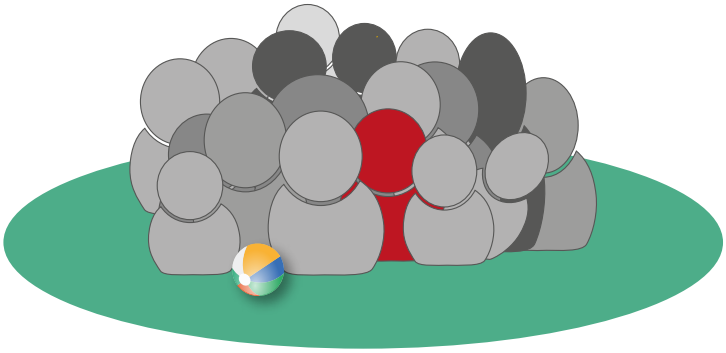
GPSU German Paediatric Surveillance Unit

Research Centre of Paediatric Epidemiology with the support of the German Society of Paediatrics and Adolescent Medicine (DGKJ)

# Annual Report 2024



JG|U UNIVERSITÄTSmedizin. MAINZ
Institute of Medical Biostatistics, Epidemiology and Informatics

DGKJ German Society of Pediatrics and Adolescent Medicine

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# Annual Report 2024

Compiled by Susanne Blomenkamp, Romina Dubrow, Anja Heß, Diana Perera Cutiño and Michael S. Urschitz

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# Contents

## Review

Dear readers, dear GPSU reporters, dear GPSU study directors, dear GPSU enthusiasts,

The past year 2024 was eventful, challenging and decisive for GPSU in many ways.

After Prof. Felderhoff-Müser took over the presidency of the DGKJ in January, Prof. Mayatepek assumed the chairmanship of the GPSU Advisory Board.

In January, we received the requested funding from the DGKJ for a redesign of our reporting portal and began the preliminary work. This had become necessary because we were unable to implement many of our reporters' requests with the old reporting portal. After overcoming numerous technical difficulties, the final switch to the new portal took place at the beginning of 2025.

Following the spring meeting of the GPSU Advisory Board on 21 March, the board was reorganised once again. This was necessary due to a new DGKJ guideline on the composition of advisory boards and commissions. We welcomed Ms PD Bruns, Prof. Grasemann and Prof. Rafat as new members. They then attended the Advisory Board meeting on 5 December for the first time. At the same time, Prof. Freisinger ended his membership of the Advisory Board. We would like to thank Prof. Freisinger for his many years of support for GPSU and look forward to working with the newly appointed Advisory Board.

On 19 September, the newly created GPSU Investigator Award was presented for the first time. It is endowed with €8,000 and was awarded to Prof. Mütze for her GPSU study on congenital vitamin B12 deficiency. Congratulations! The next award ceremony will take place again in 2026. All former GPSU study leaders are cordially invited to participate.

On 18 October, the founder and long-time director of GPSU, Prof. von Kries, passed away after a long and serious illness. He founded GPSU in 1992 – modelled on the British Paediatric Surveillance Unit – and led it until 2021. He was an honorary member of the DGKJ and was honoured in 2023 with the highest award in paediatric and adolescent medicine, the Otto Heubner Prize, for his life's work. With his passing, GPSU and the entire field of paediatric epidemiology in Germany lost the most influential person of the last decades. He was an authority, a wise advisor, a brilliant scientist, a wonderful colleague and a good friend all rolled into one. He leaves behind a void that we cannot fill.

Looking ahead to 2024, we see numerous challenges: children's hospitals and paediatric departments have closed, and long-standing reporters have taken their well-deserved retirement. We are facing major tasks that we must tackle. Further digitalisation, automatic case recording and reporting, and AI-based evaluations of health data could be solutions here.

Finally, we would like to express our sincere thanks to all GPSU supporters, especially for their dedicated participation in case reporting and clinical surveys. Our annual quality assurance shows that, despite the challenges mentioned, we have achieved high coverage and completeness in GPSU. With your help, we can continue to develop GPSU to meet the growing demands in the field of paediatric surveillance.

We hope you find this report informative and look forward to continuing our successful collaboration.

Susanne Blomenkamp and Michael S. Urschitz

# Annual Report 2024

## 1 Surveys in 2024:

A total of ten surveys were conducted in 2024 (Table 1).

The following surveys were conducted **throughout the year** and have not been completed:

- ARDS (acute respiratory distress syndrome up to 18 years of age with underlying oncological disease or after stem cell transplantation)
- Manifestation of diabetes mellitus in North Rhine-Westphalia up to age 35 and nationwide <5 years
- Heat-related illnesses
- DSD (new diagnosis of intersexuality/variants of sex development)
- Continuous renal replacement therapy
- Invasive pneumococcal disease (IPD)
- ARF/PSGN (acute rheumatic fever and post-streptococcal glomerulonephritis)
- Pleural empyema/effusion due to pneumonia
- Chronic intestinal failure

No new surveys were started or completed in 2024.

## 2 Case reports 2024

### 2.1 Participating clinics and departments in 2024

In the 2024 reporting year, 367 GPSU contact persons from participating departments at paediatric clinics in Germany were contacted. The case reports were mainly submitted online via the GPSU portal. This included 334 general paediatrics departments, 16 neonatology departments and 17 paediatric surgery departments in a total of 321 hospitals.

### 2.2 Case reports 2024

**Sending of monthly case reports**

In the 2024 reporting year, a total of 4,366 emails were sent requesting case reports for the respective month. Late submissions were possible both via the monthly queries and via the annual reporting cards sent by post at a later date (beginning of 2025). The response rate of 3,517 (80.5%) for this year exceeded the annual average for 2023 (79%; see also Fig. 1).

**Table 1:** Surveys conducted in the 2024 reporting year. All surveys were conducted continuously throughout the year.

| No. of Surveillance | 2024 | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Jan-24 | Feb-24 | Mar-24 | Apr-24 | May-24 | Jun-24 | Jul-24 | Aug-24 | Sep-24 | Oct-24 | Nov-24 | Dec-24 |
| 1 | free space | | | | | | | | | | | |
| 2 | Acute respiratory distress syndrome (ARDS) | | | | | | | | | | | |
| 3a | Diabetes mellitus nationwide <5 years | | | | | | | | | | | |
| 3b | Diabetes mellitus in North Rhine-Westphalia up to age 35 | | | | | | | | | | | |
| 4 | free space | | | | | | | | | | | |
| 5 | Heat-related illnesses requiring intensive care | | | | | | | | | | | |
| 6 | New diagnosis of intersexuality (DSD) | | | | | | | | | | | |
| 7 | Continuous renal replacement therapy | | | | | | | | | | | |
| 8 | Pneumococcal infections | | | | | | | | | | | |
| 9 | Acute rheumatic fever/post-streptococcal infections | | | | | | | | | | | |
| 10 | free space | | | | | | | | | | | |
| 11 | Pleural empyema | | | | | | | | | | | |
| 12 | Chronic intestinal failure | | | | | | | | | | | |

## Reporting routine

The response rate for case reports for 2024 peaked in the third quarter at 81.7%. In the fourth quarter, as was also observed in the previous year 2023, there was a decline in reporting, with a response rate of 78.7% (Fig. 1).

45 departments did not respond at all during the year (Fig. 2), and 73 reporters submitted incomplete reports. 249 reporters (68%) reported to GPSU every month throughout the year, and late submissions with the return of the 2024 annual reporting card enabled further completion of the case reports.

The regional distribution of the return of monthly case reports is shown in Fig. 3.

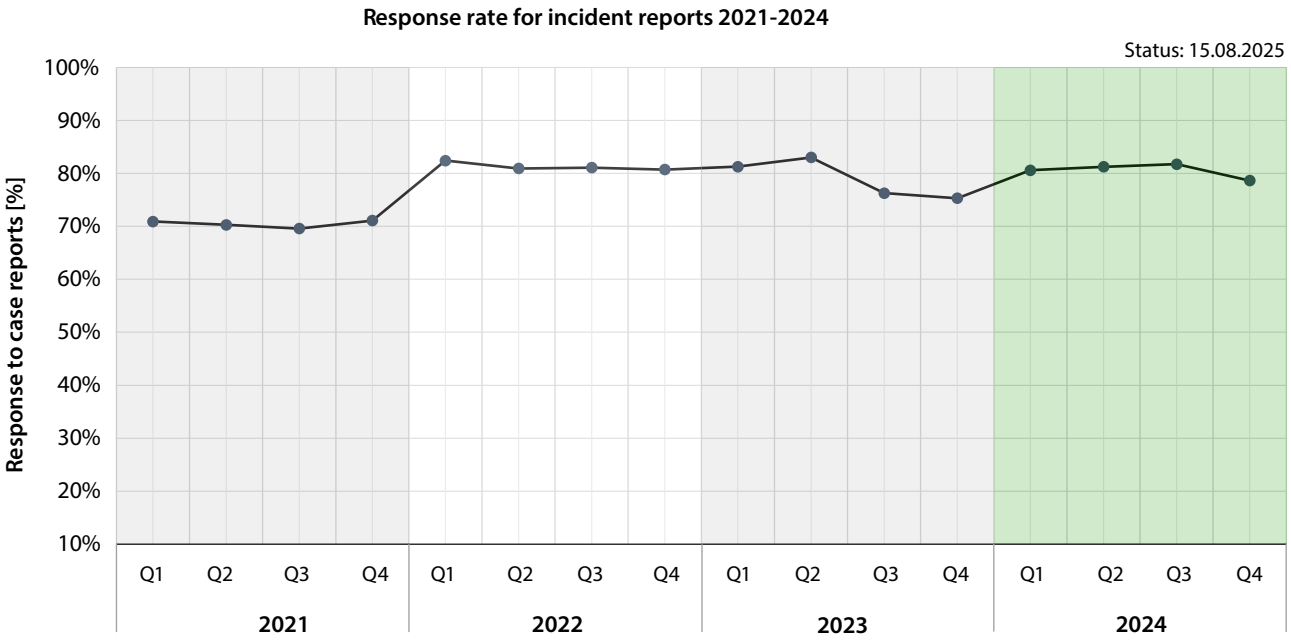


**Fig. 1:** In the 2024 reporting year (light green), the return rate for monthly case reports (reporting cards) exceeded the 80% mark again in the first three quarters. and at the end of 2024, as in 2023, there was a dip in reporting (79% vs. 75% in 2023), although it was not as pronounced as in 2023.

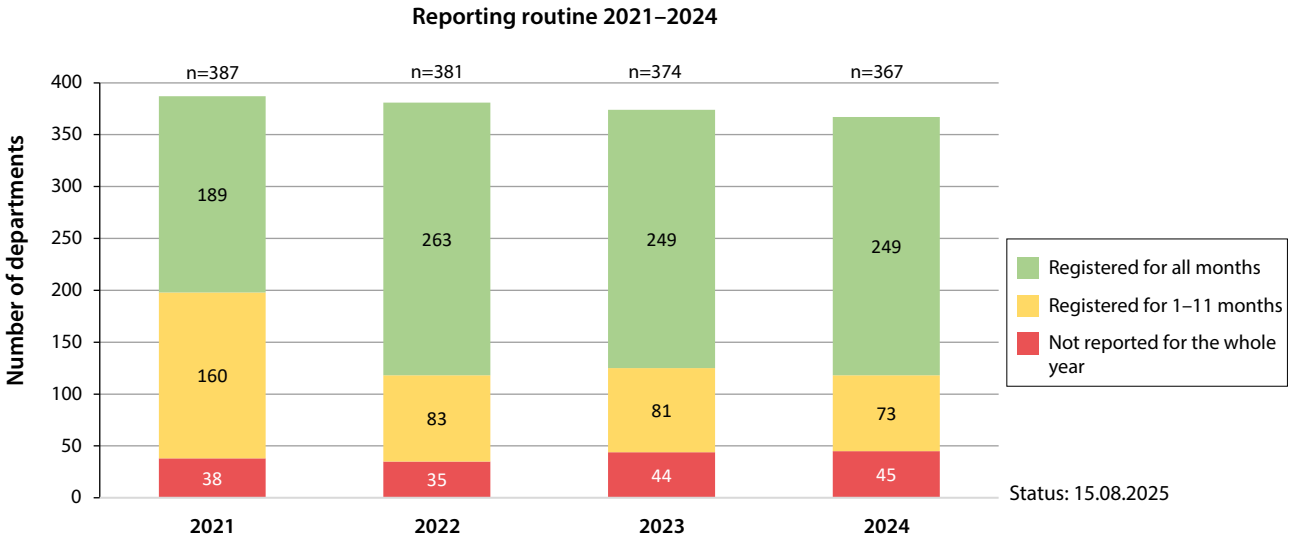


**Fig. 2:** The reporting routine of the reporters ranged from „not reported throughout the year" to „reported regularly every 12 months". The reports could still be completed using the annual reporting card sent out at the beginning of the year.

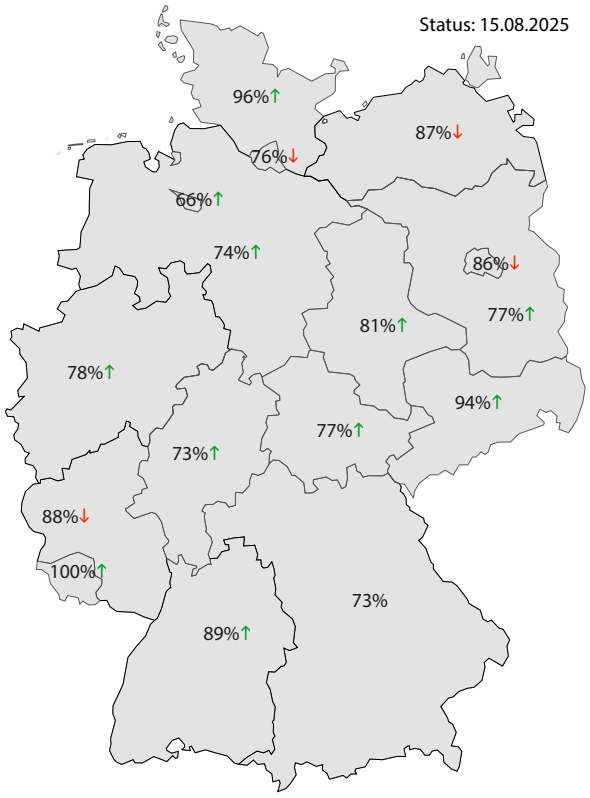


**Fig. 3:** Regional distribution of responses to requests for case reporting for 2024 (in %, arrows: trend compared to previous year 2023).

