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Surveillance of varicella-associated paediatric hospitalisations and complications in Switzerland from 2021 to 2023

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Summary

AIM: To prospectively assess varicella zoster virus-associated disease burden in hospitalised children 0–16 years of age prior to the introduction of universal varicella vaccination in Switzerland.

METHODS: We performed an observational, prospective surveillance study. Anonymised data (clinical characteristics, diagnostics, treatment and outcome) of hospitalised children were available from monthly active case reporting by 29 paediatric clinics and hospitals to the Swiss Paediatric Surveillance Unit from July 2021 to June 2023.

RESULTS: During the 2-year study period, 239 children were hospitalised with varicella (n = 224; 94%) or herpes zoster (n = 15; 6%). Mean age was 5 years, median 4.7 years (range 0–16 years). In 13 patients, varicella was concomitant and not the primary reason for hospitalisation. 199 patients (83%) were primary healthy, 138 were male (58%). Mean duration of hospitalisation for varicella patients was 5.7 days. Of the 224 children with varicella, 211 (94%) were primary hospitalised due to varicella, 120 (54%) had acute skin complications (including 52 *Streptococcus pyogenes* infections), 29 (13%) musculoskeletal and 27 (12%) neurological complications. Two patients (1%) had ischaemic strokes. 33 (14%) patients (32 with varicella and 1 with herpes zoster) required intensive care treatment (mean duration 3.5 days). 40 patients with varicella (18%) required surgical interventions. Two (1%) patients died. The calculated hospitalisation incidence rate was 7.2 per 100,000 for children and the calculated hospitalisation rate was 12.6 per 10,000 cases.

CONCLUSIONS: Varicella is associated with considerable morbidity, particularly in primary healthy children. Complications affecting the skin (mainly secondary bacterial infections), musculoskeletal and neurological systems are the main reasons for hospitalisation and may cause death even in previously healthy, immunocompetent children. The baseline burden of disease presented herein will permit evaluation of the impact of universal varicella vaccination, introduced in Switzerland in January 2023.

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Introduction

Varicella zoster virus (VZV) infection is a well-known and highly infectious childhood disease. Primary infection causes chickenpox, clinically presenting as a characteristic pruritic rash with macular, papular, vesicular and crusted skin lesions which may appear simultaneously. After primary infection, VZV persists lifelong in sensory nerve ganglia and when reactivated presents as shingles, with a characteristic dermatomal distribution, also known as herpes zoster [1]. Most people think of varicella as a benign childhood disease. However, worldwide, numerous studies have demonstrated a relevant amount of morbidity including bacterial and neurological complications leading to hospitalisation in children with or without underlying chronic conditions [2–5].

In Switzerland, the last prospective surveillance study on VZV-associated hospitalisations of children was conducted during a 3-year period from 2000 to 2003 and included 335 cases and a hospitalisation rate of 13 per 10,000. The median age of patients was 3.5 years. Secondary bacterial infections, central nervous system involvement and pneumonitis were the most common complications. Overall, 319 complications were recorded. Intensive care unit (ICU) treatment was documented in 11 (3%) patients, 12 (4%) experienced sequelae and 3 died [6].

Since January 2023, the Federal Office of Public Health (FOPH) has recommended universal varicella vaccination (UVV) for infants. The preferred immunisation is a quadrivalent measles, mumps, rubella and varicella (MMRV) vaccine with the first dose administered at 9 months and the second dose at 12 months of age. The FOPH also recommend a catch-up vaccination for all individuals 1–40 years of age who have not had varicella or two varicella vaccinations yet [7]. In addition, the FOPH and the Federal Commission for Vaccination (EKIF) have recommended vaccination against herpes zoster with the adjuvanted subunit vaccine Shingrix® since 2021. This is for healthy people aged ≥65 years, patients with immunodeficiency aged ≥50 years and patients with severe immunodeficiency aged ≥18 years [8].

The aim of this study was to assess the burden of VZV-associated hospitalisations and complications in children (0–16 years) over a 2-year period from 2021 to 2023 in Switzerland. This will allow future evaluation of the impact of universal varicella vaccination in Switzerland.

Methods

Study design

We are conducting an observational, prospective surveillance study, which started in July 2021 and is planned to continue until June 2027, on reported VZV hospitalisations in children by use of the Swiss Paediatric Surveillance Unit (SPSU) in Switzerland to assess VZV-associated disease burden in hospitalised children aged 0–16 years prior to the introduction of universal varicella vaccination in Switzerland. All 29 Swiss paediatric clinics are members of the Swiss Paediatric Surveillance Unit, participate in the study and report their cases monthly to the Swiss Paediatric Surveillance Unit [9]. This current analysis refers to the initial 2-year period (July 2021 to June 2023) without a follow-up.

The study protocol was prepared by authors MB and UH and approved by the Ethics Committee Northwestern and Central Switzerland (EKNZ) (project number: 2021-00211). It can be accessed by contacting the corresponding author (MB). According to article 34 a of the HFG (swissethics.ch), the need for individual consent was waived by the Ethics Committee.

Case definition

Hospitalised children and adolescents aged ≤16 years (in the text described as "children") with clinical manifestations of VZV infection (ICD-10: B01.-), i.e. varicella or herpes zoster.

Study population

All children who meet the case definition regardless of underlying chronic conditions or other comorbidities are eligible for reporting. Patients with VZV infection who were primarily hospitalised for a different diagnosis were also included. After reporting a case to the Swiss Paediatric Surveillance Unit, the centres receive an anonymised questionnaire (Supplementary 1. Appendix Questionnaire). Questionnaire data are collected in a central database (secuTrial®), set up by the clinical trial unit (CTU) of Cantonal Hospital Lucerne. MB, UH and the database managers are the only individuals who had access. Data cleaning was performed by MB and NS. Missing data were correctly addressed and considered as missing or unknown.

