE technology cannot be used to detect neural dysfunction (cranial nerve VIII and auditory brainstem pathway). For the diagnosis and differentiation of such a pathology, auditory brainstem responses are used. The auditory brainstem response is an auditory evoked potential that originates from the auditory nerve. It can cause impairments at the level of the cochlea, the auditory nerve and the auditory pathway in the brainstem. AABR measurements are made by attaching disposable surface electrodes on the forehead and recording brain wave activity as a response to the sound. The normal AABR shows a form of five successive nerve waves, which are designated I-V where wave I is the compound action potential of the peripheral part of the cochlear nerve. The wave is generated in the mesencephalon. The waveform of an infant is compared to the template of the AABR standard data for infants, and the result is evaluated as „pass“ or „fail“ (fail/refer). The AABR plays a major role in examining the location of the lesion - it enables to differentiate between conductive and cochlear hearing loss. This method is suitable for disorders of afferent impulses that cause hearing problems, which are described above as auditory neuropathy spectrum disorders. The presence of TOAE and concomitant major AABR abnormalities usually indicates an auditory neuropathy. The absence of TOAE and an inconspicuous AABR recording usually indicates problems in the middle ear.

Many NHS programs around the world and in Germany as well, are designed in two stages (Fig. 49 on page 78). The first stage screening is carried out in the first days of life after birth, before discharge from hospital and usually includes one- or two-stage TOAE testing or TOAE and AABR in high-risk infants. Infants who fail the screening test in the hospital are referred for repetition of screening between two and eight weeks after the discharge (second stage) and should be screened by AABR. Abnormal results of the second should be followed up by a pediatric audiological consultation (diagnostic ABR tests and other electrophysiological tests), which should be done by the third month of life. Finally, all infants who have been diagnosed with hearing loss should be treated as soon as possible after a final diagnosis. In any case an appropriate therapy and early intervention should be initiated before the age of six months.

I Studies have shown that early detection of relevant hearing loss and prompt intervention gives children the opportunity to develop significantly better language skills. Children with hearing loss, that is detected before 6 months of age, may not have speech developmental delays and may develop in the same way as their hearing peers in terms of speech and language. For this reason, these parameters have been chosen as a target in the NHS in Germany.

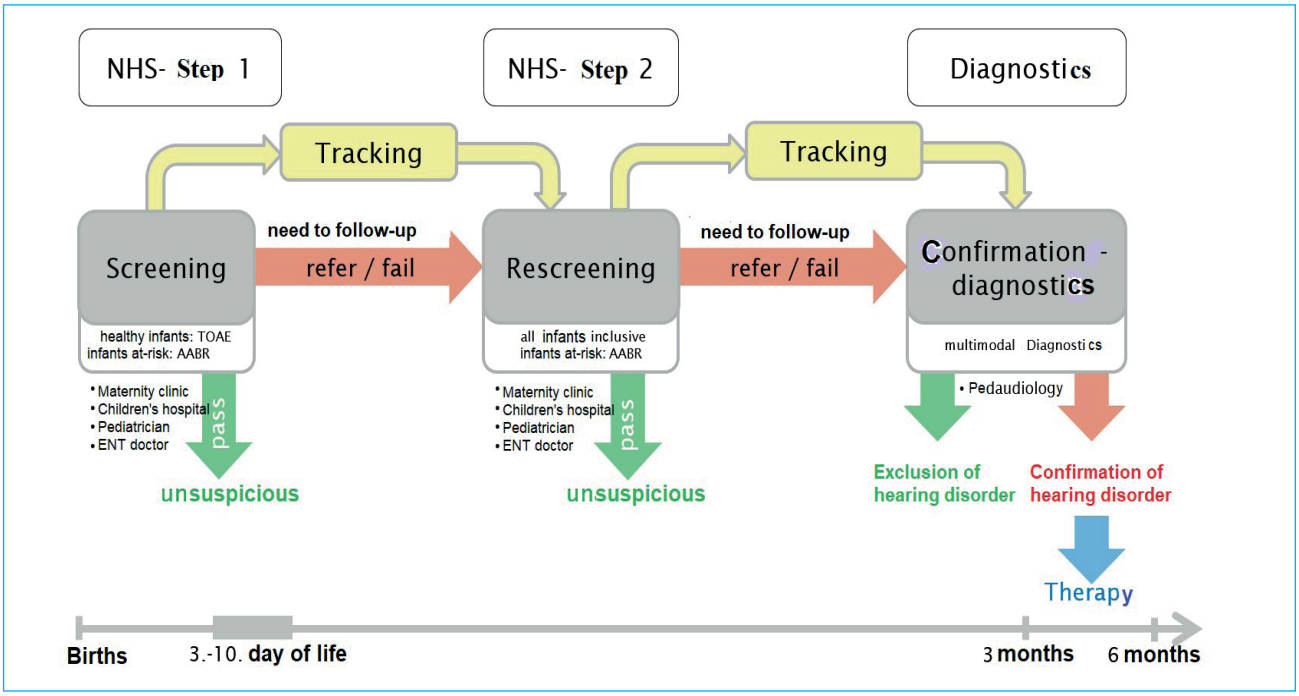


Fig. 49: Two-stage NHS program and tracking process

NHS results in Saxony-Anhalt

Saxony-Anhalt is presented here with the results of the birth cohorts 2009 to 2020. Between 2009 and 2020, a total of 202,107 newborns were screened. This corresponds to 98 % of all children born in Saxony-Anhalt who participated in the NHS with parental consent. Figure 51 (page 79) shows the results of the two-stage screening protocol here in Saxony-Anhalt at the age of the infant at initial screening, diagnosis and start of therapy. A positive effect can be observed by advancing the start of therapy for the Saxony-Anhalt data from the start of the NHS in 2009 until the birth cohort in 2019.