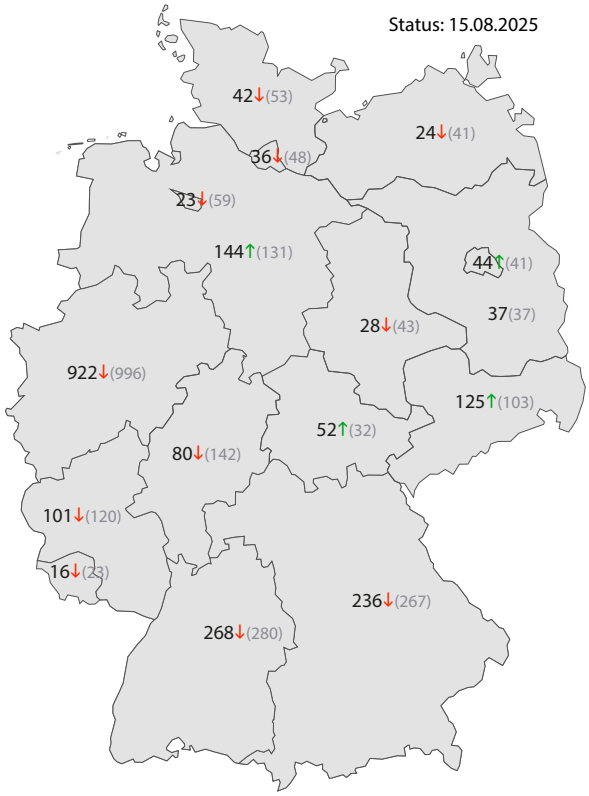


**Fig. 4:** Regional distribution of the number of reported cases for 2024 (arrows: trend compared to the previous year; in brackets: previous year's figures).

**Table 2:** Reported cases for 2024 after deduction of false reports (as of 18 August 2025).

| No. | Survey | 2024 | | | | |
|---|---|---|---|---|---|---|
| | | Q1 | Q2 | Q3 | Q4 | Total |
| 2 | Acute respiratory distress syndrome | 16 | 13 | 7 | 5 | **41** |
| 3 | Diabetes nationwide <5 years | 101 | 86 | 94 | 94 | **368** |
| | Diabetes in North Rhine-Westphalia up to age 35 | 218 | 156 | 155 | 176 | **705** |
| 5 | Heat-related illnesses requiring intensive care | 0 | 3 | 8 | 1 | **12** |
| 6 | New diagnosis of intersexuality (DSD) | 13 | 7 | 6 | 5 | **31** |
| 7 | Continuous renal replacement therapy | 0 | 4 | 3 | 7 | **14** |
| 8 | Pneumococcal infections | 105 | 59 | 32 | 56 | **252** |
| 9 | Acute rheumatic fever/post-streptococcal infection | 38 | 29 | 11 | 26 | **94** |
| 11 | Pleural empyema | 216 | 113 | 66 | 81 | **476** |
| 12 | Chronic intestinal failure | 9 | 16 | 10 | 16 | **51** |

## Case reports

A total of 2,121 cases (2023: 2,495 cases) were reported in the reporting year (Table 2). The regional distribution of reported cases is shown in Fig. 4. The number of cases of infectious or infection-associated diseases is declining again this year for the first time. The response rate for the study questionnaires in 2024 was between 29 and 87% (Fig. 5).

## Reporting effort

The reporting effort in the hospitals varies greatly (Fig. 6). Sixty-two hospitals reported no cases, the majority of hospitals (163) reported 1–10 cases per year, and 45 hospitals reported 11–20 cases in 2024. Twenty hospitals reported 21–40 cases, and five hospitals reported more than 40 cases in 2024.

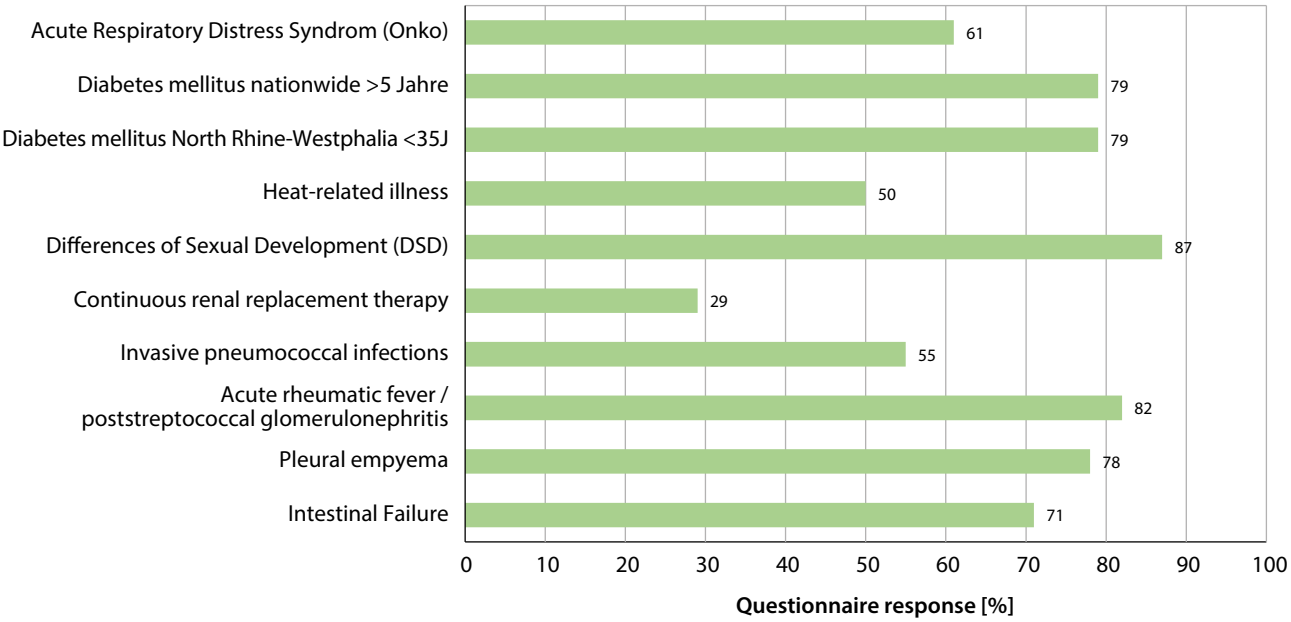


**Fig. 5:** Response rate for hospital questionnaires in 2024 (as of 18 August 2025)

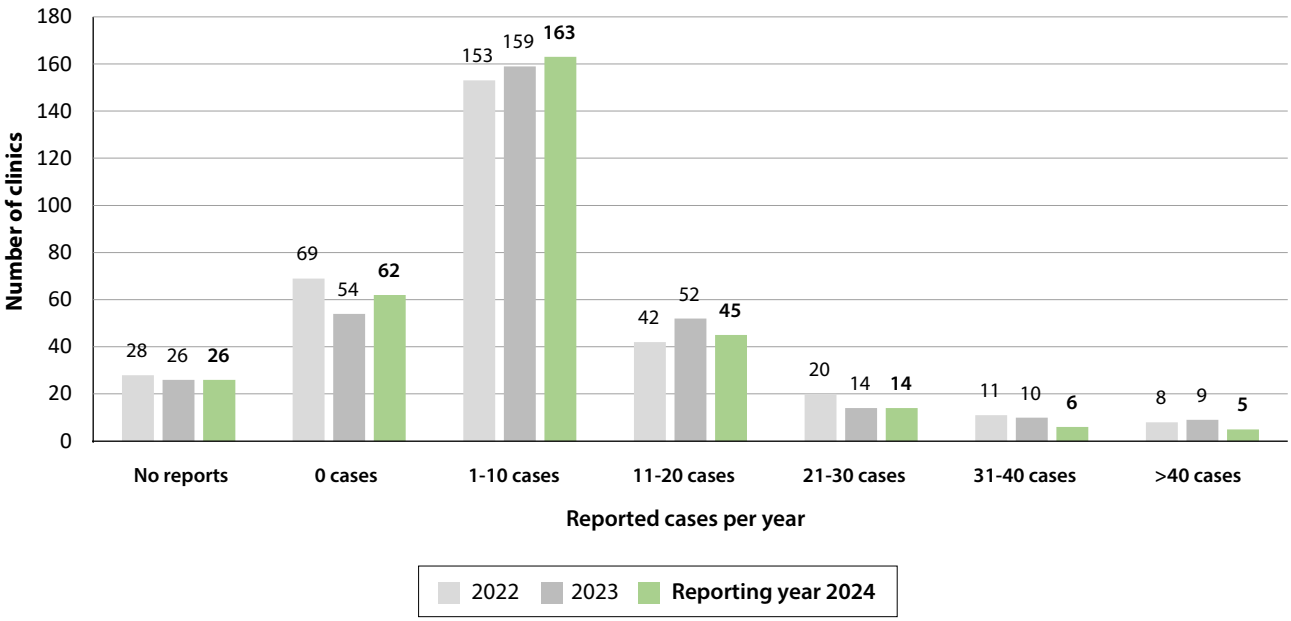


**Fig. 6:** Reporting effort of clinics participating in 2024 compared to previous years (as of 18 August 2025)

# Premiere of the Investigator Award 2024 at the Congress for Paediatrics and Adolescent Medicine in Mannheim

This year, for the first time, the GPSU Investigator Award, a new award from the German Paediatric Surveillance Unit (GPSU), was presented alongside other scientific prizes and honours.

The award winner is Prof. Dr. med. Ulrike Mütze (45) with her study „Vitamin B12 Deficiency Newborn Screening". The DGKJ jury particularly praised the innovative study design, the methodologically sound evaluation and the high clinical relevance of the research question. The benefits of screening for vitamin B12 deficiency in newborns are evident in view of the potential irreversible damage caused by delayed diagnosis and treatment. The study provides a solid basis for the introduction of appropriate screening.

In addition, the jury members emphasised that the study could also serve as a model project for the implementation of future studies in the field of rare diseases.

The results have already been taken into account in the ongoing evaluation process of the Joint Federal Committee (G-BA) on the possible expansion of newborn screening – and have been positively assessed.

**What is the Investigator Award?**
The German Society for Paediatrics and Adolescent Medicine (DGKJ) sponsors the GPSU Investigator Award, which was established on the occasion of GPSU's 30th anniversary. It can be awarded annually and is selected by members of the GPSU Scientific Advisory Board and signed by the spokesperson of the Scientific Advisory Board and the President of the DGKJ. It consists of a certificate and a monetary prize of € 8,000 for a specific purpose. The prize must The aim of the GPSU Investigator Award is to recognise high-quality publications on GPSU studies. Only publications with first authorship in a peer-reviewed journal may be submitted. Further information on participating in the GPSU Investigator Award can be found on the DGKJ website at https://www.dgkj.de/espedinvestigatoraward

Prof. Dr. Ulrike Mütze is a senior physician in the Department of Neuropaediatrics and Metabolic Medicine at the Centre for Paediatrics and Adolescent Medicine at Heidelberg University Hospital.

The GPSU Investigator Award was presented to Prof. Dr. Ulrike Mütze (left) by the President of the DGKJ, Prof. Dr. Ursula Felderhoff-Müser.

**Note:** On 15 May 2025, the GB-A completed the corresponding evaluation process and included newborn screening for vitamin B12 deficiency in the paediatric guideline. See www.g-ba.de/bewertungsverfahren/methodenbewertung/304/

# Conference impressions 2024

All photos, unless otherwise indicated: DGKJ/Hauss

Opening address by DGKJ Vice-President Prof. Dr. Ursula Felderhoff-Müser.

Opening rap with rapper Tobias Tschirneck.

Audience at the opening event.

The posters were presented and discussed at a total of seven poster sessions during the poster exhibition.

Evening event at the Technoseum Mannheim.


Lively exchange at the DGKJ conference stand.


GPSU conference stand.
Photo: A. Heß

# Brief reports from the study directors for 2024

## Acute respiratory distress syndrome in children and adolescents (paediatric ARDS) up to the age of 18 with underlying oncological disease or following stem cell transplantation

**Hendryk Schneider, Daniel Matheisl, Hans Fuchs**

**Background**

Acute respiratory failure in children (paediatric acute respiratory distress syndrome, PARDS) is a rare but serious complication in paediatric patients undergoing treatment for oncological diseases and in those who have received autologous or allogeneic stem cell transplants [1; 2].

In this heterogeneous patient population, PARDS can be triggered by a wide range of underlying causes. However, there are currently no standardized algorithms defining which diagnostic procedures should be performed in these patients. As a result, the specific cause of respiratory failure often remains unidentified.

Treatment strategies also vary considerably. There is limited consistency both in general PARDS management and in the use of specific or experimental therapeutic approaches in this group of patients.

The mortality rate of PARDS in children with underlying malignancies or following stem cell transplantation remains very high [3,4,5]. To improve outcomes, there is an urgent need for multicentre randomized studies aimed at developing evidence-based treatment strategies.

We hope that this survey will provide insight into the specific etiologies, diagnostic approaches, therapeutic interventions, and prognosis of PARDS in this unique paediatric population, thereby facilitating the design and implementation of such studies.

**Questions**

a. How many cases of PARDS due to oncological disease and/or following stem cell transplantation are there per year in the study area?
b. What is the underlying disease and acute cause of PARDS?
c. What diagnostics are performed to clarify the genesis of PARDS?
d. What therapeutic measures are taken?
e. What is the mortality rate and what are the predictors for the outcome?

**Case definition**

Patients under the age of 18 with oncological disease (solid or haematological neoplasia, including recurrence) and/or following stem cell transplantation** (for oncological or non-oncological disease)
**as well as**
PARDS according to the guideline definition [6]

- Oxygenation disorder
  - NIV* with PEEP>5cm$H_2O$ and $paO_2/FiO_2 \leq$ 300 mm Hg or $SpO_2/FiO_2 \leq$ 264%
  - IV* with OI*** (MAP x $FiO_2$ x 100 / $paO_2$) $\geq$ 4 or OSI*** (MAP x $FiO_2$ x 100 / $SpO_2$) $\geq$ 5
- Acute onset of oxygenation disorder within 7 days
- Rx or CT chest shows new infiltrates (unilateral or bilateral) in the lung parenchyma
- Oedema not caused by fluid overload or heart failure

**Results**

**Case statistics:**

From January 2024 to December 2024, there were a total of 46 reported cases. Of these reported cases, 5 were false reports. Including the cases reported from October to December 2023, this brings the total number of cases since the survey began on

* NIV = non-invasive ventilation; IV = invasive ventilation
** Stem cell transplantation within the last 360 days
*** OI = oxygenation index; OSI = oxygenation saturation index

1 October 2023 to 53 for the period up to December 2024.

A total of 31 completed questionnaires are available for the 53 valid cases. 22 questionnaires are still pending.