With regards to VZV-associated stroke cases, reports via Swiss Paediatric Surveillance Unit were supplemented by a second source of information, the Swiss Neuropaediatric Stroke Registry (SNSR) (https://snpsr.neuropaediatrie.ch/). To record and describe the epidemiological situation in Switzerland, place of residence (Switzerland or Not-Switzerland) was recorded, not patient's race or ethnicity. Analyses were performed for three subgroups, primary healthy patients, immunocompromised patients and patients with underlying disease other than immunodeficiency. The quantitative variable age was assigned to four age categories. The categories were chosen by analogy with similar studies from other countries to ensure comparability [3–6, 10–23]. Other quantitative variables were not further categorised.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics 29.0.1.0 (171). We used data editor functions, prepared and cleaned data and performed data transformation with arithmetic and statistical functions (mean, median, range). The functions are described in chapters 5, 7 and 8 of "IBM SPSS Statistics 29 Core System User's Guide" [24]. For the incidence calculation, population data were adopted from the Federal Office of Statistics [25]. We extracted age-specific numbers of inhabitants from population figures for 2021 and 2022 in Switzerland for the calculation of mean age. For the estimated number of varicella cases per year, we used varicella incidence numbers from a systematic review on estimated age-specific seroprevalence and annual varicella incidence per 100,000 in Switzerland and extrapolated this data to the mean inhabitants stated above [16]. This resulted in an estimated number of 85,398 varicella cases per year. We calculated an annual hospitalisation incidence per 100,000 inhabitants by using the calculation path *(# hospitalised patients / # inhabitants) × 100,000* where *# hospitalised patients* was the mean age-specific number of hospitalised varicella patients with a residence in Switzerland during the 2-year study period, yielding a figure of (108 / 1,493,157) × 100,000 = 7.2 per 100,000. The calculation of the annual hospitalisation rate per 10,000 varicella patients was *(# hospitalised patients / estimated # varicella cases per year) × 10,000* or (108 / 85,398) × 10,000 = 12.6 per 10,000 varicella patients. The definition for *# hospitalised patients* remained the same. The varicella hospitalisation incidence refers to Swiss residents aged 0 to 16 years while the annual hospitalisation rate refers to the estimated varicella cases per year. For further illustration, see table 1.

Tools

ChatGPT 3.5 (Version 10.01.2024) was used to improve scientific English in the discussion section. We used the prompt *Please improve the text in respect to the scientific language but keep the contents*. The text output was revised and corrected by the authors regarding the accuracy of content. We used the STROBE cohort reporting checklist guidelines before paper submission [26].

Results

During the 2-year study period, 239 hospitalised patients were reported (237 only to the Swiss Paediatric Surveillance Unit, 1 only to the Swiss Neuropaediatric Stroke Registry and 1 to both surveillance systems). Varicella was the primary admission reason for more than two thirds of all varicella patients. For only a few patients, a different diagnosis was the primary reason for their hospital admission: pneumopathy (n = 6), epilepsy (n = 2), neuroblastoma (n = 1), perforated appendicitis (n = 1), renal failure (n = 1), syndrome of inappropriate antidiuretic hormone secretion (SIADH) (n = 1) and a new diagnosis of dilated car-

diomyopathy (n = 1). All herpes zoster patients were hospitalised due to their clinical herpes zoster presentation.

Immunocompromised patients were defined as patients with primary immunodeficiency or under immunosuppressive therapy and possible other chronic disease. Underlying chronic diseases were skin disorders, cancer or leukaemia, genetic syndromes, cardiovascular diseases, HIV, inflammatory bowel disease, congenital neurological disorder, lung disorder, nephrotic syndrome, epilepsy, vasculitis, sickle cell disease and haemolytic anaemia. Skin disorders, cancer or leukaemia, genetic syndromes and cardiovascular diseases were most common over the 2-year study period. There were no significant differences between the two years of observation in the distribution of the underlying chronic diseases. Figure 1 shows that less than one fifth (40/239) of all hospitalised patients had any underlying chronic disease including immunodeficiency. Only 5 (2%) of all immunocompromised patients had no underlying chronic disease other than their immunodeficiency.

Table 2 shows the general characteristics of primary healthy patients and those with underlying chronic illnesses including immunodeficiency. For immunocompromised patients and patients with an underlying chronic disease other than immunodeficiency, median age was higher. Patients' residence was for nearly all patients in Switzerland. No patient had received vaccination prior to hospitalisation. VZV exposure was mostly unknown or via contact with family members regardless of patients' immune status and other chronic comorbidities. Almost half of all hospitalisations occurred in children aged 9 months to 4 years old. Four primary healthy patients were hospitalised with varicella due to their young age which the treating physicians considered a risk factor for a complicated course of chickenpox. Of these, two were neonates and two were 2 months old. However, none of them experienced a complication and they were discharged within five days. The mean interval between the onset of rash and hospitalisation was 4.95 days(median 4, range −1–61) and the mean duration of all varicella hospitalisations was 5.7 days (median 4, range 0–33). Patients with herpes zoster, if not primary

Table 1:
Annual varicella hospitalisation incidence and hospitalisation rate by age groups. Data from: Bollaerts K, Riera-Montes M, Heininger U, Hens N, Souverain A, Verstraeten T, et al. A systematic review of varicella seroprevalence in European countries before universal childhood immunization: deriving incidence from seroprevalence data. Epidemiol Infect. 2017;145(13):2666–77. https://doi.org/10.1017/S0950268817001546

Age group	Number of inhabitants*	Seroprevalence (%)**	Varicella incidence per 100,000**	Estimated number of varicella cases per year***	Number of hospitalised patients****	Annual hospitalisation incidence per 100,000	Annual hospitalisation rate per 10,000
<9 months	84,520	36%	7368	32,166	12	14.2	19.9
9 months – 4 years	352,048				52	14.8	
5–9 years	447,381	59%	11,798	52,782	41	9.2	7.8
10–16 years	609,028	0.7%	74###	450	3	0.5	66.7
Total	1,493,157	96.5%		85,398	108	7.2	12.6

* Mean age-specific number of inhabitants in Switzerland per year; population figures from 2021 and 2022 [25].