Live births, children with screening ID and first screening result of birth cohorts 2009 to 2020 in Saxony-Anhalt

Birth year	Live births[1]	according to tracking data base NHS Saxony-Anhalt			
		Infants with-Screening-ID[2]	First Screening		Infants with tracking measures[3]
			unsuspicious	suspicious	
2009	17,144	16,088 (93.8%)	13,137 (81.7%)	2,951 (18.3%)	1,576 (9.8%)
2010	17,300	17,055 (98.6%)	14,173 (83.1%)	2,882 (16.9%)	1,356 (8.0%)
2011	16,837	16,673 (99.0%)	13,948 (83.7%)	2,725 (16.3%)	1,255 (7.5%)
2012	16,888	16,695 (98.9%)	14,129 (84.6%)	2,566 (15.4%)	1,383 (8.3%)
2013	16,797	16,611 (98.9%)	13,806 (83.1%)	2,805 (16.9%)	1,202 (7.2%)
2014	17,064	16,903 (99.1%)	13,805 (81.7%)	3,098 (18.3%)	1,330 (7.9%)
2015	17,415	17,165 (98.6%)	14,109 (82.2%)	3,056 (17.8%)	1,308 (7.6%)
2016	18,092	17,933 (99.1%)	14,800 (82.5%)	3,133 (17.5%)	1,303 (7.3%)
2017	17,837	17,794 (99.8%)	14,956 (84.1%)	2,838 (16.0%)	1,264 (7.1%)
2018	17,410	17,084 (97.9%)	14,610 (85.7%)	2,438 (14.3%)	1,243 (7.3%)
2019	16,618	16,357 (98.4%)	14,115 (86.3%)	2,242 (13.7%)	1,138 (7.0%)
2020	16,113	15,785 (98.3%)	13,248 (83.9%)	2,537 (16.1%)	1,371 (8.7%)
Total	205,515	202,107 (98.3%)	168,836 (83.5%)	33,271 (16.5%)	15,729 (7.8%)

[1] Federal Statistical Office (Destatis), 2021 | Date: 07.09.2021 / 17:03:11
[2] uniquely assigned number, serves as a precondition for hearing screening tracking
[3] telephone calls, reminder letters to parents, inquiries at clinics or practices

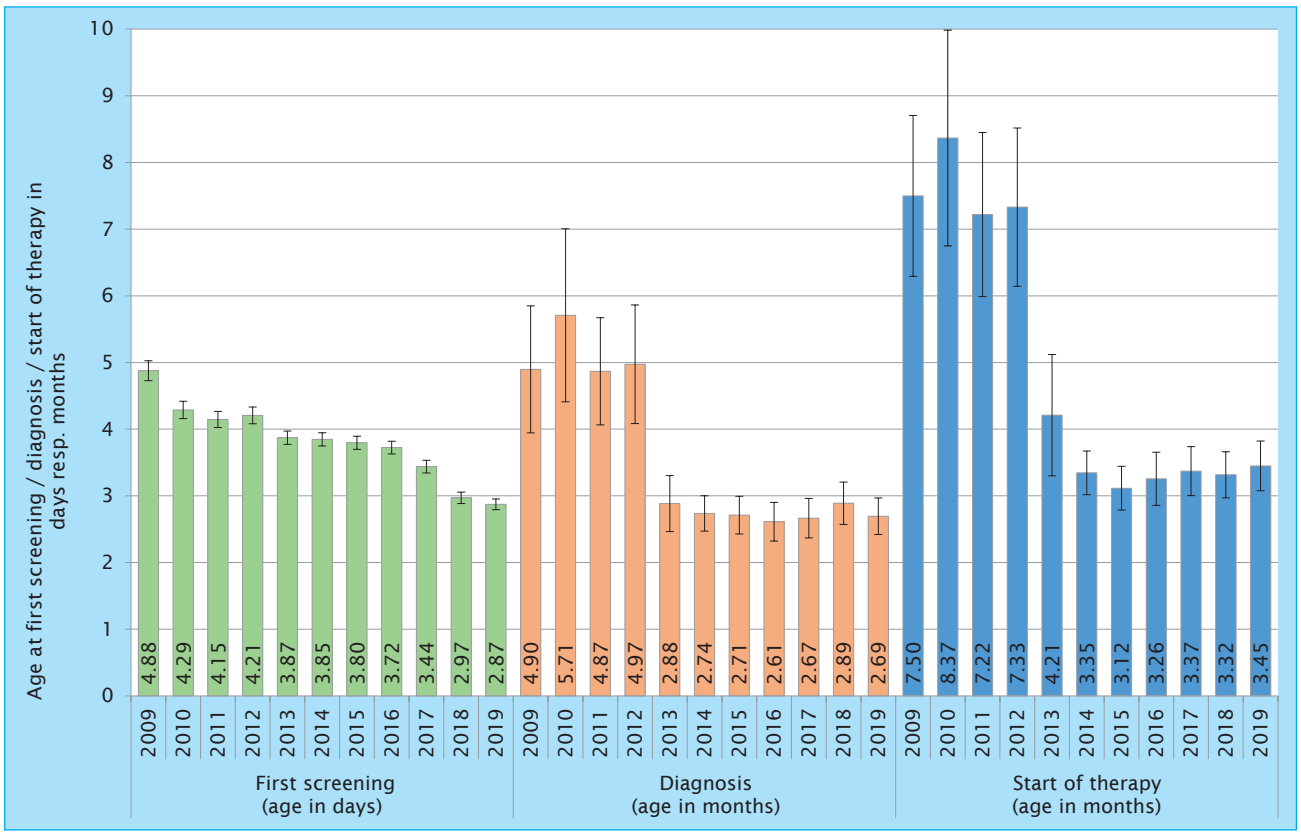


Fig. 50: Age of children born in 2009 to 2019 in days or months at first screening/diagnosis/start of therapy (average value and 95% confidence interval)