**Clinical characterisation:**

Of the 31 completed questionnaires, 21 indicated an OSI and/or an OI (corresponding to 10 incomplete responses). In 11/21 patients, only an OSI was indicated, in 5/21 only an OI, and in 5/21 patients both an OSI and an OI were indicated. Thirteen patients had severe PARDS (OSI ≥ 12 or OI ≥ 16) and 8 patients had mild or moderate PARDS (OSI 5–12 or OI 4–16) (Figure 1).

The median age of the 31 evaluable patients was 6.3 years (IQR 2.2–12.6 years), and the median body weight was 20 kg (IQR 12.75–41 kg). The highest oxygenation saturation index reported was 36, and the highest oxygenation index reported was 51.

71% (22/31) of patients were male (see also Table 1).

PARDS occurred in the reported 12 stem cell transplant patients after a median of 28 days (IQR 10–146 days).

With regard to diagnostics, the examinations performed are shown proportionally in Figure 2.

In 8 out of 31 cases (26%), the cause of paediatric ARDS remained unclear. An infectious cause was suspected in a total of 52% of cases. These included a viral infection in 6 cases (2x HMPV, 2x CMV, 1x RSV, 1x influenza) and a bacterial infection in 5 cases (VRE sepsis, Stenotrophomonas maltophilia pneumonia, Klebsiella pneumonia + E. coli sepsis, Pseudomonas aeruginosa pneumonia, Klebsiella oxytoca pneumonia). According to the report, a fungal infection appeared to be the trigger for PARDS in 3 cases (2x Aspergillus sp., 1x Candida sp.). A co-infection of viruses and fungi was suspected as the triggering cause in 2 cases (1x RSV + Aspergillus sp., 1x influenza + Candida sp.). According to the reported data, non-infectious causes appear to be present in 7 of 31 cases (22%) (see also Figure 3).

**Table 1:** Patient characteristics

| Characteristic | Value/number |
|---|---|
| **Age [years], median (IQR)** | 6.3 (2.2 – 12.6) |
| **Weighr [kg], median (IQR)** | 20 (12.75 – 41) |
| **Gender male/female** | 22/9 |
| **Underlying disease** | |
| Leukaemia or lymphoma | 18 |
| Solid tumour | 5 |
| CNS tumour | 4 |
| Solid tumour | 5 |
| Stem cell transplantation (allogeneic/autologous) | 12 |

With regard to the treatment administered, 27 of 31 patients received invasive ventilation. High-frequency oscillatory ventilation (HFOV) was performed in 2 patients. ECMO therapy was performed in 7 patients. Of these 7 patients, 2 (corresponding to 29%) survived.

The following results were obtained with regard to the ventilation strategy: The median maximum PEEP used was 14 $cmH_2O$ (IQR 11–15 $cmH_2O$), the median

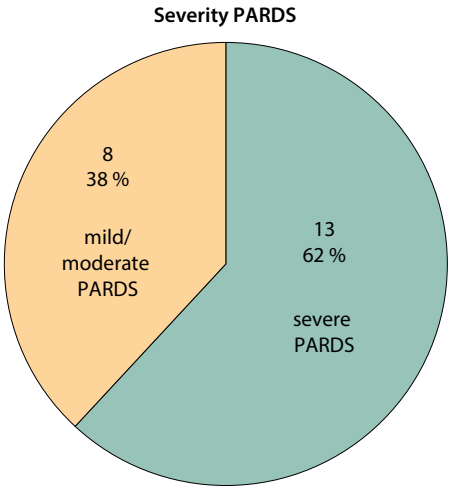


**Fig. 1:** Number and proportion of patients with mild/moderate PARDS and severe PARDS according to the maximum reported oxygenation saturation index or oxygenation index.

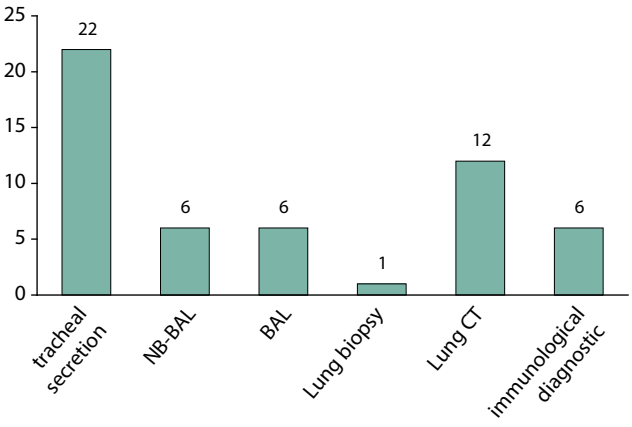


Fig. 2: Tests specified to clarify the genesis of PARDS (NB-BAL = non-bronchoscopic bronchoalveolar lavage; BAL = bronchoalveolar lavage; CT = computed tomography; immunological diagnostics = e.g. complement diagnostics / interferon signature).

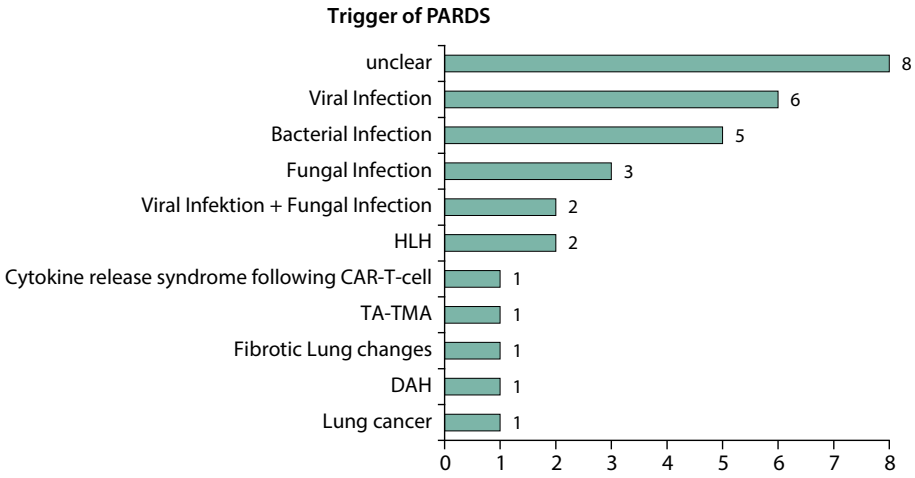


**Fig. 3:** Suspected causes of PARDS (HLH = haemophagocytic lymphohistiocytosis, TA-TMA = transplant-associated thrombotic microangiopathy, DAH = diffuse alveolar haemorrhage)

maximum peak pressure used was 34 $cmH_2O$ (IQR 29–40 $cmH_2O$), with a target tidal volume of 5 ml/kg (IQR 5–6 ml/kg). Permissive hypercapnia was targeted in 58% of ventilated patients.

An outcome was reported for 27/31 patients. In 11 of 27 cases, the patients died (mortality rate of 41%).

## Conclusions

From October 2023 to December 2024, a total of 53 cases of paediatric ARDS were reported in patients with underlying oncological disease and/or after stem cell transplantation. Completed questionnaires are available for 31 of these patients. 62% of the fully reported patients had severe lung failure (max. oxygenation index ≥ 16, max. oxygenation saturation index ≥ 12). 71% of the patients are male.

In 26% of cases, the cause of ARDS remained unclear. In 52% of cases, infection was the suspected cause of ARDS, and in 22% of cases, a non-infectious cause was identified (see Figure 3).

With regard to the ventilation strategy, it can be shown that the maximum peak pressure, with a median of 34 $cmH_2O$ (IQR 29–40 $cmH_2O$), is above the recommended range (28–32 $cmH_2O$). The same applies to the necessary driving pressure (deltaP) – the median maximum value used here is 26 $cmH_2O$ (IQR 17–32.5 $cmH_2O$) – the recommendation is < 15 $cmH_2O$ if possible [6; 7].

The median value for the maximum PEEP used was 14 $cmH_2O$ (IQR 11–15 $cmH_2O$) and the median for the target tidal volume was 5 ml/kg (IQR 5–6 ml/kg) – both of which are in line with the corresponding recommendations [6; 7].

The mortality rate in the present cohort of patients is 41%.

## Contact

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## Summary

Between October 2023 and December 2024, 53 cases of children with underlying oncological disease or following stem cell transplantation with paediatric acute respiratory distress syndrome (PARDS) were reported. Severe PARDS was present in 62% of cases, mild or moderate PARDS in 38% of fully reported cases.

The median age of the reported patients was 6.3 years, and the median weight was 20 kg. The majority of the fully reported patients (18/32) had leukaemia or lymphoma as their underlying disease, and

12 of the reported patients had undergone stem cell transplantation.

The diagnostics and therapy performed to clarify the underlying cause of PARDS present a heterogeneous picture. In 26% of reported cases, the cause of acute lung failure remained unclear. In 52% of patients, an infectious cause (6x viral infection, 5x bacterial infection, 2x fungal infection, 2x co-infection of viruses and fungi) was identified as the trigger for PARDS. A non-infectious cause was identified in 22% of patients.

Patients were ventilated with a median maximum peak pressure of 34 $cmH_2O$ (IQR 29–40 $cmH_2O$), which is above the range recommended for lung-protective ventilation. The median value for the maximum PEEP (positive end-expiratory pressure) used was 14 $cmH_2O$ (IQR 11–15 $cmH_2O$) and the median target tidal volume was 5 ml/kg (IQR 5–6 ml/kg) – both of which are in line with the corresponding recommendations [6; 7]. An outcome was reported for 27/31 fully reported patients; 11 of 27 (41%) patients died.

## Literature


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# Type 1 and type 2 diabetes mellitus

**Esther Seidel-Jacobs**

**Background**
From a health policy perspective, two forms of diabetes play a particularly important role: immune-mediated type 1 diabetes, which usually leads to absolute insulin deficiency, and type 2 diabetes, in which both insulin resistance and reduced insulin secretion play a role. The disease reduces both life expectancy and quality of life. Data on diabetes incidence therefore provide important information for planning future diabetes care. In the years prior to the COVID-19 pandemic, the incidence of type 1 diabetes in Germany showed only a slight increase in children and adolescents, while a substantial increase in new cases of type 2 diabetes was observed [1-3]. The number of new diabetes cases increased markedly during the COVID-19 pandemic, peaking in 2021 and 2022, and have since been declining in a wave-like pattern [3, 4].

**Questions**
1. What is the current incidence and incidence trend of type 1 diabetes in children under 5 years of age in Germany?
2. What is the current incidence and incidence trend of type 1 diabetes in children and adolescents under 18 years of age in North Rhine-Westphalia?
3. What is the current incidence and incidence trend of type 2 diabetes in children and adolescents aged 5 to under 18 in North Rhine-Westphalia?

**Case definition**
Clinical diagnosis of type 1 or type 2 diabetes in the period from 1 January 2024 to 31 December 2024

**Methods**
The completeness of the data collection was estimated using the capture-recapture method. Secondary data sources in North Rhine-Westphalia (NRW) included internal medicine clinics, diabetes specialist practices and general practices, and nationwide the DPV database, Ulm [5]. Incidences including 95% intervals were calculated using the person-year method [6] based on the available population data from 2022 [7], assuming a Poisson distribution of cases. Trend analyses were performed using Poisson regressions [6].

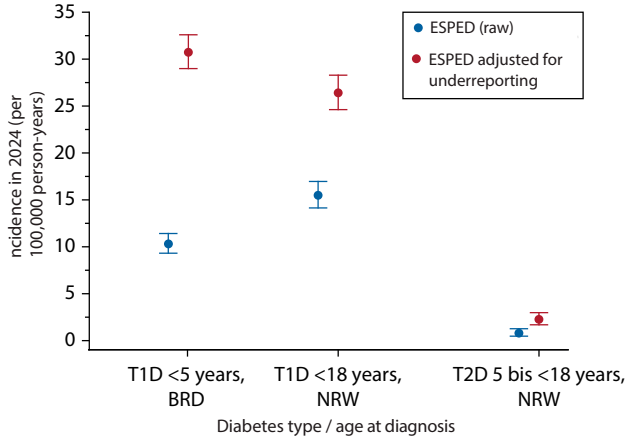
**Results**
**Incidence of type 1 diabetes in children under 5 years of age in Germany**
In 2024, 389 new cases were reported to GPSU nationwide, including 382 new cases of type 1 diabetes in children under 5 years of age in 2024 with complete basic data (gender, month and year of birth and diabetes onset). This corresponds to an incidence of 10.3 (95% CI: 9.3–11.4) per $10^5$ person-years. Based on a capture-recapture analysis, the completeness of GPSU coverage for 2024 was estimated at 33.6%. This is slightly lower than in recent years (2023: 46.5%, 2022: 45.0%). After adjusting for coverage, the incidence was 30.8 (95% CI: 29.0–32.6) per $10^5$ person-years. The GPSU-based crude incidence per $10^5$ person-years increased from 6.9 in 1993 to 15.3 in 2022 and fell markedly to 10.3 in the following years, 2023 and 2024. The coverage-adjusted incidence increased from 10.9 in 1993 to 34.1 in 2022 and fell to 30.8 in 2024. Trend analysis showed a slight but significant annual increase in incidence of 1.2% (95% CI: 0.6–1.7%), while the coverage-adjusted analysis showed a higher annual increase of 2.8% (95% CI: 2.2–3.5%) (both $p < 0.001$).

**Incidence of type 1 diabetes in children and adolescents under 18 years of age in North Rhine-Westphalia**
Of a total of 714 reports for North Rhine-Westphalia, 475 children and adolescents under the age of 18 had a new onset of type 1 diabetes in 2024 with complete baseline data. This yields to an incidence of 15.5 (95% CI: 14.1–17.0) per $10^5$ person-years. Based on a capture-recapture analysis, the completeness of GPSU coverage for 2024 was estimated at 58.7%. This is roughly in line with the completeness of coverage in recent years. After adjusting for coverage, the incidence was 26.4 (95% CI: 24.6–28.3) per $10^5$ person-years. The GPSU-based crude incidence per $10^5$ person-years increased from 11.2 in 1996 to 21.9 in

2020, then fell to 15.5 in 2023 and 2024. The coverage-adjusted incidence increased from 16.1 in 1996 to 43.0 in 2021 and fell to 26.4 by 2024. Trend analysis showed an increasing trend in incidence of 1.8% (95% CI: 1.2–2.4%), the coverage-adjusted analysis suggested a more pronounced rise of 2.6% (95% CI: 2.0–3.1%) per year (both $p < 0.001$).