** Estimated age-specific seroprevalence and annual varicella incidence per 100,000 in Switzerland;data from a systematic review [16].

*** Estimated number of varicella cases calculated via annual incidence per 100,000 extrapolated to n inhabitants per age group.

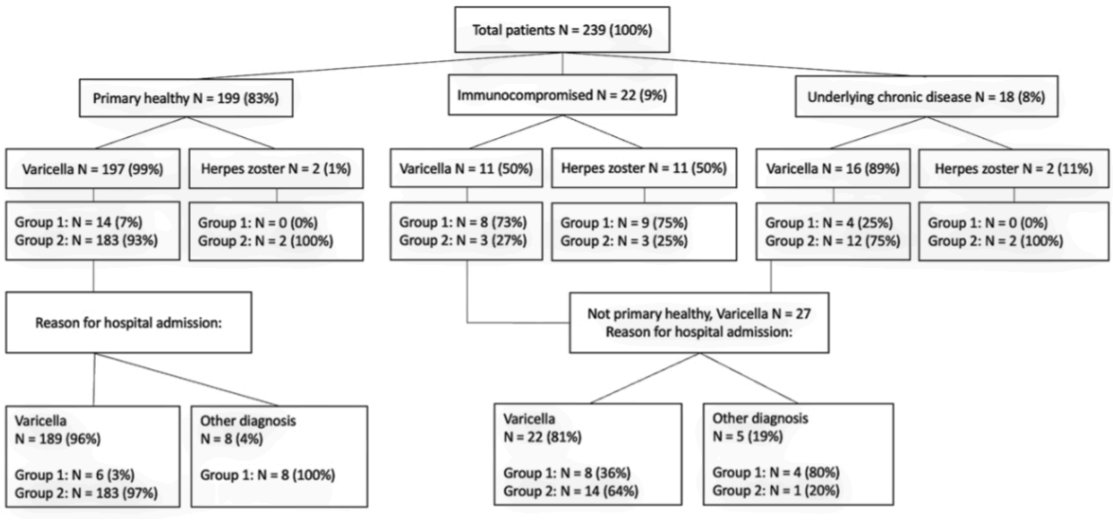
**** Mean number of hospitalised varicella patients with residence in Switzerland per year.

(Number of hospitalised patients / Number of inhabitants) × 100,000

(Number of hospitalised patients / Estimated number of varicella cases per year) × 10,000

The incidence number 74 per 100,000 refers only to patients aged 10–14 years, not 10–16 years.

Figure 1: Study flow chart of varicella zoster virus (VZV)-associated hospitalisations. Underlying chronic disease: excluding immunocompromised host who are presented separately in the figure. Group 1: no complications. Group 2: with complications. Other diagnosis: varicella was not primary reason for hospitalisation. All patients hospitalised due to another diagnosis had concomitant varicella.



healthy, stayed longer in hospital than patients with varicella. In general, immunocompromised patients stayed longer in hospital than primary healthy patients. In contrast to herpes zoster, varicella patients with underlying chronic disease other than immunodeficiency were hospitalised for a shorter period than primary healthy varicella patients.

Figure 2 shows that few varicella cases were reported during study year 1 with a nationwide outbreak during study year 2 from December 2022 to May 2023. Cantons with the highest number of varicella hospitalisations in their children's hospitals and clinics were Zurich (n = 49), Vaud (n = 29), Lucerne (n = 24), Basel (n = 22) and Bern (n = 20).

Table 3 demonstrates complications from varicella for the total study period. Complications secondary to varicella were the most common reason for hospitalisation in the majority of patients, most frequently skin disorders. From April 2022 to July 2023, invasive infections with group A Streptococcus were reported in 52 varicella cases. Musculoskeletal complications were the second most common and neurological complications the third. Several patients experienced more than one complication. Over 90% of primary healthy children experienced complications compared to less than a third of immunocompromised patients and three quarters of patients with an underlying chronic disease other than immunodeficiency. Severe complications with admission to the ICU appeared only in primary healthy children. Typical were skin infections, focal purulent collection, musculoskeletal and neurological disorders and lung involvement with pneumonia or pneumonitis. And fulminant varicella with multiorgan failure, sepsis or death only occurred in primary healthy children as well. Two patients had a varicella-associated ischaemic stroke. Two deaths occurred. One 2-year-old patient with varicella and a fulminant pneumococcal sepsis already died on day of admission in the emergency department. The other fatal case was also two years old, admitted with varicella in septic shock, who also died in the emergency unit shortly after arrival. Clinical circumstances and microbiology revealed *Streptococcus pyogenes* as the cause of the lethal sepsis.

Among the 15 patients with herpes zoster, 13 (87%) had an underlying chronic disease. Seven patients (47%) developed complications of whom five were not primary healthy. Three patients had complications that involved the central nervous system (meningitis n = 2, encephalitis n = 1). Two patients had skin complications, namely cellulitis (n = 1) and invasive *group A streptococcal* infection (n = 1). One patient had elevated liver enzyme values (AST/ALT) in the laboratory and in one patient pneumonia was detected on X-ray.