Main goal of the interventions and the early intervention at infants with hearing impairment is to establish or improve the child's ability to comunicate and to optimize the level of language development, which affects cognitive and socioemotional behavior. Currently, two main types of aids are used to improve auditory perception: Hearing aids and cochlear implants. Hearing aids are used to amplify incoming sounds so that their volume falls within the patient's usable dynamic range. Cochlear implants are used to restore hearing in cases of bilateral / unilateral severe or profound hearing loss where amplification does not provide satisfactory progress in auditory skills and spoken language. The best results with cochlea implants for permanent congenital hearing loss are achieved with early implantation, i.e., before the age of 6 months.

The benefit-cost analysis of the global NHS shows in studies, that it is a worthwhile investment for society, as the benefits clearly outweigh the disadvantages and costs associated with the Screening program.
D The NHS is a showcase example that meets all the criteria for a universal screening. 1. There is a high prevalence. 2. Hearing loss, if not diagnosed early and treated appropriately, has serious consequences for the affected child and his or her family. 3. The techniques used to diagnose hearing losses are relatively inexpensive, readily available, accurate, objective, and reliable. Before the introduction of the NHS in controlled studies of long-term outcome, severe hearing loss was diagnosed on average between two and three years of age. Mild to moderate hearing loss was often diagnosed by the age of four years [2].
Since the introduction of NHS programs in the various European countries, the average time to detect a hearing loss has become shorter. Diagnosis is made now in most cases at the age of a few months, as defined in the targets set by the NHS in Germany.

Challenges despite NHS

The NHS also shows false negative findings, which means, children pass the screening when in fact they have a relevant hearing loss. In such a situation, the diagnosis is often further delayed because the negative tests in the first few days of life provide a false sense of certainty.
The major causes of progressive late-onset are congenital CMV infection, genetic syndromes associated with progressive hearing loss, neurodegenerative diseases, trauma and bacterial meningitis during neonatal period. However, all of these conditions are known risk factors for hearing loss and, therefore, children with these conditions should be, regardless of the results of the initial screening referred for the second stage of screening at the age of four to eight weeks.
The situation is similar for children with auditory neuropathy, who are not detected in the first stage of screening. In this condition, the infant passes the TOAE tests but has an abnormal AABR. If screening is based on TOAE testing only and there are no risk factors are present, the children are not referred for AABR testing and are not diagnosed in a timely manner. However, most cases of auditory neuropathy involve neonates at high risk who have been treated in neonatal intensive care.
It is also recommended that all infants who are readmitted to the hospital during the first month of life and who have conditions associated with possible hearing loss (sepsis, bacterial meningitis or treatment with ototoxic drugs). Re-screening of hearing is performed prior to discharge. Another point of weakness of the NHS programs in global comparison is the percentage of newborns who do not pass the first test but who are not

tested further on and are „lost“ to follow-up. See also the details on the latest status of children in need of control of the birth cohorts 2009 to 2020 from Saxony-Anhalt (Fig. 51) with a low lost to follow-up rate.

In some study populations where central tracking was not implemented, up to 50% of children who failed hearing screening did not receive a follow-up [2]. Socioeconomic factors also have a significant impact on the effectiveness of hearing screening programs, especially in developing countries. Last but not least, mild hearing losses between 20 and 35 dB are usually not detected by the NHS, regardless of the protocol used.
E There is significant evidence in studies that in case of mild hearing impairment, including unilateral hearing loss, prompt interventions show a better outcome [10]. Unilateral affectedness can cause disturbance in background perception and auditory comprehension disorder, unilateral and bilaterally mildly affected children may also show deficits in short-term memory. It also seems particularly important to involve these families in therapy programs and the equivalent treatment of the patient with mild or unilateral disorder. A 10-year longitudinal study [10] showed dissatisfied parents especially in this group, parents who felt that they were not taken seriously compared to affected families with deaf children. Still without a fixed guideline, when and if a hearing aid fitting is indicated, studies show that there is an improvement in the detection of whispered speech in bilateral mild hearing loss [10]. Consensus is to prescribe speech therapy and to consider technical aids such as cross-over devices, hearing amplification with FM systems, or conventional hearing aid prescriptions, including training hearing aids and, if necessary, also to use this hearing perception training, if appropriate.