### Incidence of type 2 diabetes in children and adolescents aged 5 to under 18 in North Rhine-Westphalia

Of a total of 714 reports for North Rhine-Westphalia, 18 children and adolescents aged 5 to <18 years with a new onset of type 2 diabetes in 2024 and complete baseline data were reported to GPSU. This corresponds to an incidence of 0.8 (95% CI: 0.5–1.3) per $10^5$ person-years. Based on a capture-recapture analysis, the completeness of GPSU coverage for 2022 was estimated at 35%, comparable to last year's estimate (36%). The coverage-adjusted incidence for 2024 was 2.3 (95% CI: 1.7–3.0) per $10^{(5)}$ person-years. The GPSU-based crude incidence per $10^{(5)}$ person-years rose from 0.2 in 2002 to 1.0 in 2021 and has since shown a wave-like decline. The coverage-adjusted incidence rose from 0.8 in 2002 to 6.6 in 2021 and fell sharply to 2.3 by 2024. Trend analysis of the incidence data showed an annual increase of 6.7% (95% CI: 5.3%–8.0%) during this period; coverage-adjusted, the increase was 6.8% (95% CI: 4.3%–9.4%) per year (both $p < 0.001$).




| | | | |
|---|---|---|---|
| Incidence (raw) | 10.3 | 15.5 | 0.8 |
| Incidence (corrected) | 30.8 | 26.4 | 2.3 |
| Cases (raw) | 382 | 475 | 18 |
| Cases (corrected) | 1138 | 809 | 51 |

Figure 1: Observed and coverage-adjusted incidence of type 1 and type 2 diabetes in children and adolescents in 2024 for Germany (BRD) and North Rhine-Westphalia (NRW).

## Discussion

In 2024, the incidence of type 1 and type 2 diabetes in young people remained to be lower than those observed during the COVID-19 pandemic [8-12]. In line with an analysis of the diabetes incidence register in young people for North Rhine-Westphalia, a stronger increase in incidence for type 2 diabetes compared to type 1 diabetes in children and adolescents was observed for the entire observation period of the last 30 years [4]. After implementing data corrections of some diabetes cases reported in 2023 and adjustments to the population figures from the Federal Statistical Office [13], the analyses yielded slightly different estimates compared to the previous GPSU report.

On average, the completeness of data collection for type 1 diabetes for the years 2021-2024 was noticeably lower than in the years 1993-2020 (nationwide: 36% vs. 66%; North Rhine-Westphalia: 52% vs. 71%). This could be due to reduced participation by children's hospitals following the switch to the online-based GPSU system in 2021, or due to the coarser data collection in GPSU as a result of stricter data protection requirements. This circumstance complicates the comparison with secondary data sources required for capture-recapture analyses and presumably leads to distorted, lower completeness of data collection and thus possibly to an overestimation of the coverage-adjusted incidences since 2021. No significant differences of data completeness are apparent for type 2 diabetes (2021-2024: 25%; 1993-2020: 30%).

### Contact details for the study management

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### Summary

The incidence of type 1 and type 2 diabetes in children and adolescents was estimated using GPSU and adjusted for underreporting using capture-recapture analyses based on secondary data sources (internal medicine clinics, diabetes specialist practices and general practices in North Rhine-Westphalia, and the DPV database nationwide). The GPSU-based incidence per 100,000 person-years of type 1 diabetes in children under 5 years of age was 10.3 (95% CI: 9.3–11.4) [coverage-adjusted 30.8 (29.0–32.6)], for

children and adolescents <18 years in North Rhine-Westphalia 15.5 (14.1–17.0) [26.4 (24.6–28.3)], and for type 2 diabetes in children and adolescents aged 5 to <18 years in North Rhine-Westphalia, it was 0.8 (95% CI: 0.5–1.3) [2.3 (1.7–3.0)]. The less detailed data collection since the switch of the GPSU system of in 2021 makes it more difficult to compare with secondary data sources and may lead to an overestimation of the coverage-adjusted incidence rates .

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# Heat-related illnesses in children and adolescents from 0-18 years leading to the necessity of intensive care treatment in Germany

**Kathrin Zangerl, Dorothy Wasike, Christian Staufner, Chelsea Williams, Ilan Kelman & Till Bärnighausen**

**Background**

Human-made climate change and the subsequent rise in global temperatures pose significant health risks among vulnerable groups like children [1]. As the number and days of heatwaves are increasing in Germany, there is not only a rise of heat-related illnesses but also in overall morbidity and mortality rates during extreme heat [2]. Due to major gaps in research and emergency preparedness, young children and adolescents are particularly vulnerable to the impacts extreme heat can have [1, 2]. A study examining climate change national adaptation policies for inclusion of child-relevant measures across 160 countries, including Germany, noted the inadequacies and the urgency of child specific heat adaptation measures [3]. Currently, no existing studies have provided primary data on the incidence of heat-related illnesses treated at intensive care units among children within Germany. Addressing this knowledge gap is essential for the development and implementation of heat adaptation measures that are responsive to children's health needs, ultimately helping to reduce the burden of morbidity and mortality due to heat-related illnesses among children [2].

**Research questions and aims**

1. To estimate the incidence of heat-related illnesses in children from 0 – 18 years leading to the necessity of intensive care treatment
2. To explore the primary health outcome in terms of morbidity and mortality

**Case definition**

Children from 0 to 18 years who needed intensive care treatment due to one of the following diagnoses:

**Heat Edema, Cramps** [4]**:**

- Symptoms: Temperature < 38 °C, swelling extremities, clammy skin, cramps (muscular, cerebral), miliaria
- Physiological Reaction: Blood circulation of the skin surface increase, sweating, incipient vascular leak, incipient cerebral edema, muscular hyperactivity, fluid-electrolyte imbalance

**Heat syncope** [5]**:**

- Symptoms: Dizziness, lightheadedness, brief loss of consciousness immediately after stopping activity or exposure to sun/heat
- Physiological Reaction: Severe peripheral vasodilation, volume depletion and reduced vasomotor tone, reduced venous return and subsequent syncope or presyncope, rapid recovery

**Heat exhaustion** [5, 6]**:**

The ICD-10 distinguishes between two forms:

- Anhydrotic heat exhaustion (mainly fluid deficiency),
- Salt-loss heat exhaustion (electrolyte loss through sweating)
- Symptoms: Temperature 38.3° – 40 °C, photophobia, orthostasis, lethargy or restlessness, syncope, dizziness, brief loss of consciousness, nausea, vomiting, tachycardia (fast and weak pulse), cold and clammy skin, muscle cramps, no altered mental status
- Physiological Reaction: Marked peripheral vasodilation, vasomotor tone decrease, venous return decrease, splanchnic vasoconstriction, hypovolemia, beginning organ dysfunction

**Heat stroke** [1]**:**

- Exertional heatstroke: occurs after intense physical activity
- Classic heatstroke: occurs due to passive heat stress without sufficient cooling
- Symptoms: Temperature > 40 °C, quantitative and qualitative disturbance of consciousness, seizures, coma, tachycardia (rapid, strong), hyperventilation, diaphoresis, oliguria, hot and dry skin
- Physiological Reaction: Severe thermoregulatory failure, endotoxin leak, SIRS, cellular apoptosis, multiorgan dysfunction

**Preliminary results**

Since the commencement of the national registry in 2023, there have been 55 reported cases, with 29 having been incorrectly reported. Of the 26 cases, there is yet to be a response for the questionnaires of 14 cases. The full dataset is available for 12 documented cases of children admitted to an intensive care unit in Germany due to a heat related illness.

Of these cases there were five females and seven males. The children's age ranged from 2 years to 17 years, including nine cases involving children over 10 years old, two cases involving six-year-olds, and one case involving a 2-year-old child. BMI percentiles were documented for nine cases: five children had a healthy weight, two were classified as overweight, and two were classified as obese.

The primary reasons for admission were prolonged exposure to high ambient temperatures during outdoor activities, including school-organized events such as amusement park visits and sports, as well as family activities like swimming, water fights, and biking. Other contributing factors included dehydration and secondary acute illnesses such as tonsillitis (two cases), influenza, sinusitis, conjunctivitis, and adenovirus infection (one case). Three of the children had pre-existing chronic conditions: type 1 diabetes mellitus, bronchial asthma, and teratoblastoma.

The duration of intensive care unit stays varied from 1 to 2 days, with an average of 1.4 days. Diagnosis indicated that five children suffered from heat stroke, one child was diagnosed with heat exhaustion, two were diagnosed with heat syncope, two were diagnosed with heat cramps, and two were diagnosed with insolation. Upon discharge, no child was identified with consequential damage.

**Preliminary conclusions**

From the limited data set, preliminary conclusions showcase that there may be an increase in risk for heat-related illnesses during pre-teen and adolescent years. This risk is exacerbated by factors such as prolonged activities outside in the sun, such as sports and exercise. The presence of secondary illnesses may also suggest an increased vulnerability to heat-related illnesses, compounding the effects of heat exposure. The presence of a chronic disease, as well as an elevated BMI, was also identified as potential risk factors. Due to over half of the cases being incorrectly reported, it indicates uncertainty about the criteria for diagnosing heat-related illnesses. A higher number of cases were expected by this point in the study, and this limited data set indicates an increased risk of underdiagnosis and misdiagnosis amongst pediatrics. There is an urgent need to educate and train health care professionals, along with families and educational staff who regularly interact with children to better recognize the signs and symptoms for heat-related illnesses. Enhanced surveillance is also necessary to better understand morbidity associated with heat related illnesses in children.

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**Summary**

Human-made climate change and the subsequent rise in global temperatures pose significant health risks and consequences especially among vulnerable groups like young children. Despite limited research on the health impacts of climate change on children, they are disproportionately affected due to their physiological, developmental, and social characteristics.

The primary aim of this study is to assess the incidence, clinical presentation and outcome of heat-related illnesses among newborns, infants, children, and adolescents (0-18), who need intensive care treatment in Germany.

Preliminary data since 2022 indicates that long periods outdoors during hot weather, engaging in outdoor activities and sports, above average BMI, secondary acute illnesses, and having chronic health conditions may be potential risk factors for heat-related illnesses, with a potential peak during pre-teen and adolescent years.

The preliminary results indicate that there is a high likelihood that heat related illnesses are being underreported and misdiagnosed in children. This uncertainty obscures and underestimates the actual scale and impact of how heat is impacting children throughout Germany. This insufficient data on the morbidity risks to children limits the ability to plan effective and directed public health responses to better protect children from heat-related health risks. There is an urgent need for greater awareness and training for health care professionals, along with families and educational staff who regularly interact with children to better recognize the signs and symptoms

for heat-related illnesses amongst pediatric populations. Enhanced surveillance is also necessary to better understand morbidity associated with heat related illnesses in children.

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# Newborns and children newly diagnosed with intersex/variants of sex development or 46,XX adrenogenital syndrome (AGS) with virilised genitals

**Uta Neumann, Clemens Kamrath & Annette Richter-Unruh**

**Background**

The term "variants of sex development" (DSD) encompasses a wide range of diagnostic groups in which the sex chromosomes, genitals or gonads are incongruent. The causes can be manifold: numerical chromosome abnormalities, gonadal development disorders, sex hormone biosynthesis disorders or sex hormone resistance, as well as inadequately increased or decreased production of sex hormones or their precursors. The variants of sex development are divided into three categories according to karyotype: chromosomal DSD, 46, XX-DSD, 46, XY-DSD.

The main symptoms and clinical indications for the presence of DSD after birth are ambiguous male or female genitalia, a female-like phenotype with an enlarged clitoris, posterior fusion of the labia majora, urogenital sinus or inguinal/labial resistance, or a male-pattern phenotype with bilateral undescended testes, hypoplastic scrotum, hypoplastic penis, isolated penoscrotal or perineal hypospadias.

Tests for DSD should be performed if there is a discrepancy between the prenatal karyotype and genital findings. In addition, in cases of a primarily female phenotype, pubertal virilisation and/or primary amenorrhoea and/or lack of breast growth may indicate a DSD. In cases of a primarily male phenotype, pubertal hypovirilisation may be a symptom of a variant of sex development.

DSD is a rare condition. It is estimated that around 10,000 people in Germany are affected. It is estimated that around 150 children are born with intersex genitalia each year, meaning that the incidence is approximately 1:4,500.

The possibilities for surgical treatment in children who are unable to give consent are significantly restricted by the 2021 law on the protection of children from gender reassignment surgery [1] and are only possible in special cases after approval by the family court. Surgical treatment of the genitals is not usually indicated in newborns. To date, there have been only limited studies on surgical interventions in newborns and children, and research on long-term prognosis in particular is insufficient.

The primary objective of the study is to determine the prevalence of children with DSD at birth and during the first 28 days of life. Secondary objectives of the study are to record the phenotype, karyotype, molecular genetic tests, and recommendations of the centres/specialists for further care/counselling.

**Questions**

1. To examine the prevalence of children with 46,XX-AGS and virilisation, as well as suspected DSD, at birth and during the first 28 days of life.
2. How were the children noticed and recording of the phenotype (external genitalia)?
3. Were genetic tests requested and, if so, which ones and, if applicable, what were the results?
4. Recording whether they were referred to specialist centres/specialists and, if so, the type of centres/specialists

**Case definition**

Newborns with 46,XX AGS and virilisation, as well as newborns and children with DSD (according to the AWMF guideline Variants of Sex Development [2], excluding Ullrich-Turner and Klinefelter syndromes) with a date of birth within the survey period and an initial diagnosis of DSD within the first 28 days of life, defined as follows:

- in the event of a discrepancy between the prenatally determined karyotype and genital findings
- after birth, genitals that are not clearly male or female
- a female-patterned phenotype with enlarged clitoris, posterior fusion of the labia majora, urogenital sinus or inguinal/labial resistance
- Pronounced hypospadias (penoscrotal or perineal)

- 46,XX-AGS with virilised genitals
- ICD 10 Chromosomal DSD: Q93.3, Q99.8, Q99.0
- ICD 10: 46,XY DSD: Q99.1, Q56.1, Q97.3, Q56.0, Q56.1, Q56.3, E34.5, E34.51, E34.59, Q54.2, Q54.3, E25.08
- ICD 10 46,XX DSD: Q99.1, Q56.0, E25.00, E25.08, E25.9, E25.8, Q87.8, 52.4

**Preliminary results**

In the first 18 months (07/2023-12/2024), 44 reports were received (50 in total, 6 error reports). Of these, 38 questionnaires were returned (2023: 11, 2024: 27).