ICU treatment was necessary for 33 (14%) patients, 32 (14%) with varicella and 1 (7%) with herpes zoster. For varicella and herpes zoster patients, the mean length of stay in the ICU was 3.5 days (median 2, range 0–14). The herpes zoster patient stayed in the ICU for 6 days and improved status after infection. For varicella patients, the mean length of stay was 3.4 days (median 2, range 0–14). Skin complications like cellulitis and soft tissue abscess and musculoskeletal complications were the most common reason for ICU admission (n = 10). Most varicella patients in the ICU (91%) did not experience sequelae or die.

Table 2:
General characteristics. Study year 1 (July 2021–June 2022). Study year 2 (July 2022–June 2023).

		Study year 1	Study year 2	Total study period	Primary healthy	Immunocompromised	Underlying chronic disease other than immunodeficiency
Patients (n)		51	188	239	199	22	18
Female sex, n (%)		22 (43%)	79 (42%)	101 (42%)	80 (40%)	10 (45%)	9 (50%)
Age (in years)	Mean	4.3	5.2	5.0	4.6	7.9	6.2
	Median	3.6	4.8	4.7	4.6	7.0	6.9
	Range	0–14	0–16	0–16	0–15	1–16	0–12
Age group distribution, n (%)	<9 months	10 (20%)	15 (8%)	25 (10%)	22 (11%)	0 (0%)	3 (17%)
	9 months – 4 years	27 (53%)	83 (44%)	110 (46%)	97 (49%)	9 (41%)	4 (22%)
	5–9 years	8 (16%)	78 (41%)	86 (36%)	73 (37%)	5 (23%)	8 (44%)
	10–16 years	6 (12%)	12 (6%)	18 (8%)	7 (4%)	8 (36%)	3 (17%)
Residence, n (%)	Switzerland	49 (96%)	182 (97%)	231 (97%)	192 (97%)	22 (100%)	17 (94%)
	Not-Switzerland	2 (4%)	6 (3%)	8 (3%)	7 (4%)	0 (0%)	1 (6%)
Varicella vaccination history, n (%)	Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	No	48 (94%)	176 (94%)	224 (94%)	187 (94%)	20 (91%)	17 (94%)
	Unknown	3 (6%)	12 (6%)	15 (6%)	12 (6%)	2 (9%)	1 (6%)
Varicella zoster virus exposure*, n (%)	Within family	17 (37%)	62 (35%)	79 (35%)	68 (35%)	5 (45%)	6 (38%)
	Outside family	5 (11%)	14 (8%)	19 (8%)	13 (7%)	4 (36%)	2 (13%)
	Unknown	24 (52%)	103 (58%)	126 (56%)	116 (59%)	2 (18%)	8 (50%)
Varicella, n				224	197	11	16
– Hospitalisation days	Mean			5.7	5.8	6.3	3.4
	Median			4	4	5	3
	Range			0–33	0–33	2–16	1–10
Herpes zoster, n				15	2	11	2
– Hospitalisation days	Mean			8.4	2.5	9.1	10.5
	Median			8	2.5	8	10.5
	Range			2–16	2–3	3–16	10–11

* Varicella cases only.

In total, 214 varicella patients had a favourable outcome, i.e. had recovered (n = 117) or improved when discharged (n = 97). Only 8 patients experienced sequelae, mainly remaining skin defects (n = 5), residual loss of the vestibulocochlear nerve (n = 1), pain (n = 1) or ataxia (n = 1). With regards to herpes zoster, 13 of 15 patients had a favourable outcome. Six patients recovered and seven had improved status when discharged; only two had sequelae, one a right peripheral facial nerve palsy and the other pain.

During hospitalisation, cerebrospinal fluid was obtained from 22 (9%) patients. They were 2 times positive with varicella zoster virus evidence. Table 4 shows the number and type of pathogens from blood cultures and other site cultures for varicella patients. In total, 56 *Streptococcus pyogenes,* 15 *Staphylococcus aureus* and 16 other bacteria were reported. None of the 15 herpes zoster patients had a positive blood culture.

Table 5 lists therapies for varicella and herpes zoster patients. Varicella patients were prescribed more antibiotic therapy while herpes zoster patients received more antiviral therapy. All immunocompromised patients received intravenous antiviral therapy. Antifungal therapy was only prescribed once for an immunocompromised herpes zoster patient.