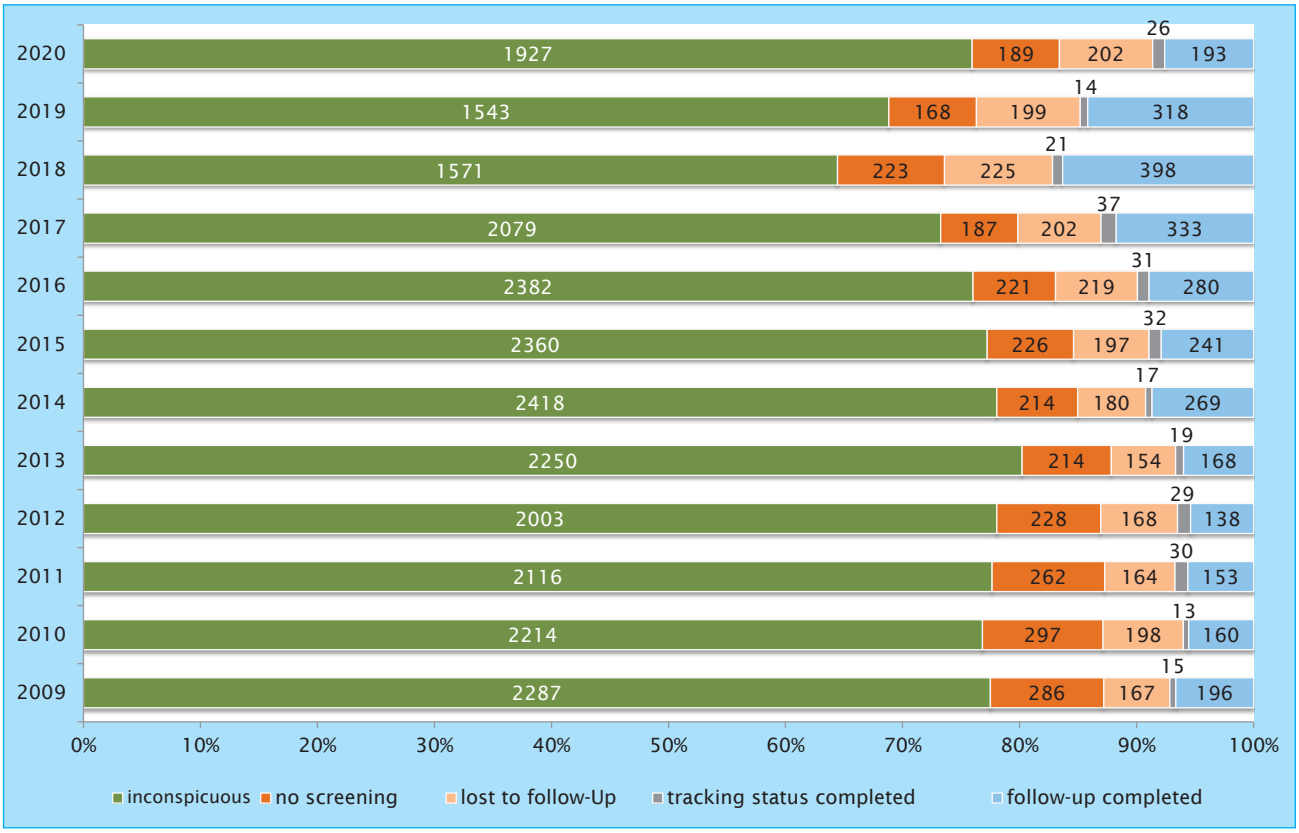


Fig. 51: Last status of infants in need of control in the birth cohorts 2009 to 2020 in Saxony-Anhalt

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14.2 Current recommendations on SARS-CoV-2/COVID-19 during pregnancy, childbirth and post-partum period

COVID-19 is associated with increased maternal mortality and increased miscarriage rates

After 21 months of COVID-19 pandemic, data about risks of a SARS-CoV-2 infection during pregnancy are accumulating. Nationwide, approximately 10,000 cases of SARS-CoV-2 positive pregnancies have been reported in Germany, many of which required intensive care and some died [1]. The German Society for Perinatal Medicine's (DGPM) initialized the COVID-19 and Pregnancy Registry Study „Covid-19 Related Obstetric and Neonatal Outcome Study" (CRONOS) which confirms with German data that pregnant women should generally be considered a „high-risk" group, as they are at increased risk for severe COVID-19 events and adverse pregnancy outcomes [2]. The CRONOS study, as of November 2021, includes approximately 122 reporting centers and 3,397 patients registered, of whom 2,826 have already given birth (37% sectio rate) [3]. This corresponds to about 23% of all pregnancies and births treated in Germany [4].
In one report of COVID-19-related deaths in the United States, pregnant patients had a higher mortality rate than non-pregnant patients (9 versus 2.5 deaths per 1,000 SARS-CoV-2 infections). Fourteen of the 15 maternal deaths involved patients with comorbidities and none of the 15 patients was fully vaccinated [5].
In an analysis of more than 8,000 stillbirths among 1.2 million deliveries in the United States, pregnant COVID-19 patients had a higher rate of stillbirth than those without COVID-19 (1.26 vs. 0.64% of deliveries) [6].
Although incomplete information and recording errors (Texas Snapshooter Procedure) have hampered the interpretation of these retrospective observational studies, these results provide further arguments in support of vaccination of pregnant women and those who are planning a pregnancy.

No increased risk of miscarriage after COVID-19 vaccination

Further epidemiological evidence for the safety of the COVID-19 vaccine in pregnancy could be provided by the following studies. In one study, which included 2,500 pregnancies were included, the age-standardized cumulative risk of miscarriage was at 12.8% of those who had received before conception or before 20 weeks' gestation an mRNA vaccine, which corresponds to the expected value of the general obstetric miscarriage rate in the general population [7]. I In another study, which included more than 105,000 pregnancies, women who experienced a miscarriage had a similar likelihood of having been exposed to a COVID-19 vaccine in the preceding 28 days than women with complication-free pregnancies [8]. The results were consistent with either exposure to the mRNA-1273 or the BNT162b2 vaccine, specific risks for the Ad26.COV.2.S vaccine could not be assessed due to the small number of exposures.
Pregnant and lactating women were excluded from the initial COVID-19 vaccine studies as usual and data for this vulnerable population must be recollected. More than 139,000 participants of the „V-safe After Vaccination Health Checker" of the Center for Disease Control and Prevention (CDC) of the USA (roughly equivalent to the Robert Koch Institute in Germany) have indicated that they were pregnant at the time of vaccination [9]. Data on 827 completed pregnancies were evaluated (mostly of women who were vaccinated in the third trimester). In these cases there were no obvious clusters in terms of miscarriages, congenital anomalies, fetal growth retardation, preterm birth, and stillbirth [10]. In contrast, the „Vaccine Adverse Event Reporting System" (reporting system of adverse events with vaccinations) of the CDC has, as published in March 21, data of 154 pregnancies in which there were compared to the national birth data, no notable adverse events or adverse reactions. In a retrospective cohort study from Israel, BNT162b2 mRNA vaccination during pregnancy was associated with a lower incidence of maternal SARS-CoV-2 infections [11].