**Clinical characterization**

Six children were not assigned a sex/diverse after birth. In two of these children, no karyotype could be specified, two children had chromosomal DSD, and two children had a karyotype of 46,XY.

Five of 38 children (13%) were diagnosed postpartum with 46,XX adrenogenital syndrome (AGS) with virilised genitals. All of them were referred to a specialist centre for paediatric endocrinology and one family was referred to a child psychologist.

Five of 38 children (13%) had pronounced hypospadias with 46,XY. Three children were referred to paediatric surgery and three children to paediatric endocrinology.

Three children had chromosomal DSD, two of whom had mosaic 46,XY/46,XX and an unbalanced chromosome set due to an X derivative from a cryptic translocation (XX-male, SRY positive).

In eight children, no genetic testing had been arranged at the time of reporting, or no results were available.

Of all cases, eleven children were referred to experts or centres with the relevant expertise for DSD. Of the 8 children, where investigations were not done or were pending, 2 families had been referred to a DSD-centre.

22/38 children were referred to the pediatric endocrinology, 8/38 to the surgery/urology.

The incidence of newborns with AGS is well known thanks to newborn screening. Approximately 55 children with AGS are born each year, of whom approximately 25–27 are assumed to have 46,XX AGS. Over the entire study period of 1.5 years, only 5 children with virilised genitals were reported via the GPSU notification system. Although not all children with 46,XX AGS exhibit virilisation, with an expected number of approximately 40 children with 46,XX AGS in 1.5 years, the feedback from 5 children is clearly insufficient and suggests inadequate reporting of newborns.

**Conclusion**

During the 18-month study period, only 38 questionnaires were returned, which does not allow any conclusions to be drawn about prevalence. No genetic variant was listed for any child with severe hypospadias. The timing of the survey is too soon after birth; follow-up examinations after one year would be informative.

**Contact**

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**Summary**

The incidence of newborns with intersex genitalia is estimated at 1:4,500. This corresponds to approximately 150 children per year. In 2024, we were only able to record 27 children, of whom approximately 40% were diagnosed with 46,XX-AGS and severe hypospadias. This would mean that the prevalence is significantly lower than assumed. Most families were referred to specialised centres with DSD expertise.

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# Use of continuous renal replacement therapy in the first 28 days of life

**Mark Dzietko**

**Background**

The aim of the study is to record all newborns who were treated with any form of continuous renal replacement therapy during the neonatal period (within the first 28 days of life). The need for continuous dialysis treatment increases mortality in newborns and infants (1). Numerous possible conditions that may require dialysis treatment are described in the literature, including electrolyte imbalances, metabolic acidosis, fluid overload, renal failure of various origins, and congenital metabolic disorders (2). Congenital renal malformations do not necessarily increase the mortality of a newborn after haemodialysis treatment (3). The development of innovative dialysis machines with reduced dialysis circuit volumes has made it possible to further reduce the weight limit for critically ill children in recent years. The risks of treatment have also been reduced, allowing for more generous indications (4). In metabolic diseases, continuous dialysis appears to be superior to peritoneal dialysis without increasing the risks (5, 6). This raises medical and ethical questions about when and for whom continuous renal replacement therapy is appropriate. There is no valid data in Germany on the frequency of continuous dialysis in newborns, the frequency of complications associated with it, or guidelines for its use and practical implementation.

**Questions**

1. How often is continuous renal replacement therapy used in newborns in Germany?
2. What are the diseases that necessitate the use of continuous renal replacement therapy?
3. What forms of continuous renal replacement therapy are used?
4. What complications or side effects arise from the use of continuous renal replacement therapy in the neonatal period?

**Case definition**

Performance of any form of continuous dialysis (e.g. haemodialysis, haemofiltration, haemodiafiltration, ECMO combined with dialysis/filtration, plasmapheresis, immunoadsorption) in newborns within the first 28 days of life.

**Results**

By December 2024, a total of 27 cases had been reported, of which 6 turned out to be false reports. Of the remaining 21 reported and valid cases, 10 responses had been received to date.

The 10 children included 7 girls and 3 boys. Seven of the 10 children were assigned to the reporting clinic. The age of the children at the time of admission to dialysis varied between 1 and 23 days. In 6 out of 10 cases, symptoms began on the first day of life. Oligohydramnios as a possible prenatal symptom occurred in 2 of the 10 children. Prenatal sonography was abnormal in 4 of the 10 children. One child underwent prenatal vesicoamniotic shunting for lower urinary tract obstruction (LUTO). One mother had taken candesartan during pregnancy as a possible cause of foetal renal dysfunction. The gestational age at birth ranged from 30+2 to 41+6 weeks. Six children were born by primary or secondary caesarean section/emergency caesarean section and four children were born spontaneously. , birth weight ranged from 290 g to 3585 g. Weight at the start of haemodialysis ranged from 1990 g to 6460 g. Two of the five children were also treated with ECMO. Three of the five children had additional complications such as congenital heart defects, asphyxia, trisomy 21, pulmonary hypoplasia with PPHN or abnormalities in the central nervous system. The indications for haemodialysis in the neonatal period were severe hyperhydration in six children, a metabolic disorder in one child and hyperkalaemia and metabolic acidosis in three children.

An ultrasound scan of the kidneys before the start of treatment showed varying findings, including renal dysplasia and severe urinary transport disorders. The maximum creatinine levels before the start of dialysis were 1 to 4.9 mg/dl. The catheters used were inserted either via the umbilical vein, the femoral vein or the jugular vein. The preferred dialysis machine is the Plasauto Sigma with CVVH or CVVHD. Continuous

renal replacement therapy was performed for a minimum of 4 days and a maximum of 13 days with or without anticoagulation. Dialysis-associated complications mainly included thrombocytopenia, anaemia and circulatory instability, which required transfusions in 4 children. Five of the 10 children died and 5 were discharged home, 4 of whom continued to require dialysis and all of whom continued to be treated with peritoneal dialysis.

## Conclusions

The low number of patients recorded to date illustrates that only a few patients are treated or can be treated with a continuous replacement therapy in the neonatal period. Birth weight and additional diseases are the most significant limitations for the use of dialysis in newborns. The procedure is also associated with considerable complications and death, so it should be reserved for specialised centres. Overall, however, the recorded cases to date only provide an initial impression of the care situation in Germany, and their statistical significance is limited at this stage.

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## Summary

To date, there is no data available from Germany that would allow for a statistical evaluation of the use of continuous renal replacement therapy in newborns. In the first 18 months of the survey, 10 children were reported whose characteristics provide an initial impression of the care structure, treatment and outcomes.

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# Invasive pneumococcal disease (IPD)

**Delphine Perriat & Johanna Schlaberg**

## Background

Invasive pneumococcal disease (IPD) occurs frequently in young children and older people and can occasionally take a very severe course of infection, manifesting clinically as meningitis, septic arthritis or sepsis. Residual effects are not uncommon. The Standing Committee on Vaccination (STIKO) recommends for infants a vaccination against pneumococci with a conjugate vaccine (PCV) [1]. After the introduction of the infant vaccination programme in 2006, there was a significant decrease in IPD caused by the serotypes contained in PCV in the group of vaccinated infants, as well as in all other age groups. On the other hand, in the following years there was an increase in diseases caused by pneumococci with serotypes not contained in the vaccine (replacement phenomenon). Initially, this negative effect was out balanced by an increasing vaccination rate and the positive effects of "herd protection". However, once the increase in the incidence of serotypes not contained in the vaccine exceeds the maximum reduction in IPD incidence of serotypes contained in the vaccine, the peak benefit of the vaccination programme has been exceeded. This was the case, for example, for the serotypes contained in the 13-valent PCV in 2014 [2]. Higher-valent vaccines are gaining in importance.

In Germany, a 7-valent PCV was initially available, which was replaced by a 13-valent PCV at the beginning of 2010. In addition, 10-, 15- and 20-valent PCVs are currently available. For primary immunisation in infants, STIKO recommends using PCV13 or PCV15 in a 2+1 schedule [1]. PCV20 was approved for infants in spring 2024 exclusively in a 3+1 vaccination schedule due to its lower immunogenicity compared to PCV13. It is currently not possible to say what additional benefits the seven additional serotypes contained in PCV20 may have despite the vaccine's lower immunogenicity. STIKO will continue to address this issue and evaluate data on effectiveness and modelling in the future.

## Case definition

Cases are defined as children up to the age of 16 who have fallen ill, in whom a *Streptococcus* pneumoniae strain could be isolated and cultured from physiologically sterile body tissue such as blood, cerebrospinal fluid or tissue puncture (e.g. empyema) and who were reported to GPSU by a children's hospital or paediatric department of another hospital in Germany.

## Results

### Reporting rates by age group

As of 13th of June 2025, 134 IPD cases admitted in 2024 have been reported by paediatric clinics to GPSU. After exclusion of two cases that did not meet the case definition (1 case aged 16 years or older and 1 case with no age specified), 132 data sets could be evaluated. This are 19 cases less than in the previous year (2023: n = 151) and yet about 33% more than the average for the pre-COVID-19 pandemic years 2013-2019 (Ø n = 99) (Fig. 1).

### Epidemiology

The number of reported IPD cases in 2024 was distributed across the three age groups studied as followed: 32 cases were younger than 2 years (2023: n = 47), 45 cases were aged 2 to 4 years (2023: n = 51) and 55 cases were aged 5 to 15 years (2023: n = 53). While the incidence rates in the 2 to 4 and 5 to 15 year-old age groups were above pre-pandemic levels, the IPD incidence rate in the under-2-year-old age group was well below the average level of the years 2013-2019 and declined slightly compared to the previous year (Fig. 1). Fifty-eight cases were girls, 73 were boys, and one case was reported as diverse. The most common clinical diagnosis was pneumonia, with 74 reports out of a total of 128 cases for which information on symptoms was available (74/128, 58%), followed by pleural empyema (47/148, 37%), sepsis (46/128, 36%) and meningitis (42/128, 33%) (Table 1).

Various co-morbidities were present in 31/132 (23%) children. Severe neurological co-morbidities

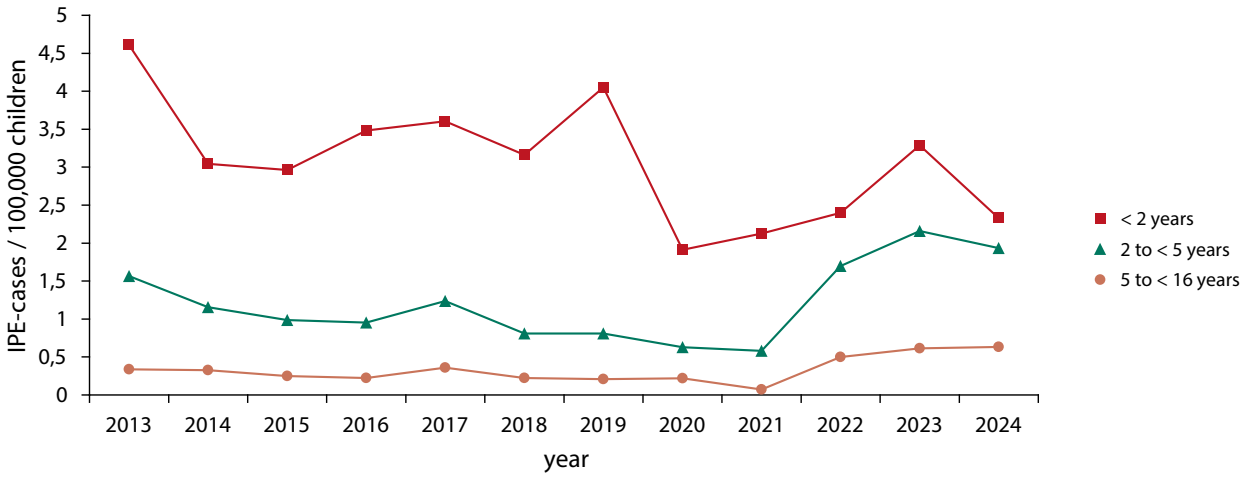


**Fig. 1:** Age-specific GPSU reporting rates (incidence rates) for invasive pneumococcal disease in Germany (per 100,000 children), 2013-2024.

were the most frequently reported (n = 8). Residual damage was reported in eight children upon discharge from hospital after IPD (10 reports): four neurological, two auditory and four other residual symptoms. More than one sequela was reported in two children. The children with permanent impairments at discharge were distributed across the three age groups as follows: younger than 2 years: n = 2, 2 to 4 years: n = 2, 5 to 15 years: n = 4. According to the information provided, two of these children had a co-morbidity. For the other children, it was stated that there were no pre-existing risk factors. Five children died of IPD in 2024 (2023: n = 7). Four of them were younger than 2 years of age and one child was between 2 to 4 years of age. Only one of the children who died had a known co-morbidity: a congenital immunodeficiency.

**Table 1:** Clinical diagnoses. GPSU survey on invasive pneumococcal disease in children in Germany, 2024 (n=132) Duplicate entries are possible.

| | Age group | | | |
|---|---|---|---|---|
| Diagnosis | 0 bis < 2 years | 2 bis < 5 years | 5 bis < 16 years | all |
| Pneumonia | 16 | 29 | 29 | 74 |
| Sepsis | 12 | 13 | 21 | 46 |
| Pleural empyema | 6 | 21 | 20 | 47 |
| Meningitis | 10 | 9 | 23 | 42 |
| Mastoiditis | 2 | 1 | 9 | 12 |
| Osteoarthritis | 1 | 0 | 2 | 3 |
| Peritonitis | 0 | 0 | 2 | 2 |

## Serotype distribution

For 39 of 132 cases, it was stated that serotype testing was attempted (30%). In one case each, the pneumococci could not be cultured or finally differentiated, and in four cases it was stated that the investigation had not yet been completed. Valid information on serotypes was available for 25% of cases (33/132) (2023: 18%). In twelve cases (12/33, 36%), serotypes contained in PCV13 or PCV15 were reported: serotype 3 in seven cases, serotypes 19A and 22F in two cases each, and serotype 14 in one case. Seven children had evidence of a serotype that is not contained in PCV13 or PCV15 but is contained in PCV20 (serotype 10A three times and serotypes 8 and 15B twice each). Serotypes not contained in PCV13, PCV15 or PCV20 were detected in 14 children: serotype 38 four times, serotypes 7C and 24F three times each, and serotypes 9N, 10B, 23B and 35F once each. Among the deceased children, information on the serotype was available for one child: 10B – not preventable by vaccination.