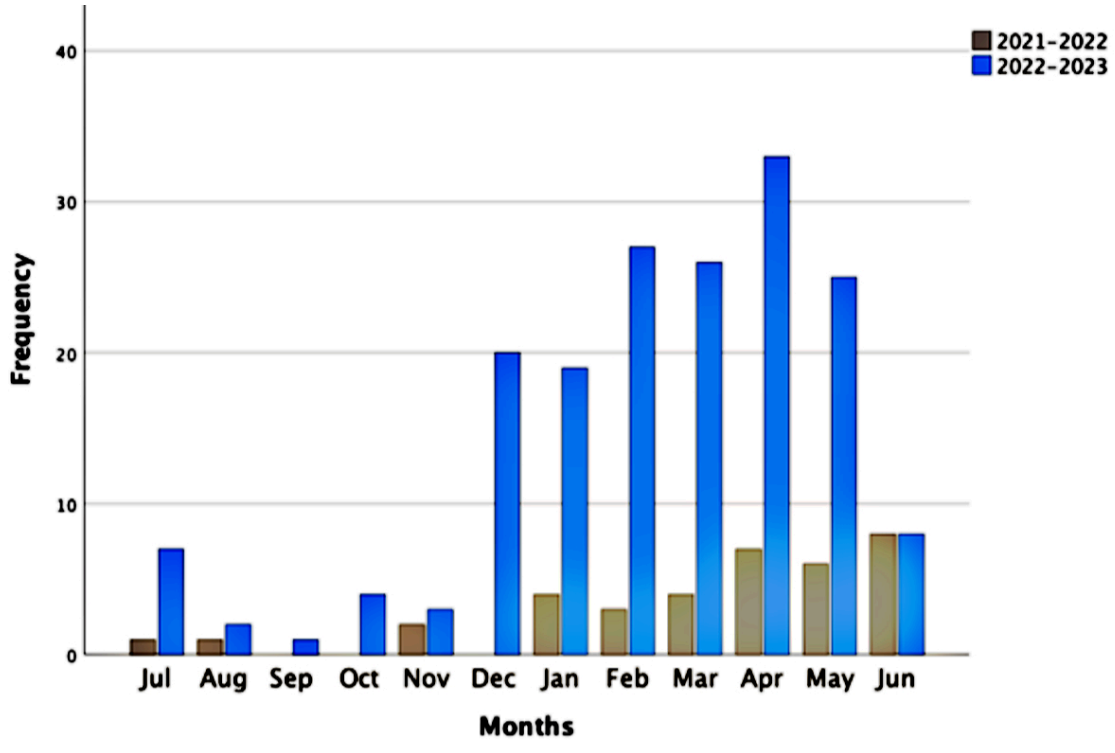
With data from a systematic review on varicella prevalence in European countries before universal childhood vaccination, population data from Switzerland and the Swiss Paediatric Surveillance Unit reports, we estimated the number of varicella cases per year and calculated the annual hospitalisation incidence per 100,000 inhabitants and the annual hospitalisation rate per 10,000 varicella patients by age groups and present them in table 1 [16, 25]. Only children with varicella and resident in Switzerland were included in these calculations (n = 216). The calculated annual varicella hospitalisation incidence for our 2-year study period was 7.2 per 100,000 and the estimated annual hospitalisation rate 12.6 per 10,000.

Discussion

This observational prospective 2-year surveillance study, encompassing reports from all Swiss children's hospitals within the Swiss Paediatric Surveillance Unit, elucidates the morbidity rate of varicella, particularly manifesting in previously healthy (>80%) children. The study shows a comprehensive portrayal of hospitalisations and associated complications of varicella in Switzerland, prior to the implementation of universal varicella vaccination recommendations. Furthermore, it illustrates the seasonal and yearly variations in varicella epidemiology with a nationwide outbreak during the second study year from December 2022 to May 2023. Paediatric varicella hospitalisation frequencies increased 4- to 7-fold in these months compared to the first study year. The seasonal distribution of varicella hospitalisations adhered to its well-established pattern, with a peak incidence during the winter and spring months [2, 11, 12, 14, 17, 18]. Since 2005, there have been no descriptive national epidemiological studies pertaining to varicella-related hospitalisations. Hereby we give an up-to-date epidemiological investigation on varicella morbidity and mortality in children in Switzerland.

The annual hospitalisation rate of 13 per 10,000 remains consistent with the findings of the preceding prospective surveillance study conducted in Switzerland in 2005. Looking at European studies and a study from New Zealand, characterised by either the absence of universal varicella vaccination or low vaccination coverage, the an-

Figure 2: Seasonality of varicella hospitalisations. Varicella as primary reason for hospitalisation: study year one n = 45; study year two: n = 179.



nual varicella hospitalisation incidence ranges from 0.82 to 29.5 per 100,000 [2–5, 11, 13, 14, 19]. Our calculated annual varicella hospitalisation incidence, quantified at 7.2 per 100,000, falls within this broader range. This incidence closely aligns with figures reported in the Netherlands (6.8 per 100,000) and New Zealand (8.6 per 100,000) and underscores the idea of comparability of varicella-related hospitalisation rates across nations with analogous demographic and infrastructural characteristics [3, 19].

Comparative analysis of baseline characteristics among patients revealed that the sex ratio (male:female) was often almost evenly distributed [5, 13, 17, 27]. Our cohort manifested a slight male predominance (58%).

The median age within our cohort, 4.7 years, diverges by 1 to 3 years from the reported median age in other stud-

Table 3:
Complications in 224 patients with varicella. n = 224 patients. Total: total study period (July 2021 – June 2023).

Varicella patients, n (%)	**Total**	**Primary healthy**	**Immunocompromised**	**Underlying chronic disease other than immunodeficiency**
	224 (100%)	**197 (100%)**	**11 (100%)**	**16 (100%)**
Complication, n (%)	198 (88%)	183 (93%)	3 (27%)	12 (75%)
Skin infection[2]	120 (61%)	111 (61%)	1 (33%)	8 (67%)
– Invasive Group A Streptococcal infection[3]	52 (43%)	47 (42%)	1 (33%)	4 (50%)
Musculoskeletal[4]	29 (15%)	26 (14%)	0 (0%)	3 (25%)
Neurological[5]	27 (14%)	25 (14%)	1 (33%)	2(17%)
Focal purulent collection[6]	21 (11%)	19 (10%)	0 (0%)	2 (17%)
Fulminant, with multiorgan failure	19 (10%)	19 (10%)	0 (0%)	0 (0%)
Pneumopathy[7]	16 (8%)	15 (8%)	1 (33%)	0 (0%)
Sepsis	13 (7%)	13 (7%)	0 (0%)	0 (0%)
Haematological[8]	7 (4%)	5 (3%)	0 (0%)	2 (17%)
Lymphadenitis	5 (3%)	5 (3%)	0 (0%)	0 (0%)
Keratitis	2 (1%)	2 (1%)	0 (0%)	0 (0%)
Hepatitis	1 (0.5%)	0 (0%)	0 (0%)	1 (8%)
Reye's syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Deaths, n	2	2	0	0
ICU admission, n (%)	32 (16%)	32 (17%)	0 (0%)	0 (0%)
Varicella complication of ICU patients, n (%)				
Skin	10 (31%)	10 (31%)	0 (0%)	0 (0%)
Musculoskeletal[4]	10 (31%)	10 (31%)	0 (0%)	0 (0%)
Focal purulent collection	7 (22%)	7 (22%)	0 (0%)	0 (0%)
Fulminant, with multiorgan failure	7 (22%)	7 (22%)	0 (0%)	0 (0%)
Pneumonia	6 (19%)	6 (19%)	0 (0%)	0 (0%)
Toxic shock syndrome	6 (19%)	6 (19%)	0 (0%)	0 (0%)
Neurological[5]	5 (16%)	5 (16%)	0 (0%)	0 (0%)
Septic shock	2 (6%)	2 (6%)	0 (0%)	0 (0%)
Cardiovascular[9]	1 (3%)	1 (3%)	0 (0%)	0 (0%)
Haematological[8]	1 (3%)	1 (3%)	0 (0%)	0 (0%)
SIADH	1 (3%)	1 (3%)	0 (0%)	0 (0%)
Patients with surgical intervention, n (%)	40 (18%)	38 (19%)	0 (0%)	2 (13%)