The Standing Committee on Vaccination (STIKO) recommends that women of childbearing potential, pregnant women in the 2nd trimester and and breastfeeding women to be vaccinated as soon as possible, see www.rki.de/SharedDocs/FAQ/COVID-Impfen/FAQ_Liste_Impfung_Schwangere_Stillende.html.

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16 Newborn Hearing Screening 2020

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 Directive determines the **process of the newborn hearing screening** in the following way:

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

According to the Children Directive performance and results of the newborn hearing screening as well as 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:
Joint Committee on Infant Hearing: Year 2008 position statement: Principles and guidelines for early hearing detection and intervention programs. PEDIATRICS 2008; 120: 898–921

Participating institutions

22 maternity clinics existed in Saxony-Anhalt in 2020. All these clinics offer a newborn hearing screening already for several years by TEOAE or AABR. These maternity clinics all participated 2020 in the newborn hearing screening.
A screening-ID is assigned to each child - if there is no denial of this examination and /or data transmission by the parents/guardians - and the hearing screening results are forwarded to the tracking centre of newborn hearing screening Saxony-Anhalt.

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

The following table on page 86 gives an overview about the single maternity clinics and number of births with a screening ID..

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

Maternity Clinic	Tracking period 2020	Live births with screening ID in this period*
AMEOS Klinikum Aschersleben	01.01.-31.12.2020	422
Gesundheitszentrum Bitterfeld/Wolfen	01.01.-31.03.2020	85
HELIOS Klinik Jerichower Land Burg	01.01.-31.12.2020	429
Städtisches Klinikum Dessau	01.01.-31.12.2020	922
Altmark-Klinikum Krankenhaus Gardelegen	01.01.-31.12.2020	279
AMEOS Klinikum Halberstadt	01.01.-31.12.2020	423
Krankenhaus St. Elisabeth und St. Barbara Halle	01.01.-31.12.2020	2,020
Universitätsklinikum Halle (Saale)	01.01.-31.12.2020	1,219
HELIOS Klinik Köthen	01.01.-31.12.2020	505
Krankenhaus St. Marienstift Magdeburg	01.01.-31.12.2020	1,051
Klinikum Magdeburg	01.01.-31.12.2020	1,300
Universitätsklinikum Magdeburg	01.01.-31.12.2020	1,242
Carl-von-Basedow-Klinikum Saalekreis Merseburg	01.01.-31.12.2020	929
Saale-Unstrut Klinikum Naumburg	01.01.-31.12.2020	399
Harzklinikum Dorothea Christiane Erxleben, Klinikum Quedlinburg	01.01.-31.12.2020	509
Altmark-Klinikum Krankenhaus Salzwedel	01.01.-31.12.2020	401
HELIOS Klinik Sangerhausen	01.01.-31.12.2020	622
AMEOS Klinikum Schönebeck	01.01.-31.12.2020	316
Johanniter-Krankenhaus Genthin-Stendal	01.01.-31.12.2020	739
Harzklinikum Dorothea Christiane Erxleben, Klinikum Wernigerode	01.01.-31.12.2020	737
Evangelisches Krankenhaus Paul Gerhardt Stift Wittenberg	01.01.-31.12.2020	777
Georgius-Agricola Klinikum Zeitz	01.01.-31.12.2020	327
Total number of live births with Screening-ID in Saxony-Anhalt		**15,653**

Further live births with Screening-ID: e.g. home births / births in a birthing centre resp., infants not born in Saxony-Anhalt	01.01.-31.12.2020	132

Tracked infants, in total	**15,785**

In total, **15.653 births** received a screening ID in their maternity clinic in Saxony-Anhalt in 2020. In this way, these infants could participate in the hearing screening tracking. Furthermore, **133 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 **96 senders** in 2020.

Births with screening-ID and number of incoming results

2020	Infants with screening ID	Number of incoming results
January	1,380	1,627
February	1,205	1,619
March	1,271	1,598
April	1,318	1,704
May	1,281	1,668
June	1,355	1,778
July	1,357	1,490
August	1,371	1,785
September	1,394	572
October	1,335	2,958
November	1,240	1,243
December	1,278	1,230
total	**15,785**	**19,266**

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. 1,606 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, **2568 letters resp. faxes** were forwarded in 2020 (one up to ten letters per infant). With reference to all infants with screening ID this corresponds to an average of 0.16 letters per infant. Additionally, the parents and attending physicians of the infants born in 2020 were contacted by telephone. In total, **655 calls** were made in connection with the hearing screening tracking (one up to nine calls per infant).