## Vaccination status

For 103/132 (78%) children, at least partial information on pneumococcal vaccination was available. At least one vaccine dose had been administered to 86/132 children (65%). Of these, 69/132 (52%) were fully vaccinated according to their age (i.e. the children had received the number of pneumococcal vaccine doses appropriate for their age at the time of illness), 17/132 (13%) were incompletely vacci-

nated and 17/132 (13%) had no information on vaccination dates or vaccine doses administered. In addition, 20/132 (15%) children had an unclear vaccination status and 9/132 (6%) were unvaccinated. Among the unvaccinated children, one child was too young to have had received a vaccine dose before onset of illness. Of the 31 children with co-morbidities, 17 were fully vaccinated and six were incompletely vaccinated. In eight children with co-morbidities , the vaccination status was unclear or unknown. Among the 12 cases caused by a serotype contained in PCV13 or PCV15, seven were fully vaccinated according to STIKO recommendations. Serotype 3 was the causative agent in four cases, and serotypes 14, 19A and 22F were the causative agent in one case each.

**Conclusions**

Compared to the previous year, the total number of reported IPD cases in children and adolescents in 2024 has decreased slightly, but remains above the average for the pre-COVID-19 pandemic years. In the age groups of 2 to 4-year-olds and 5 to 15-year-olds, the figures remain significantly higher than in the pre-COVID-19 pandemic years and have changed only marginally compared to the previous year. This high proportion of IPD in these two age groups remains a cause for concern. The number of IPD cases among infants under 2 years of age has fallen significantly compared to the previous year (incidence in 2024: 2.3 cases/100,000 versus 2023: 3.3 cases/100,000) and is at the same level as during the COVID-19 pandemic years. The reasons for this are difficult to determine. Overall, it is possible that the low number of cases in the respective age groups may lead to distortions and fluctuations. In addition, changes in testing behaviour could have an impact on IPD case numbers.

The information on serotypes is very incomplete. In less than half of the reports, an investigation of the serotype was attempted. In order to differentiate between IPD caused by vaccine serotypes and other serotypes, it is important that treating physicians ensure that serotyping is performed and the results are reported to GPSU. Serotype 3 plays the most significant role as a disease trigger among the serotypes contained in PCV13/PCV15. It is known that the effectiveness of the available vaccines against serotype 3 is insufficient. In addition, serotype 38 was detected more frequently for the first time. This is consistent with reports from other European countries [3, 4]. It is essential to continue monitoring the epidemiology of IPD in order to evaluate the vaccination programme and the possible additional benefits of higher-valent vaccines currently in development. The GPSU project is an important component of IPD surveillance in Germany due to its comprehensive reporting on clinical symptoms, existing underlying conditions (co-morbidities), data on the pathogen serotype and vaccination status [5].

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**Summary**

*Streptococcus pneumoniae* causes various diseases in childhood. Invasive pneumococcal disease (IPD) is rare. It mainly affects infants and young children and can be severe or fatal. Pneumococcal vaccines are the most effective form of prevention. Since the main burden of IPD is in early childhood, STIKO recommends a pneumococcal vaccination as early as possible for all infants and for children and adolescents with certain co-morbidities.

Data from the German Rare Paediatric Diseases Surveillance Unit (GPSU) on IPD in children and adolescents under the age of 16 in 2024 were evaluated. A total of 132 cases were reported in children under the age of 16. The number of cases has not increased further compared to 2023, but it is still above the average for the pre-COVID-19 pandemic years (2013-2019). The most common clinical diagnoses were pneumonia (58%), pleural empyema (37%) and sepsis (36%). Five children died from IPD. The data on serotypes and vaccinations is quite incomplete. Slightly more than one-third of cases with serotype data (12/33; 36%) were caused by serotypes included in the 13-valent or 15-valent conjugate vaccines (PCV13/PCV15) recommended for infants. Serotype 3 was the most frequently identified (n = 7). Only 52% of all IPD cases (69/132) were fully vaccinated according to age-appropriate guidelines. Continuous epidemiological surveillance of IPD is essential in order to evaluate the vaccination programme and the potential added benefit of higher-valent vaccines. The GPSU project is an important component of IPD surveillance in Germany.

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# Acute rheumatic fever (ARF) and post-streptococcal glomerulonephritis (PSGN) in Germany

**Maximilian Hoffmann, Nicole Töpfner & Reinhard Berner**

**Background**
The estimated incidence of ARF and PSGN in Germany before the pandemic was 0.05/100,000 and 0.7/100,000, respectively. From winter 2022 onwards, there was a massive increase in non-invasive and invasive infections caused by group A streptococci (GAS) in Germany and many other European countries; according to Saxony's health reporting system, reported cases of scarlet fever increased approximately 25-fold between 2021 and 2023 [1]. The exact incidence figures for non-purulent, immunogenic sequelae are not known for children and adolescents in Germany or in many other European countries. The aim of this survey is therefore to determine the frequency and burden of disease of these post-streptococcal diseases in Germany so that they can be taken into account in treatment recommendations.

**Question**

1. What are the current incidence rates of ARF and PSGN in Germany?
2. Are there regional differences or other risk factors associated with the occurrence of ARF or PSGN in Germany?
3. What is the ARF- and PSGN-associated morbidity and mortality in Germany?

**Case definition**

Patients aged 0 to 18 years with one of the following conditions:

- Acute rheumatic fever **or**
- post-streptococcal glomerulonephritis

In addition, there must be a previous, confirmed A streptococcal infection based on ≥ 1 of the following criteria: (1) Cultural evidence of group A streptococci, (2) Positive streptococcal antigen detection, (3) Elevated or rising streptococcal antibody titre.

**Case definition 1:** Diagnosis of acute rheumatic fever 1.1) according to the Jones criteria, if 2 major criteria or 1 major criterion and 2 minor criteria are met. Major criteria: clinical (or echocardiographic) carditis, polyarthritis, chorea minor, erythema annulare, subcutaneous nodules. Minor criteria: arthralgia, fever, elevated erythrocyte sedimentation rate (ESR) and/or elevated C-reactive protein (CRP), prolonged PQ interval. **Or** 1.2) outside the Jones criteria, if ≥ 1 of the following criteria is met: carditis (with clear anamnestic reference to previous streptococcal infection), chorea minor (after exclusion of other CNS diseases), recurrence of rheumatic fever.

**Case definition 2:** Diagnosis of post-streptococcal glomerulonephritis 2.1) (Highly probable clinical) diagnosis of glomerulonephritis due to nephritic syndrome: Micro-/macrohaematuria, pathological proteinuria, possibly elevated renal retention parameters, C3 reduction (transient), hypertension, elevated ASL and/or anti-DNaseB titres **Or** 2.2) Histologically confirmed glomerulonephritis (rarely performed).

**Methods**

Nationwide surveillance of ARF and PSGN cases in Germany through GPSU reporting.

**Results**

**Case statistics**

During the observation period from December 2023 to December 2024, a total of 115 cases were reported, including 3 false reports/exclusions. Of the 112 valid reports, 90 questionnaires were completed, including 14 reports for ARF and 76 reports for PSGN.

**Clinical characterisation**

The gender ratio for ARF was almost balanced (female (f), n = 8, male (m), n = 6). The median age for ARF was 10 years (IQR 8.2–13.3 years).

Patients with ARF met the Jones criteria [2] in 13/14 cases; one case was included based on symptoms of chorea minor (Sydenham). The leading symptom in 11 of the 14 cases was fever and laboratory abnormalities with elevated CRP (mean 113.75 mg/dl, minimum 10 mg/dl – maximum 362 mg/dl). Clinically, six patients presented with polyarthralgia, four of whom

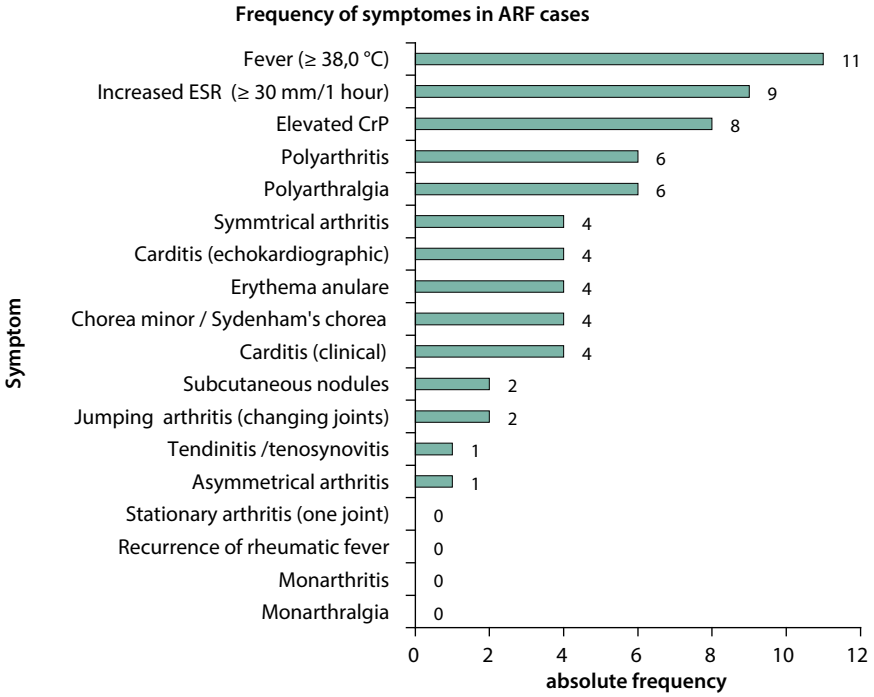


**Fig. 1:** Frequency of symptoms in ARF cases.

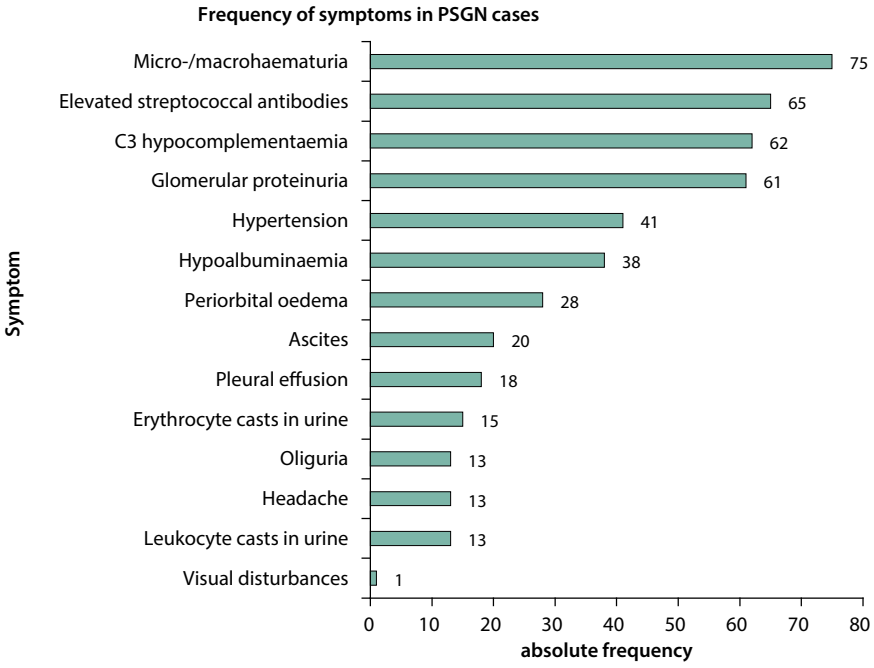


**Fig. 2:** Frequency of symptoms in PSGN cases.

had polyarthritis as the main criterion of the Jones criteria, and two further cases were reported as isolated polyarthritis without polyarthralgia. These manifested predominantly in the knee (n = 7) and ankle joints (n = 8). Four cases presented with clinical carditis, two of which were confirmed by echocardiography. In two other cases, carditis was diagnosed exclusively by echocardiography. ECG abnormalities were reported in three of all ARF cases.

In PSGN, the affected individuals were predominantly male (m, n = 51 to f, n = 25; 2:1). The median age was 6.3 years (IQR 4.5-8.2 years). The leading clinical symptoms were micro-/macrohaematuria (n = 75), hypertension (n = 41) and periorbital oedema (n = 28). Diagnostically, 62 cases showed C3 hypocomplementaemia, frequently glomerular proteinuria (n = 61) and hypoalbuminaemia (n = 38). Renal biopsies were performed in three cases, confirming

PSGN in one case and IgA glomerulonephritis in two cases.

The majority of patients had no pre-existing conditions. One PSGN case had pre-existing uropathy, and 11 other cases had other pre-existing conditions (including two cases each of obesity and ADHD). The aetiology was determined by detecting GAS pathogens in 25 of all cases via throat swab, in seven cases by other means (wound swab, empyema puncture). In 57 cases, no pathogen was detected – here, the high degree of clinical suspicion was based primarily on the clinical presentation (including tonsillitis, fever, scarlet fever), positive environmental history and serological detection. The median initial antistreptolysin O titre was higher in ARF at 1555.50 IU/ml (IQR 731.00-2200.25) than in PSGN (918 IU/ml, IQR 596-1575). In cases with a history of GAS infection, the median time between infection and onset of ARF/PSGN was 8 days (IQR 5.3-17.5), and in these cases, a median of 3 days (IQR 0-7) of fever ≥ 38.5 °C was reported in the last 6 weeks before ARF/PSGN manifestation. Recurrent tonsillitis (≥1 in 6 months prior to onset of illness) was reported eighteen times, twelve of which were treated with anti-infective agents.

The majority ($_{nARF}$ = 11, $_{nPSGN}$ = 65) were treated as inpatients (median length of stay 6 days (IQR 4.5-9.50)), a few of them in an intensive care unit ($_{nARF}$ = 2, $_{nPSGN}$ = 7). In PSGN, dialysis therapy was not performed in any case, and albumin substitution was reported in one case. The majority of cases ($_{nARF}$ = 11, $_{nPSGN}$ = 34) did not suffer any sequelae; in two ARF and 11 PSGN cases, these were reversible; in the other cases, the outcome was unknown.