ICU: Intensive care unit; SIADH: Syndrome of inappropriate antidiuretic hormone secretion.

[1] The number of complications does not refer to the absolute number of complications, but to the number of varicella patients who experienced at least one complication.

[2] Skin, soft tissue abscess, cellulitis, purpura fulminans.

[3] Bacterial complications secondary to varicella with *Streptococcus pyogenes*.

[4] Necrotising fasciitis, septic arthritis, osteomyelitis, pyomyositis, myositis, other musculoskeletal complication.

[5] Varicella-associated ischaemic stroke, encephalitis, cerebellitis (ataxia), meningitis, other neurological complication.

[6] Bacterial complications secondary to varicella.

[7] X-ray evidence of pneumonia or X-ray evidence of pneumonitis.

[8] Coagulopathy, heamorrhagic, other abnormal haematology laboratory parameters.

[9] Dilated cardiomyopathy of the left ventricle of undetermined origin.

Table 4:
Pathogen detection in blood cultures and cultures from other sites. Blood cultures in 151 (63%) of 239 patients. Other-site cultures in 81 (35%) of 239 patients.

Pathogen	**Positive blood culture**	**Positive other-site culture**
n (%)	18 (100%)	63 (100%)
Streptococcus pyogenes	10 (56%)	41 (65%)
Others	6 (33%)	9 (14%)
Staphylococcus aureus	2 (11%)	7 (11%)
Streptococcus pyogenes and *Staphylococcus aureus*	0 (0%)	5 (8%)
Staphylococcus aureus and others	0 (0%)	1 (2%)

ies [2–4, 11, 13, 14, 19]. The peak frequency of hospitalisations was observed in patients aged 9 months to 4 years. This aligns with findings from several studies, thus illustrating a recognised pattern of elevated varicella hospital admission rates within younger age cohorts. These observations challenge the conventional presumption that severe complications are exclusive to older children, thereby highlighting the vulnerability of younger age groups to varicella-related complications [2–5, 11, 13].

The majority of children requiring hospitalisation due to varicella were primary healthy. Comparative analyses with studies conducted in Germany, the Netherlands, Belgium and Ireland reveal proportions of hospital admissions for primary healthy patients ranging from 61% to 96.3% [2–5, 11]. In our 2-year study period, 83% of all observed hospitalised patients and 88% of the varicella patient subset were healthy. These findings substantiate the assumption that primary healthy children are at risk of severe varicella infections.

Our investigation revealed an augmented occurrence of invasive Group A Streptococcus (iGAS) infections concomitant with varicella compared to pre-COVID-19 years. Specifically, in the second study year, 49 cases of iGAS infections were registered. This noteworthy increase aligns with findings reported in a Dutch study [28]. Other European countries documented an increase of iGAS as well. Cameron et al. documented a notable proportion of infectious complications involving iGAS [11]. McCarthy et al. observed a rise in iGAS infections too [5]. These collective observations underscore the complex interplay between varicella and iGAS infections, emphasising the need for heightened vigilance and surveillance in monitoring such infectious dynamics.

Prevalent underlying chronic diseases in other European studies include congenital anomalies, skin disorders and pneumopathies [2, 3, 11]. We found these categories in our study too; however skin disorders, particularly atopic dermatitis, cancer or leukaemia, genetic syndromes and cardiovascular diseases were the most common. Notably, hospitalisations occurred primarily due to complications from varicella. Varicella complications commonly involve the skin, central nervous system and lungs, with variations in the order and frequency of affected organ systems across studies. Our investigation showed predominant skin infections, followed by musculoskeletal and neurological complications. The observed spectrum of complications in our study aligns with that of comparable studies from other countries [2–5, 11, 13, 14, 17, 19]. During our analysed period, no patient had a history of prior VZV vaccination. All patients admitted to the ICU were primary healthy. The severity of complications concentrating in primary healthy patients has been described in similar studies [4, 11, 19]. Further, the ICU admission rate at 14% for all patients in our study falls within the range observed in European countries and New Zealand (2.5% to 24%) [4, 5, 11, 19].

The fatality rate, observed at 4.5% in 2021–2022 and 0.5% in 2022–2023, closely mirrors the outcomes reported from Switzerland in 2005 and therefore underscores the notion of an unchanged epidemiology of varicella in Switzerland [6]. Fatalities resulting from varicella hospitalisations are documented in various studies [2, 4, 11, 13].

As a limitation, the interpretative scope of our findings is constrained by the abbreviated 2-year study period, marked by fluctuations in the frequency of varicella-related hospitalisations. An extended observation period will provide a more nuanced and accurate description of the epidemiological dynamics. Comparative analyses with other studies are circumscribed by variations in case definitions and methodological approaches. The absence of a follow-up questionnaire or a capture-recapture analysis introduces the potential for underestimating the true burden of disease. Assignment errors may have transpired during the codification process, emphasising the need for cautious interpretation.