Results (date October 2021)

All results that were reported to the hearing screening tracking centre about infants that were born in 2020 are included in our analyses 2020 of the newborn hearing screening:

13.248 infants out of **15,785 infants** with screening ID had an **unsuspicious newborn hearing screening result.** In **2,537 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 2,537 infants showed in **1,927 cases** an **unsuspicious result.** The remaining **610 infants** had again a **suspicious result.**
193 of these 610 infants received a **complete paediatric audiological confirmation diagnostic.**
According to our knowledge, **186 infants** did **not receive a confirmation diagnostic** and therefore are considered as **lost to follow-up**. In **7 cases**, the **further examinations were refused** by the parents.

189 infants did **not participate in the screening** (no reaction of parents to reminder letters or refusal of examination) and in **9 cases** the **status** is still **pending**, i.e. the examinations were not finished in October 2020 or the tracking process still requires more time.
In **26 cases** the **tracking** was closed from our side **without any result**, because we could not get into connection with the parents because the parents could not be contacted, or the infant had died.

In total, the **follow up-examinations** of **207 infants** who were born in 2020 could be **completed (confirmations diagnostics).** Among 193 infants with a suspicious result, 14 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 **170 cases.** In **37 cases** a **hearing disorder was diagnosed** (25 x bilateral and 12 x unilateral hearing disorder) and the corresponding therapy was initiated. For instance, **30 infants** received a **hearing aid** (20 times hearing aid bilateral, 10 times hearing aid unilateral).

17 Annual Report 2020 of the Newborn Screening Centre Saxony-Anhalt

according to §13 to § 42 inclusive attachments of the valid Children Directive of the Federal Joint Committee about early detection of diseases at infants

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Kompetenznetz Neugeborenen-Screening

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Introduction

The Newborn screening is a population-based preventive measure with the aim of a complete and early detection as well as quality-assured therapy of all newborns with severe, congenital metabolic disorders (Tab. 1).
The Directive of the Joint Federal Committee about the early detection of childhood diseases (Children's Directive) stipulates the details of the newborn screening (NGS) and screening for cystic fibrosis (CF) in paragraphs 13 to 42.
The German Society of newborn screening (DGNS) compiles annually a national screening report in cooperation with the German screening laboratories (http://screening-dgns.de/reports.php). The statistical processing of the screening data is based on the quality criteria defined in the Directive for the implementation of NGS and CF screening in Germany.

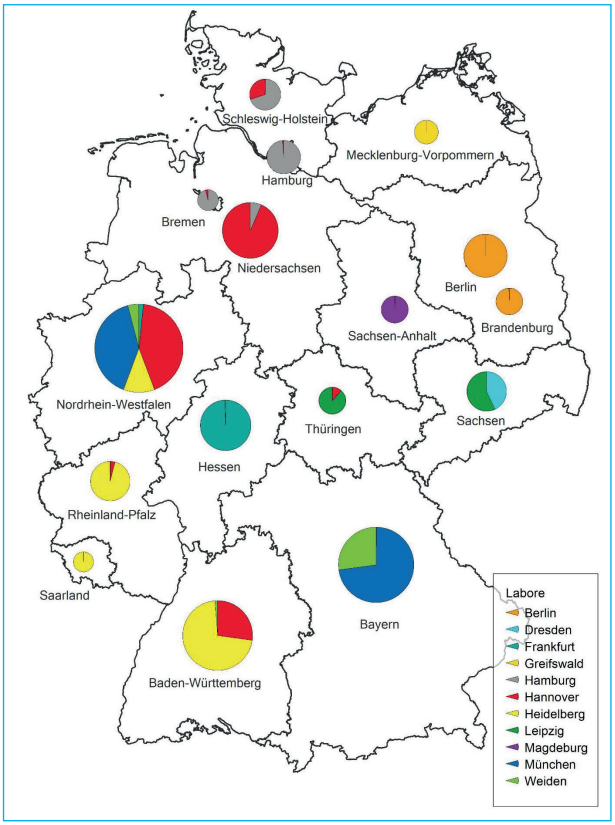

Fig. 1: Sample distribution of the screening centers in Germany[1]

The report only refers to congenital metabolic and endocrinologic diseases which are defined as „target" diseases by the Directive. Furthermore, it gives a complete statistical compilation of related screening figures, recall rates and confirmed diagnoses for the current year. Additionally, data about process quality for whole Germany is presented.
Screening samples from the single Federal States are divided to the laboratories as it is presented in figure 1 1.
The screening laboratory in Magdeburg handles the dry blood samples of all infants born in Saxony-Anhalt.
Table 1 shows the frequencies 2019 of the screening target diseases in Germany1 for a total number of 778,090 screened births.

Tab. 1: Frequency of diseases detected in screening in Germany 20191 (including mild forms)

Disease	v	Prevalence
Congenital hypothyroidism (CH)	258	1 : 3,016
Congenital adrenal hypoplasia (CAH)	46	1 : 16,915
Biotinidase deficiency (incl. partial defects)	21	1 : 37,052
Galactosemia (classical)	10	1 : 77,809
Hyperphenylalaninemia (HPA) [of which phenylketonuria (PKU)]	151 [59]	1 : 5,153 [1 : 13,188]
Maple syrup urine disease (MSUD)	4	1 : 194,523
Medium-Chain-Acyl-CoA-Dehydrogenase deficiency (MCAD)	79	1 : 9,849
Long-Chain 3-OH-Acyl-CoA-dehydrogenase deficiency (LCHAD)	3	1 : 259,363
(Very-)Long-Chain-Acyl-CoA-dehydrogenase deficiency (VLCAD)	8	1 : 97,261
Carnitin-Palmitoyl-CoA-Transferase I deficiency (CPTI)	-	
Carnitin-Palmitoyl-CoA-Transferase II deficiency (CPTII)	2	1 : 389,045
Carnitin-Acylcarnitin-Translocase deficiency (CACT)	-	
Glutaric aciduria type I (GA I)	4	1 : 194,523
Isovaleric acidaemia (IVA)	7	1 : 111,156
Cystic Fibrosis (CF) / CFSPID	151	1 : 5,153
Severe combined immunodeficiency (SCID)	18	
Total	**768**	**1 : 1,013**