## Conclusions

Based on the 2022 census (14,567,998 persons <18 years of age), the estimated incidence of ARF is 0.1/100,000 and that of PSGN is 0.52/100,000. With the number of cases remaining low, the incidence of ARF has thus doubled compared to the last comparable survey period (01/2019 – 12/2020; 0.05/100,000 in each year). The incidence of PSGN was similar to that in the survey period (01/2019 – 12/2019; 0.59/100,000), but showed a decline compared to the survey period (01/2020 – 12/2020; 0.88/100,000). These incidence estimates for ARF and PSGN are below the current estimates for Europe [3]. Even in relation to the significantly increased incidence of acute GAS infections in the post-pandemic period, the incidence of these post-streptococcal diseases remained far below these levels.

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## Summary

GPSU was used to record inpatient ARF and PSGN cases. Following the significant increase in invasive and non-invasive GAS infections in Europe in 2022/23, this GPSU survey also showed a slight increase in ARF cases compared to previous years (2019-2020). However, potential fluctuations due to the low number of cases must be taken into account. ARF and PSGN remain very rare in Germany.

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# Pleural empyema and complicated parapneumonic pleural effusions in children and adolescents <18 years of age (14th year of study, 1 July 2023–30 June 2024)

**Andrea Streng & Johannes Liese**

**Background**
Parapneumonic pleural effusions and pleural empyema (PPE/PE) in children are rare but serious complications of mostly bacterial pneumonia, most commonly associated with *Streptococcus pneumoniae* and *S. pyogenes* [1, 2]. In Germany, the introduction of general pneumococcal conjugate vaccination for young children led to an initial decline in PPE/PE, but the incidence has risen again since 2014/15, associated with an increase in both *S. pneumoniae* serotype 3-associated PPE/PE [2] and *S. pyogenes*-associated PPE/PE [3]. The outbreak of the SARS-CoV-2 pandemic led to a strong decline in both overall respiratory diseases [4] and paediatric bacterial PPE/PE from April 2020 onwards and during the 2020/21 season as a result of the implementation of non-pharmaceutical pandemic prevention measures. In the 2021/22 season, the incidence of paediatric PPE/PE rose again slightly, mainly due to *S. pneumoniae*-associated PPE/PE; *S. pyogenes*-associated PPE/PE, on the other hand, hardly occurred [5]. In the 2022/23 season, following the widespread lifting of non-pharmaceutical protective measures, there was an exceptionally sharp resurgence in PPE/PE incidence, reaching 2.3 times the highest pre-pandemic level observed, due in particular to the sharp increase in *S. pyogenes* PPE/PE. This report from 2023/24 (study year 14) describes paediatric PPE/PE in the first study year after the official end of the SARS-CoV-2 pandemic in May 2023.

**Questions (study year 14)**
- Incidence (total and pathogen-specific)
- Clinical characteristics and management
- *S. pneumoniae* serotypes, pneumococcal vaccine breakthroughs

in hospitalised children with PPE/PE in Germany, 2023/24.

**Case definition (study year 14)**
- Children and adolescents < 18 years of age in paediatric hospitals in Germany with PPE/PE lasting longer than 7 days or requiring drainage
- Hospital admission between 1 July 2023 and 30 June 2024

**Methodology**
- Case reports from paediatric hospitals via the GPSU system
- Collection of clinical data
- Additional pathogen diagnostics from pleural effusion:
  - Molecular biological pathogen detection from pleural fluid (eubacterial 16s rDNA PCR with sequencing); Institute for Hygiene and Microbiology, University of Würzburg
  - Serotyping of *Streptococcus pneumoniae* detected by culture or PCR; Reference Centre for Streptococci, Aachen.

**Results (interim evaluation 11 July 2025)**
**Case statistics**
In the period from study year (SY) 1 (2010/11) to SY 14 (2023/24), 4564 children with PPE/PE were reported via the GPSU system and 3454 (75.8%) with valid reports (i.e. according to the case definition) were included in the study.

For the period from 1 July 2023 to 30 June 2024 (SY 14), 574 children with PPE/PE were reported; 405 (70.6%) reports were valid (as of 11 July 2025; Table 1).

**Epidemiological and clinical data**
The monthly distribution of reports for SY 1-14 is shown in Fig. 1. In SY 14 (July 23 to June 24), the number of monthly reports ranged from 14 children (August 2023) to 98 children (February 2024). Based on the 405 case reports assessed as valid in SY 14, the minimum incidence of paediatric PPE/PE in SY 14 was estimated as 29.0 (95% CI 26.2-32.0) per $10^6$ children (Table 2). For the 92 children with *S. pneumoniae*-associated PPE/PE, the minimum incidence in SY 14 was 6.6 (95% CI 5.3-8.1) per $10^6$ children, for

**Table 1:** Case reports / exclusions / valid cases of children <18 years with PPE/PE in Germany; per completed study year (July-June); GPSU-PPE/PE study*.

| Study year (SY) | 1 2010/ 2011 | 2 2011/ 2012 | 3 2012/ 2013 | 4 2013/ 2014 | 5 2014/ 2015 | 6 2015/ 2016 | 7 2016/ 2017 | 8 2017/ 2018 | 9 2018/ 2019 | 10 2019/ 2020 | 11 2020/ 2021 | 12 2021/ 2022 | 13 2022/ 2023 | 14 2023/ 2024 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Reports (raw) | 272 | 285 | 314 | 244 | 245 | 297 | 315 | 301 | 273 | 322 | 80 | 236 | 806 | 574 |
| • Duplicate entries | 13 | 14 | 20 | 12 | 11 | 12 | 9 | 13 | 22 | 11 | 7 | 17 | 41 | 23 |
| • Errors | 31 | 23 | 32 | 26 | 28 | 24 | 25 | 20 | 26 | 29 | 11 | 20 | 52 | 58 |
| • No questionnaire | 13 | 37 | 33 | 28 | 25 | 33 | 38 | 25 | 15 | 27 | 6 | 28 | 84 | 88 |
| • inclusion (valid) | 215 | 211 | 229 | 178 | 181 | 228 | 243 | 243 | 210 | 255 | 56 | 171 | 629 | 405 |

*Minor changes in the number of patients included compared to previous reports are due to ongoing data corrections (e.g. late registrations, identification of duplicate entries, etc.; status as of 11 July 2025).

the 62 children with *S. pyogenes*-associated PPE/PE it was 4.4 (95% CI 3.4-5.7), and 3.1 (95% CI 2.2-4.1) for the 43 children with PPE/PE caused by other bacterial pathogens (Table 3).

A total of 405 children were included in the evaluation of clinical data in SY 14. The median age was 4.8 years (IQR 3.0-8.4); 202 (49.9%) of the 405 children with PPE/PE were male; 74 (18%) had a defined underlying disease. In SY 14, the children were admitted to hospital a median of 5 days (IQR 3-8) after the onset of symptoms; the length of stay was 16 days (IQR 11-22). 271 (66.9%) children received intensive care treatment for a median of 7 days (IQR 4-14). 395 (97.5%) of the 405 children received parenteral antibiotics for a median of 14 days (IQR 9-20). In 327 (80.7%) children, the pleural space was opened; 90 children (22.2%) were treated using video-assisted thoracoscopy (VATS) and/or thoracotomy. In 322 (79.5%) children, pulmonary (305; 75.3%), pleural (124; 30.6%) or infectious complications (48 (11.9%) with sepsis/SIRS/septic shock) occurred. In 53 (13.1%) children, possible sequelae were reported, primarily pleural/pulmonary impairments. Four (1.0%) of the children (two of whom had pre-existing conditions) died (three of them with sepsis/septic shock).

In 198 (48.9%) of the 405 children in SY 14, at least one bacterial pathogen could be identified from blood culture or pleural fluid (by culture or PCR) (Table 3). *S. pneumoniae* was detected in 92/198 (46.5%) and *S. pyogenes* in 62/198 (31.3%). In 44/198 (22.2%) children with other bacterial pathogens, the most common were *Staphylococcus aureus* (13/198; 6.7%), *Haemophilus influenzae* (10/198; 5.1%) and *Streptococcus intermedius* (9/198; 4.5%).

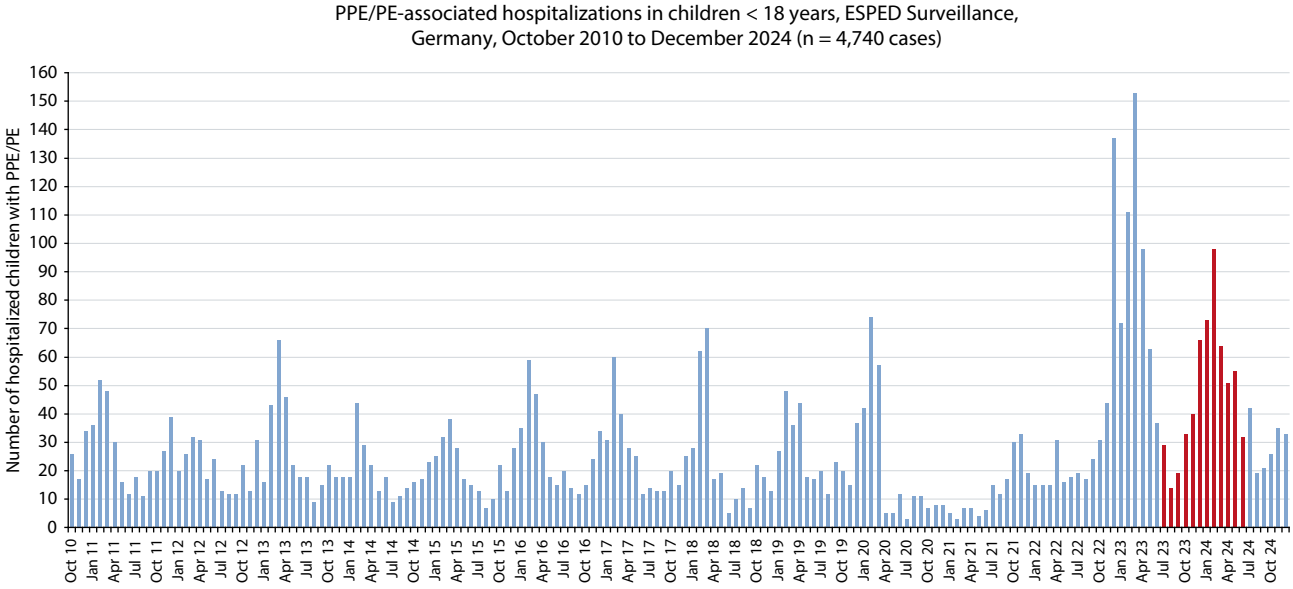


**Fig. 1:** Reports of paediatric hospital admissions due to PPE/PE in Germany in study years 1 to 14 (Oct. 2010 to June 2024, n = 4,566), as well as preliminary reporting data for the first half of study year 15 (July 2024 to Dec. 2024, n = 176). Study year 14 (GPSU reporting year) is highlighted in red color. GPSU-PPE/PE study.

**Table 2:** Incidence per 1,000,000 children <18 years with PPE/PE in paediatric hospitals in Germany, based on the number of cases included in the study as "valid" and cases with pathogen detection (minimum incidence); per study year (July-June); GPSU-PPE/PE study*.

| Study year (SY) | 1 2010/ 2011 | 2 2011/ 2012 | 3 2012/ 2013 | 4 2013/ 2014 | 5 2014/ 2015 | 6 2015/ 2016 | 7 2016/ 2017 | 8 2017/ 2018 | 9 2018/ 2019 | 10 2019/ 2020 | 11 2020/ 2021 | 12 2021/ 2022 | 13 2022/ 2023 | 14 2023/ 2024 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Children <18 years with PPE/PE (all)** | 215 | 211 | 229 | 178 | 181 | 228 | 243 | 243 | 210 | 255 | 56 | 171 | 629 | 405 |
| **Inzidenz per $10^6$ children <18 years** | | | | | | | | | | | | | | |
| • PPE/PE (all) | 16,1 | 16,1 | 17,5 | 13,6 | 13,8 | 17,1 | 18,0 | 18,0 | 15,4 | 18,6 | 4,1 | 12,3 | 45,2 | 29,0 |
| • PPE/PE associated with *S. pneumoniae* | 3,4 | 2,9 | 2,7 | 1,5 | 1,6 | 2,1 | 2,8 | 2,2 | 2,4 | 3,7 | 0,4 | 3,5 | 8,5 | 6,6 |
| • PPE/PE associated with *S. pyogenes* | 0,4 | 0,6 | 1,5 | 0,8 | 1,0 | 2,6 | 1,3 | 2,2 | 1,8 | 3,3 | 0,0 | 0,2 | 12,4 | 4,4 |
| • PPE/PE associated with other bacteria | 1,2 | 1,5 | 2,2 | 1,6 | 1,5 | 2,0 | 2,6 | 2,4 | 2,1 | 2,0 | 0,9 | 2,2 | 4,2 | 3,1 |

*Minor deviations in the number of patients compared to previous reports are due to ongoing data corrections (e.g. late registrations, identification of duplicate entries, etc.; status as of 10 July 2025).

Of all 405 children with PPE/PE in SY 14, 317 (78%) had been vaccinated against pneumococci at least once, 33 (8%) had not been vaccinated, and no vaccination data was available for 55 (14%). For 225 of the vaccinated children, additional information on the number of doses was available; 48 (21%) had received 4 doses each, 140 (62%) had received 3 doses each, and 37 (16%) had received <3 doses.

Of the 92 children with *S. pneumoniae*-associated PPE/PE, 77 (84%) had been vaccinated against pneumococci at least once, 6 (6%) had not been vaccinated, and the vaccination status of 9 (10%) was unknown. Of the 77 vaccinated children, 61 had received PCV-13, 1 had received PCV-10 and 1 child had received various vaccines (PCV-13 and PCV-15); the vaccine was not specified for 14 children. Information on the number of doses was available for 67 of the vaccinated children; 10 (15%) had received 4 doses each, 49 (73%) had received 3 doses each, and 8 (12%) children had received <3 doses.