Nations that have already instituted universal varicella vaccination strategies have consistently reported a decline in hospitalisations [12, 15, 18, 21–23, 29–31]. Universal varicella vaccination has been proposed and implemented as a measure against severe complications, thereby diminishing the overall burden on healthcare resources and reducing hospitalisation rates [4, 5, 11, 19].

Data sharing statement

Anonymised study data can be shared on request by contacting the corresponding author (MB). Apart from soft-

Table 5:
Therapies listed for varicella and herpes zoster patients for the total study period.

Number of patients, n (%)	Varicella	Primary healthy	Immunocompromised	Underlying chronic disease other than immunodeficiency	Herpes zoster	Primary healthy	Immunocompromised	Underlying chronic disease other than immunodeficiency
	n = 224	n = 197	n = 11	n = 16	n = 15	n = 2	n = 11	n = 2
Antiviral therapy	44 (20%)	29 (15%)	11 (100%)	4 (25%)	14 (93%)	1 (50%)	10 (91%)	2 (100%)
– Intravenous*	40 (18%)	25 (13%)	11 (100%)	4 (25%)	14 (93%)	1 (50%)	11 (100%)	2 (100%)
– Oral**	25 (11%)	12 (6%)	9 (82%)	4 (25%)	11 (73%)	0 (0%)	10 (91%)	1 (50%)
Antibiotic therapy	168 (75%)	156 (79%)	4 (36%)	8 (50%)	8 (53%)	2 (100%)	5 (45%)	1 (50%)
– Intravenous	165 (74%)	155 (79%)	3 (27%)	7 (44%)	8 (53%)	2 (100%)	5 (46%)	1 (50%)
– Oral	134 (60%)	123 (62%)	3 (27%)	8 (50%)	3 (20%)	2 (100%)	1 (9%)	0 (0%)
Antifungal therapy								
– Intravenous	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (7%)	0 (0%)	1 (9%)	0 (0%)
– Oral	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other treatment	25 (11%)	19 (10%)	1 (9%)	5 (31%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

* *For varicella patients:* acyclovir (n = 39), acyclovir (n = 1). *For herpes zoster patients:* acyclovir (n = 14).

** *For varicella patients:* valacyclovir (n = 19), acyclovir (n = 5), oseltamivir (n = 1), Tamiflu (n = 1). *For herpes zoster patients:* valacyclovir (n = 10), acyclovir (n = 1).

ware and tools described above in the analysis and tools subheadings, no additional software libraries, frameworks or packages were used in this study.

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References

1. Heininger U, Seward JF. Varicella. Lancet. 2006 Oct;368(9544):1365–76. http://dx.doi.org/10.1016/S0140-6736(06)69561-5.
2. Liese JG, Grote V, Rosenfeld E, Fischer R, Belohradsky BH, v Kries R; ESPED Varicella Study Group. The burden of varicella complications before the introduction of routine varicella vaccination in Germany. Pediatr Infect Dis J. 2008 Feb;27(2):119–24. http://dx.doi.org/10.1097/INF.0b013e3181586665.
3. van Lier A, van der Maas NA, Rodenburg GD, Sanders EA, de Melker HE. Hospitalization due to varicella in the Netherlands. BMC Infect Dis. 2011 Apr;11(1):85. http://dx.doi.org/10.1186/1471-2334-11-85.
4. Blumental S, Sabbe M, Lepage P; Belgian Group for Varicella. Varicella paediatric hospitalisations in Belgium: a 1-year national survey. Arch Dis Child. 2016 Jan;101(1):16–22. http://dx.doi.org/10.1136/archdischild-2015-308283.
5. McCarthy KN, Ó Maoldomhnaigh C, Butler KM, Gavin PJ. Varicella Related Hospital Admissions in Ireland. Ir Med J. 2019 Aug;112(7):966.
6. Bonhoeffer J, Baer G, Muehleisen B, Aebi C, Nadal D, Schaad UB, et al. Prospective surveillance of hospitalisations associated with varicella-zoster virus infections in children and adolescents. Eur J Pediatr. 2005 Jun;164(6):366–70. http://dx.doi.org/10.1007/s00431-005-1637-8.
7. Bundesamt für Gesundheit. Neue Empfehlungen zur Impfung gegen Varizellen (Windpocken). BAG-Bulletin. 2022 Oct 31;44.
8. Bundesamt für Gesundheit. Neue Empfehlungen zur Impfung gegen Herpes zoster: impfstoff Shingrix. BAG-Bulletin. 2021 Nov 22;47:8–15.
9. Swiss Paediatric Surveillance Unit (SPSU). Internet: https://www.spsu.ch/en/home
10. Riera-Montes M, Bollaerts K, Heininger U, Hens N, Gabutti G, Gil A, et al. Estimation of the burden of varicella in Europe before the introduction of universal childhood immunization. BMC Infect Dis. 2017 May;17(1):353. http://dx.doi.org/10.1186/s12879-017-2445-2.
11. Cameron JC, Allan G, Johnston F, Finn A, Heath PT, Booy R. Severe complications of chickenpox in hospitalised children in the UK and Ireland. Arch Dis Child. 2007 Dec;92(12):1062–6. http://dx.doi.org/10.1136/adc.2007.123232.
12. Streng A, Grote V, Rack-Hoch A, Liese JG. Decline of Neurologic Varicella Complications in Children During the First Seven Years After Introduction of Universal Varicella Vaccination in Germany, 2005-2011. Pediatr Infect Dis J. 2017 Jan;36(1):79–86. http://dx.doi.org/10.1097/INF.0000000000001356.
13. Fontoura-Matias J, Moreira RS, Reis-Melo A, Freitas A, Azevedo I. Varicella Admissions in Children and Adolescents in Portugal: 2000-2015. Hosp Pediatr. 2021 Aug;11(8):856–64. http://dx.doi.org/10.1542/hpeds.2020-004275.
14. Pierik JG, Gumbs PD, Fortanier SA, Van Steenwijk PC, Postma MJ. Epidemiological characteristics and societal burden of varicella zoster virus in the Netherlands. BMC Infect Dis. 2012 May;12(1):110. http://dx.doi.org/10.1186/1471-2334-12-110.
15. Waye A, Jacobs P, Tan B. The impact of the universal infant varicella immunization strategy on Canadian varicella-related hospitalization rates. Vaccine. 2013 Oct;31(42):4744–8. http://dx.doi.org/10.1016/j.vaccine.2013.08.022.
16. Bollaerts K, Riera-Montes M, Heininger U, Hens N, Souverain A, Verstraeten T, et al. A systematic review of varicella seroprevalence in European countries before universal childhood immunization: deriving incidence from seroprevalence data. Epidemiol Infect. 2017 Oct;145(13):2666–77. http://dx.doi.org/10.1017/S0950268817001546.
17. Bernal JL, Hobbelen P, Amirthalingam G. Burden of varicella complications in secondary care, England, 2004 to 2017. Euro Surveill. 2019 Oct;24(42):1900233. http://dx.doi.org/10.2807/1560-7917.ES.2019.24.42.1900233.
18. Spackova M, Muehlen M, Siedler A. Complications of varicella after implementation of routine childhood varicella vaccination in Germany. Pediatr Infect Dis J. 2010 Sep;29(9):884–6. http://dx.doi.org/10.1097/INF.0b013e3181e2817f.
19. Wen SC, Best E, Walls T, Dickson N, McCay H, Wilson E. Prospective surveillance of hospitalisations associated with varicella in New Zealand children. J Paediatr Child Health. 2015 Nov;51(11):1078–83. http://dx.doi.org/10.1111/jpc.12937.
20. van Lier A, van Erp J, Donker GA, van der Maas NA, Sturkenboom MC, de Melker HE. Low varicella-related consultation rate in the Netherlands in primary care data. Vaccine. 2014 Jun;32(28):3517–24. http://dx.doi.org/10.1016/j.vaccine.2014.04.034.
21. Heywood AE, Wang H, Macartney KK, McIntyre P. Varicella and herpes zoster hospitalizations before and after implementation of one-dose varicella vaccination in Australia: an ecological study. Bull World