Screening data 2020 of Saxony-Anhalt is outlined in the following:

Process quality

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

- complete coverage of target population
  - coverage method and rate
  - blank card systems
- completeness of control (recall)- and follow up examinations
- registration of examination parameter and standard values / cut-offs
- according to disease, laboratory and age/gestational age stratified recall rates, positive
- predictive values, prevalences
- specificity and sensitivity of test methods
- process times (here only in the preanalytic and laboratory field: age at time of blood taking, time between blood taking, arriving at laboratory and result transmission)
- individual screening results of newborns, which 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. The test card is sent to the responsible laboratory; however, it differs between the single Federal States how successful this method is.

We collected the following registration rates in Saxony-Anhalt in 2020:
According to the Federal Statistical Office 16,113 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	15,951
Non-resident in Saxony-Anhalt	1,167
Screening of children living in Saxony-Anhalt	**14,784**

The discrepancy between the number of live births and screened infants with residence in Saxony-Anhalt amounts to 1329.

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

Tab. 3: Registration rates by blank cards

Blank cards in total	**487**
Blank card: infant deceased/ stillbirth	45
Blank card: refusal of early taking	402
Blank card: transfer to another hospital	25
Blank card: screening refused by parents	15
Screening took place	417

As a result of follow-up (telephone calls, faxes, letters), only 1% of the blank cards sent in remained without result. All other live births participated later successfully in the newborn screening and the CF screening in our or in a neighbouring screening laboratory. Furthermore, the tracking of missing screening examinations is performed successfully according to the reasons mentioned in table 4.

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

Reason for second screening	suspicious first screening	First screening < 36h or < 32 WOG
Requested	105	510
Received at own laboratory	98	451
Deceased before control examination	1	6
Received at another laboratory	5	43
Without result, feedback missing	1	10

WOG = weeks of gestation

Examination numbers, recall rates and assured cases

I Table 5 shows recall rates of the single parameter and assured cases. A total of 142 control examinations had to be carried out in 2020.

Tab. 5: Recall-rate 2020 and diagnosed patients with a metabolic disease in reference to 15,951 screening examinations (includes also early withdrawal < 36 h and preterm births < 32 WOG), prevalence 1997-2020

Target disease incl. all forms of disease	Number of recalls 2020	Assured cases 2020	Prevalence in Saxony-Anhalt 1997-2020
Hypothyroidism (CH)	51	4	1 : 4,033
Phenylketonuria (PKU/ HPA)	3	3	1 : 5,287
Galactosemia (classical)	2	-	1 : 118,968
Biotinidase deficiency	2	1	1 : 88,407
Congenital adrenal hypoplasia (CAH))	51	3	1 : 17,924[I]
Medium-Chain-Acyl-CoA-Dehydrogenase deficiency (MCAD)	1	1	1 : 10,716[II]
Long-Chain 3-OH-Acyl-CoA-dehydrogenase deficiency (LCHAD)	-	-	1 : 70,725
(Very-)Long-Chain-Acyl-CoA-dehydrogenase deficiency (VLCAD)	5	-	1 : 176,814
Maple syrup urine disease (MSUD)	-	-	
Carnitin-Palmitoyl-CoA-Transferase I and II deficiency (CPTI)	-	-	
Carnitin-Acylcarnitin-Translocase deficiency (CACT)	-	-	
Glutaric aciduria type I (GA I)	1	-	
Isovaleric acidaemia (IVA)	5	-	
Mucoviscidosis	8	2	1 : 6,098[III]
Tyrosinemia type I[IV]	2	-	
Severe combined immunodeficiencies (SCID)[V]	2	-	
Other	9	-	

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

Process times

Point of taking blood samples

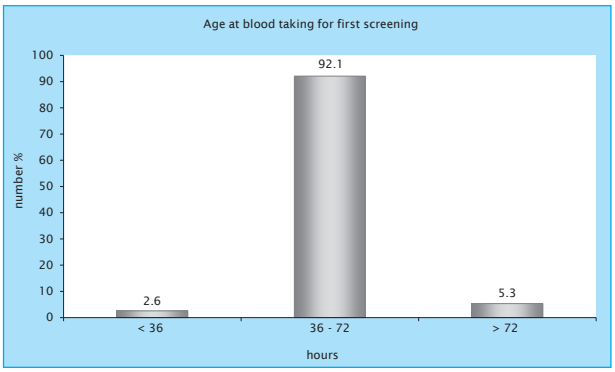

Fig. 2: Age at point of blood taking for first screening

The optimal point of taking blood samples for the newborn screening (36 –72 hours of life, §20 Children`s Directive) took place within the required period of time at 92.1 % (2019: 93.8 %) of all cases. At a total number of 7.9% the taking of blood samples took not place within the required period of time (2016: 7.6%).