**Table 3:** Bacterial pathogens in 1,448 children with PPE/PE included in the study with positive bacterial pathogen detection in blood/pleural fluid over 14 study years (10/2010–06/2024), GPSU-PPE/PE study.

| Study year (SY) | Children with at least 1 bacterial pathogens n (%) | Children with PPE/PE with *S. pneumoniae*# n (%)* | Children with PPE/PE with *S. pyogenes*# n (%)* | Children with PPE/PPE with other bacterial pathogens n (%)* |
|---|---|---|---|---|
| **1 (2010/11)** | **67 (100)** | 45 (67,2) | 6 (9,0) | 16 (23,9) |
| **2 (2011/12)** | **66 (100)** | 38 (57,6) | 8 (12,1) | 20 (30,3) |
| **3 (2012/13)** | **84 (100)** | 35 (41,7) | 20 (23,8) | 29 (34,5) |
| **4 (2013/14)** | **52 (100)** | 20 (38,5) | 11 (21,2) | 21 (40,4) |
| **5 (2014/15)** | **54 (100)** | 21 (38,9) | 13 (24,1) | 20 (37,0) |
| **6 (2015/16)** | **89 (100)** | 28 (31,5) | 34 (38,2) | 27 (30,3) |
| **7 (2016/17)** | **91 (100)** | 38 (41,8) | 18 (19,8) | 35 (38,5) |
| **8 (2017/18)** | **93 (100)** | 30 (32,3) | 30 (32,3) | 33 (35,5) |
| **9 (2018/19)** | **86 (100)** | 33 (38,4) | 25 (29,1) | 28 (32,6) |
| **10 (2019/20)** | **122 (100)** | 50 (41,0) | 45 (36,9) | 27 (22,1) |
| **11 (2020/21)** | **17 (100)** | 5 (29,4) | 0 (-) | 12 (70,6) |
| **12 (2021/22)** | **81 (100)** | 48 (59,3) | 3 (3,7) | 30 (37,0) |
| **13 (2022/23)** | **348 (100)** | 118 (33,9) | 172 (49,4) | 58 (16,7) |
| **14 (2023/24)** | **198 (100)** | **92 (46,5)** | **62 (31,3)** | **44 (22,2)** |
| **Total** | **1448 (100)** | 601 (41,5) | 447 (30,9) | 400 (27,6) |

* Percentages refer to the respective total number per study year
# In cases of multiple infection, *S. pneumoniae* or *S. pyogenes* was considered the primary pathogen.

In SY 14, 28 serotypes of *S. pneumoniae* PPE/PE were detected, of which 25/28 (89.3%) were ST3, 1 (3.6%) was ST19A, 1 (3.6%) ST22F and 1 (3.6%) ST23F. Of the 25 ST3 detections, 17/25 (68%) were vaccine breakthroughs (fully vaccinated with a vaccine containing the serotype); the child with ST19A detection was also a vaccine breakthrough.

**Conclusions**

After the exceptional increase in the overall incidence of paediatric PPE/PE following the lifting of most non-pharmaceutical measures in the last year of the SARS-CoV-2 pandemic in 2022/23 (SY 13) to 45 PPE/PE cases per $10^6$ children, the overall incidence in the first post-pandemic study year 2023/24 (SY 14) decreased to 29 per $10^6$ children, but was still approximately 1-5 times higher than the pre-pandemic maximum incidence of 19 PPE/PE cases per $10^6$ children in SY 10. This still elevated incidence is most likely due to continued reduced herd immunity as a result of the reduced circulation of various respiratory pathogens in the first two years of the pandemic due to pandemic prevention measures.

When comparing the demographic and clinical characteristics of SY 14 vs. SY 13, the median age of children with PPE/PE was slightly higher in SY 14 (4.8 vs. 4.0 years); the data on treatment and outcome largely corresponded to the results of the previous year, with pleural space opening in 81% vs. 86% (of which 22% each by VATS/thoracotomy), intensive care treatment in 67% vs. 74% (median duration of intensive care treatment 7 days in both years), and a median duration of hospitalisation of 16 days in both years; possible sequelae were diagnosed in 13% vs. 17%.

The lower incidence of PPE/PE compared to SY 13, but still significantly higher than in pre-pandemic years, was also evident in the three pathogen groups analysed (PPE/PE associated with *S. pneumoniae* / *S. pyogenes* / other bacterial pathogens).

For *S. pneumoniae*-associated PPE/PE, the incidence fell from 8.5 per $10^6$ children to 6.6 per $10^6$ children, which was still 1.8 times higher than the pre-pandemic maximum (SY 10). In SY 14, *S. pneumoniae* was again the most frequently detected pathogen in paediatric PPE/PE. As in the previous 7 study years, ST3 was the most frequently detected serotype in SY 14 (25/28; 89%); most vaccine breakthroughs in SY 14 were attributable to ST3 (17/18; 94%).

For *S. pyogenes*-associated PPE/PE, the incidence fell from an exceptionally high 12.4 per $10^6$ children in SY 13 to 4.4 in SY 14, but was still 1.3 times higher than the pre-pandemic maximum in SY 10. As in SY13, detailed analyses of clinical parameters (not shown here) in SY 14 revealed no evidence of a significant increase in severity compared to pre-pandemic disease progression [5].

Continuing PPE/PE surveillance will enable the assessment of changes in the overall incidence of PPE/PE, serotype replacement and its impact on the effectiveness of vaccine prevention, as well as further shifts in the bacterial pathogen spectrum. In the first post-pandemic SY 14 (2023/24), a decline in paediatric PPE/PE was recorded compared to the exceptional SY 13, but the incidence remained at a higher level than in the pre-pandemic years. Even for the still ongoing SY 15, there are already more reports/inclusions than in the pre-pandemic years.

It is not yet possible to assess whether this is still an "after-effect" of the pandemic due to still reduced herd immunity and whether the incidence level will return to the pre-pandemic level of 2019/20 in the longer term, or whether the pre-pandemic increase in PPE/PE observed since 2014/15 will continue.

The continued increase in pneumococcal serotype 3 indicates suboptimal effectiveness of the pneumococcal conjugate vaccines used to date; it is still unclear whether the new, recently approved, partly more immunogenic vaccines will show an improvement in this regard.

Further surveillance is therefore necessary, both with regard to the increase in paediatric PPE/PE overall and *S. pyogenes*-associated PPE/PE, and with regard to the frequent vaccine breakthroughs in *S. pneumoniae*-associated PPE/PE.

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**Summary**

Non-pharmaceutical preventive measures targeting the SARS-CoV-2 pandemic initially led to a sharp decline in the incidence of complicated parapneumonic pleural effusions and pleural empyema (PPE/PE) in children in the study years 2020/21 and 2021/22.

After the exceptionally sharp resurgence in the overall incidence of PPE/PE following the lifting of non-pharmaceutical preventive measures in the last pandemic study year 2022/23, the incidence declined significantly again in 2023/24 (from 45 to 29 per $10^6$ children), but was still considerably higher than the highest pre-pandemic incidence observed in the study (19 per $10^6$ children in 2019/20).

A decline in incidence compared to 2022/23, but with values still significantly higher than the pre-pandemic maximum values, was also observed within the three pathogen groups (*S. pneumoniae, S. pyogenes*, other pathogens).

*S. pneumoniae* was again the most common single pathogen in paediatric PPE/PE in 2023/24 (47% of all pathogen detections). Serotype 3 was again the most common pneumococcal serotype in 2023/24 (89% of all serotype detections); most vaccine breakthroughs were associated with ST3.

Initial data from the ongoing second post-pandemic study year 2024/25 indicate that the incidence remains higher than before the pandemic. It is not yet possible to conclusively assess whether this is still an after-effect of the pandemic due to reduced herd immunity or whether the pre-pandemic increase in PPE/PE observed since 2014/15 is continuing.

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# Chronic intestinal failure in children and adolescents

**Victor Bildheim**

**Background**

Chronic intestinal failure (CIF) is a rare disease in children characterised by a reduction in functional intestinal mass. This leads to an inability to absorb the necessary nutrients and fluids for survival, growth and development, resulting in the need for artificial nutrition [1]. Intestinal failure is defined as dependence on parenteral nutrition for more than 60 days due to an intestinal disease [2]. The most common cause in children is short bowel syndrome (SBS), followed by intestinal motility disorders and mucosal enteropathies [3, 4]. There is insufficient epidemiological data on incidence and prevalence, and none is available for Germany [5, 6]. The prevalence in Europe is estimated at 1.4–5.6 per 100,000 children [7]. Due to improved survival rates, even in severely ill children, an increase in CIF is assumed [8, 9].

The goals of treatment are normal growth and development, avoiding complications, and achieving independence from parenteral nutrition ('enteral autonomy') [10]. Interdisciplinary 'intestinal rehabilitation' programs have proven to be the most successful strategy [11].

In Germany, the incidence and distribution of causes, disease characteristics, and initial care, in terms of both medical content and structure, are unknown.

**Research question(s)**

The study aims to record the incidence, aetiology, intestinal anatomy, drug and nutritional therapy, complications, and medical care of children under the age of 18 with CIF in Germany.

**Case definition**

Patients under the age of 18 with the first occurrence of CIF, in the sense of requiring parenteral support for more than 60 days or who are expected to require it for more than 60 days.

**Preliminary results**

**Case statistics**

Between July 2023 and December 2024, a total of 73 cases were reported. Of these, 4 were false reports. The response questionnaires for 19 cases are still pending. Therefore, a total of 50 questionnaires are available for evaluation (2023: 16; 2024: 34).

**Clinical characterisation**

Of the 50 cases that could be evaluated, 24 involved girls and 25 involved boys. In one case, the sex is not specified. Thirty-five of the children were born prematurely (before completing 37 weeks of gestation). The gestational age at birth ranged from 23+1 weeks to 40+0 weeks, and the birth weight ranged from 460 g to 3,910 g. The gestational age at birth was unknown in seven cases, and the birth weight was unknown in six cases.

46 of the children were younger than 1 year old at the time of diagnosis. The remaining 4 patients were between 11 and 15 years old. 4 children (8%) died within the reporting period.

The aetiology of CIF was short bowel syndrome in 37 cases (74%), intestinal motility disorder in 8 cases (16%) and mucosal enteropathy in 1 case (2%). In 4 cases (8%), no information was provided regarding the cause of the CIF.

The causes of short bowel syndrome can be summarised as follows (multiple entries per case possible): necrotising enterocolitis (n = 14), volvulus (n = 8), congenital intestinal atresia (n = 6), gastroschisis (n = 5), meconium ileus (n = 2), extensive o agangli-onosis (n = 2), mesenteric ischaemia (n = 2), focal intestinal perforation (n = 1), anorectal malformation (n = 1), chronic inflammatory bowel disease (n = 1). Causes of intestinal motility disorders: megacystis microcolon intestinal hypoperistalsis syndrome (n = 4), paediatric intestinal pseudo-obstruction without further specification (n = 1), gastroschisis (n = 1), volvulus (n = 1), meconium ileus (n = 1). Causes of mucosal enteropathies: microvillus inclusion disease (MVID) (n = 1).

At least one abdominal surgical procedure was necessary for 47 out of 50 children (94%) (7 children underwent surgery once, 12 children underwent

**Table 1:** Causes of CDV (multiple selections possible)

| | N | (%) |
|---|---|---|
| **Short bowel syndrome** | 37 | (74) |
| Necrotising enterocolitis | 14 | (28) |
| Volvulus | 8 | (16) |
| Congenital intestinal atresia | 6 | (12) |
| Gastroschisis | 5 | (10) |
| Meconium ileus | 2 | (4) |
| Extensive aganglionosis | 2 | (4) |
| Mesenteric ischaemia | 2 | (4) |
| Inflammatory bowel disease | 1 | (2) |
| Anorectal malformation | 1 | (2) |
| Focal intestinal perforation | 1 | (2) |
| **Intestinal motility disorder** | 8 | (16) |
| Megacystis-microcolon-intestinal hypoperistalsis syndrome | 4 | (8) |
| Intestinal pseudo-obstruction | 1 | (2) |
| Gastroschisis | 1 | (2) |
| Meconium ileus | 1 | (2) |
| **Mucosal enteropathies** | 1 | (2) |
| Microvillus inclusion disease | 1 | (2) |
| **Unclassified** | 4 | (8) |

surgery twice, 10 children underwent surgery three times, and 15 children underwent surgery ≥4 times). Forty-three of the 50 children who underwent surgery had an intestinal stoma created, which could be removed in 16 cases by the time the case was reported.

In 39 cases (78%), a permanent central venous catheter was implanted. In all cases, this was a Hickman catheter. 39 of the 50 children (78%) were also fed orally or enterally. In 8 of the 39 children, this oral-enteral nutrition provided more than 50% of the daily calorie requirement, which was not possible in the remaining children. In 5 children (10%), it was possible to discontinue parenteral nutrition during the course of treatment, but 33 of the 50 children had already been discharged home at the time of reporting.

23 patients (46%) developed catheter-associated sepsis during the course of treatment. Hepatopathy was also reported in 21 cases (42%), concomitant failure to thrive in 20 cases (40%), and nephropathy in 3 cases (6%).

In 30 cases, treatment was provided in university hospitals, in 25 cases in maximum care hospitals, in 6 cases in specialist care hospitals and in 4 cases in basic and standard care hospitals. The following specialist disciplines were involved in each case: paediatric surgery in 48/50, neonatology in 48/50, paediatric intensive care medicine in 6/50, general paediatrics in 24/50, paediatric gastroenterology in 42/50, nutritional counselling or dietetic assistance in 29/50 and speech therapy in 5/50 cases.

## Preliminary conclusions

In Germany, 50 cases of chronic intestinal failure in children were documented over a period of 18 months. Children in their first year of life are particularly affected. The most prevalent etiological factor is short bowel syndrome. We attribute the wide range of specialist disciplines involved in care to the diverse needs of patients on the one hand and the necessity of multidisciplinarity on the other. The rate of catheter-associated sepsis, hepatopathy, nephropathy and failure to thrive is noteworthy, and must be monitored with ongoing recording. At the time of reporting, 4 children had succumbed to the disease, thus highlighting its severity. The fact that only 5 children were able to be weaned off parenteral nutrition, but 33 of the patients had already been discharged home at the time of reporting, implies high medical expertise requirements for further care, including in the outpatient sector.

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## Summary

In Germany, 50 cases of chronic intestinal failure in children were recorded within a 18-month period (2023: 16 cases, 2024: 34 cases), with children in their first year of life being particularly affected. The most prevalent etiological factor is short bowel syndrome. The majority of patients were discharged home at

the time of reporting, but very few were weaned off parenteral nutrition. The wide range of specialist disciplines involved in care is indicative of the varied needs of patients and the necessity for a multidisciplinary approach. It is anticipated that the findings of this study will facilitate a more comprehensive characterisation of this rare patient cohort.

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