Health Organ. 2014 Aug;92(8):593–604. http://dx.doi.org/10.2471/BLT.13.132142.

22. Sheridan SL, Quinn HE, Hull BP, Ware RS, Grimwood K, Lambert SB. Impact and effectiveness of childhood varicella vaccine program in Queensland, Australia. Vaccine. 2017 Jun;35(27):3490–7. http://dx.doi.org/10.1016/j.vaccine.2017.05.013.
23. Streng A, Grote V, Carr D, Hagemann C, Liese JG. Varicella routine vaccination and the effects on varicella epidemiology - results from the Bavarian Varicella Surveillance Project (BaVariPro), 2006-2011. BMC Infect Dis. 2013 Jul;13(1):303. http://dx.doi.org/10.1186/1471-2334-13-303.
24. IBM. IBM SPSS Statistics 29 Core System User's Guide.
25. Sozialdienst und Migration. Ständige Wohnbevölkerung nach Geschlecht und Alter, 1860-2022. Available from: https://www.pxweb.bfs.admin.ch/pxweb/de/px-x-0102030000_101/px-x-0102030000_101/px-x-0102030000_101.px
26. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007 Oct;370(9596):1453–7. http://dx.doi.org/10.1016/S0140-6736(07)61602-X.
27. Grote V, von Kries R, Springer W, Hammersen G, Kreth HW, Liese J. Varicella-related deaths in children and adolescents—Germany 2003-2004. Acta Paediatr. 2008 Feb;97(2):187–92. http://dx.doi.org/10.1111/j.1651-2227.2007.00595.x.
28. de Gier B, Marchal N, de Beer-Schuurman I, Te Wierik M, Hooiveld M, de Melker HE, et al.; ISIS-AR Study Group; GAS Study group; Members of the GAS study group; Members of the ISIS-AR study group. Increase in invasive group A streptococcal (*Streptococcus pyogenes*) infections (iGAS) in young children in the Netherlands, 2022. Euro Surveill. 2023 Jan;28(1):2200941. http://dx.doi.org/10.2807/1560-7917.ES.2023.28.1.2200941.
29. Hirose M, Gilio AE, Ferronato AE, Ragazzi SL. Impacto da vacina varicela nas taxas de internações relacionadas à varicela: revisão de dados mundiais [The impact of varicella vaccination on varicella-related hospitalization rates: global data review]. Rev Paul Pediatr. 2016 Sep;34(3):359–66. http://dx.doi.org/10.1016/j.rpped.2015.12.006.
30. Quinn HE, Gidding HF, Marshall HS, Booy R, Elliott EJ, Richmond P, et al.; PAEDS (Paediatric Active Enhanced Disease Surveillance) Network. Varicella vaccine effectiveness over 10 years in Australia; moderate protection from 1-dose program. J Infect. 2019 Mar;78(3):220–5. http://dx.doi.org/10.1016/j.jinf.2018.11.009.
31. Marshall HS, Clarke M, Heath C, Quinn H, Richmond PC, Crawford N, et al.; PAEDS Investigators. Severe and Complicated Varicella and Associated Genotypes 10 Years After Introduction of a One-Dose Varicella Vaccine Program. J Infect Dis. 2019 Jan;219(3):391–9. http://dx.doi.org/10.1093/infdis/jiy518.