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 20,8 % (2019: 18,6 %) of all transmittals reached the laboratory more than three days after the blood taking. On average, samples from 21 clinics reach the laboratory in the required time window, although in some cases there are major differences in the shipping time (table 6). Fortunately, the times have improved compared to 2019.
Although there were dry blood cards that took more than 10 days to arrive at the laboratory, the average transport times for 20 of the 21 clinics are within the required ran-

ge. Only one clinic continued to have significantly too high shipping times (< 72 hrs, up from 3 clinics in 2019), which could not be changed even after several consultations. 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

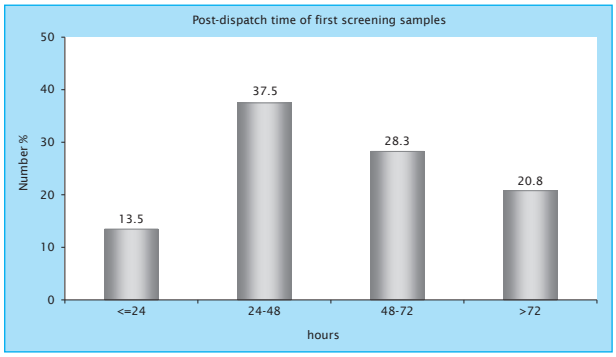

Fig.3: Post-dispatch time of the dry blood cards (first screening) Time from blood collection to arrival at the laboratory

Tab. 6: Post-dispatch time of dry blood cards per sending hospital (average value of all wards of a hospital), comparison 2020 to 2015

Maternity clinic	Average shipping time h	
	2020	2015
Magdeburg St. Marienstift*	22	12.1
Magdeburg Universitätsklinikum*	27	28.9
Magdeburg Klinikum*	43	25.4
Gardelegen	44	41.5
Quedlinburg	44	44.1
Schönebeck	45	40.8
Zeitz	46	49.2
Halle St. Elisabeth und St. Barbara	46	50.1
Salzwedel	50	45.1
Köthen	51	48.8
Lutherstadt Wittenberg	53	56.0
Naumburg	54	40.9
Aschersleben	56	49.7
Merseburg	56	50.5
Stendal	58	46.0
Sangerhausen	60	49.6
Burg	61	44.2
Halle Universitätsklinikum	62	53.4
Wernigerode	64	49.8
Dessau-Roßlau	65	44.0
Halberstadt	100	62.1

* Clinic with a courier service

Transmission of Results

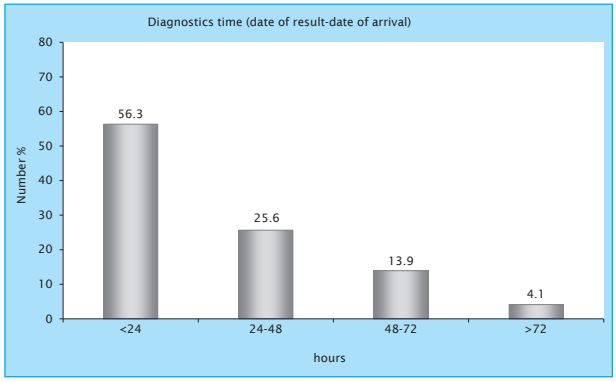

Fig.4: Duration of findings transmission

Figure 4 shows the duration of laboratory analysis of all initial screening examinations. 18 % (2019: 12.8 %) of all findings, that leave the laboratory after more than 48 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.). The increase compared to 2019 is due to the introduction of the new target disease SCID, as there are more internal repeats in qPCR analysis.

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

	2020	2019
Screening, in total	15,951	16,312
CF screening included	99.7 %	99.7 %
CF screening positive	8	17
sweat test performed	8	16
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 2020 no parent or guardian rejected the participation in the CF screening. 0.3 % of CF analyses were not carried out due to the special fact that midwives are not allowed to take blood samples for this screening without permission from a doctor. Usually, the cooperation between midwifes and paediatricians works well. All children received a sweat test after a positive CF screening. A sweat test showed

highly abnormal findings in 2 children. A genetic analysis subsequently confirmed the diagnosis of severe cystic fibrosis.

Confirmation diagnostics and therapy of screening-positive patients

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

Tab. 8: Diagnosis, confirmation diagnostics and therapy starting

Diagnosis	Confirmation diagnostics	Age at start of therapy
4 x Hypothyroidism	Serum TSH, fT3, fT4, sonography, thyroid antibodies	7-25 days
2 x Phenylketonuria 1 x Hyperphenylalanemia	Serum Phe, BH4 test, DHPR activity, pterins, partial mutation analysis	4-7 days
1 x Biotinidase deficiency	Enzymaktivität im Plasma	10 days
3 x Adrenogenital syndrome 1 x salt wasting syndrome 2 x without salt wasting syndrome	Mutation analysis, steroid analysis 1 x missing feedback	5-6 days
2 x x Mucoviscidosis 1 x classical homocygotic mutation 1 x compound heterozygous mutation	Sweat test Mutation analysis	16-20 days

Summary

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

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

The 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.

Since 2019, the laboratory has been equipped with a qPCR device, which is used for screening for SCID. In October 2021 two new target diseases have been added to the expanded newborn screening: Sickle Cell Disease (SCD) and spinal muscular atrophy (5q-SMA). For this purpose, new laboratory equipment was purchased and the spectrum of qPCR analysis was extended to include the SMN1 gene.

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

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

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

www.stwz.ovgu.de

We would like to inform senders, parents and interested people here about the Newborn Screening and about special metabolic diagnostics and provide downloads/ forms.
The national screening report of the DGNS1 is available on the Society's own website (http://screening-dgns.de) two years after the respective period of time

[1] Quelle: Deutsche Gesellschaft für Neugeborenenscreening e.V. (DGNS): Nationaler Screeningreport Deutschland 2019
http://www.screening-dgns.de/Pdf/Screeningreports/DGNS-Screeningreport-d_2019.pdf