Type 1 diabetes incidence curves differ by age for girls and boys between 1996 and 2022: Results from the North Rhine-Westphalia Diabetes Registry, Germany

Anna Stahl-Pehe, Christina Baechle, Stefanie Lanzinger, Michael S. Urschitz, Reinhard W. Holl, Joachim Rosenbauer

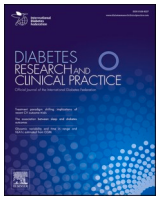
Article - Version of Record

diabetesresearchandclinicalpractice 220 (2025) 111996

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.journals.elsevier.com/diabetes-research-and-clinical-practice



Brief Report

Type 1 diabetes incidence curves differ by age for girls and boys between 1996 and 2022: Results from the North Rhine-Westphalia Diabetes Registry, Germany

Anna Stahl-Pehe [a,b,*], Christina Baechle [a,b], Stefanie Lanzinger [b,c], Michael S. Urschitz [d], Reinhard W. Holl [b,c], Joachim Rosenbauer [a,b]

[a] Institute for Biometrics and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany
[b] German Center for Diabetes Research (DZD), Munich-Neuherberg, Germany
[c] Institute of Epidemiology and Medical Biometry, CAQM, Ulm University, Ulm, Germany
[d] German Paediatric Surveillance Unit, Division of Paediatric Epidemiology, Institute of Medical Biostatistics, Epidemiology, and Informatics, University Medical Centre of the Johannes Gutenberg University Mainz, Mainz, Germany

A B S T R A C T

The type 1 diabetes incidence was analyzed in 0- to 14-year-old children in North Rhine-Westphalia, Germany, from 1996 to 2022. The data revealed an overall increasing trend, with variations by age and sex. The incidence increased in boys across age groups but peaked in girls in the 5–9-year age group.

1. Introduction

The diagnosis of type 1 diabetes (T1D) in children represents a considerable burden for affected children, their families, and the healthcare system. Children with T1D require specialized pediatric diabetes treatment and continuous medical care. Reliable estimates of the incidence of T1D are essential for health service planning, and targeted strategies that can reduce the future morbidity and mortality associated with diabetes onset in childhood [1]. A recent systematic review and meta-analysis revealed a worrying upward trend in the incidence of T1D among children younger than 15 years in most European countries. For Germany, the incidence was estimated to increase from 16.2 cases (95 % confidence interval [95 % CI] 13.9; 18.6) per 100,000 person-years (PYs) in the period 1994–2003 to 25.3 cases (22.4; 28.2) per 100,000 PYs in the period 2013–2022. This estimate was based on several reports, but not a single study has focused on the incidence of T1D in 0–14-year-old children over the last three decades including the period of the coronavirus disease 2019 (COVID-19) pandemic [2].

The aim of this study was to investigate the incidence of T1D in North Rhine-Westphalia (NRW), Germany's most populous federal state with 18 million inhabitants, by using the longest available data series and to analyze age group-specific trends by sex.

2. Materials and methods

For this study, registry data on physician-diagnosed T1D in children younger than 15 years were used; these data have been collected in NRW since 1996. The registry is based on data from the hospital-based German Paediatric Surveillance Unit [3], annual inquiries among medical practices, and the Diabetes Prospective Follow-up Register [4], as described in detail elsewhere [5]. Children younger than 15 years at the time of diagnosis who permanently resided in NRW between January 1, 1996, and December 31, 2022, were eligible for inclusion. The type of diabetes was determined by the treating physicians in accordance with international diagnostic criteria [6].

The annual completeness of coverage was estimated with a capture–recapture method, and the number of cases corrected for the degree of underreporting was estimated with common formulas [7]. The rates of incident T1D are expressed as the number of cases per 100,000 PYs.

Incidence rates with 95 % CIs were estimated by assuming a Poisson distribution of cases and directly age- and sex-standardized. We present incidence rates with correction for underreporting, log-linear incidence trends as annual percentage changes (APCs) with 95 % CIs estimated from negative binomial regressions [8], segmented log-linear trends identified from joinpoint analysis as described previously [5], and fitted curves estimated with flexible B-splines [9] that allowed us to modulate

* Corresponding author at: Institute for Biometrics and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Germany, Auf'm Hennekamp 65, D-40225 Düsseldorf, Germany.
E-mail address: anna.stahl@ddz.de (A. Stahl-Pehe).

https://doi.org/10.1016/j.diabres.2025.111996
Received 11 October 2024; Received in revised form 21 December 2024; Accepted 6 January 2025
Available online 11 January 2025

even short-term fluctuations.

The data were analyzed with SAS® software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

From 1996 to 2022, 18,394 children with incident T1D were recorded, resulting in 18,694 cases after adjustment for underreporting. The mean completeness of coverage was 98.7 % (range 91.7 %; 99.7 %). The overall T1D incidence was 26.1 cases per 100,000 PYs, slightly higher in boys than in girls and lowest in children aged 0–4 years (Table 1, year-specific data in Supplementary Table S1 and Supplementary Table S2). According to the joinpoint analysis, there was an overall steady increase in incidence from 1996 to 2012, followed by a phase with approximately stable incidence until 2019, a steep increase at the beginning of the COVID-19 pandemic, and finally a decline in 2022, resulting in an overall APC of 3.0 % (Fig. S1, sex-specific data in Supplementary Fig. S2).

Fig. 1 shows that the incidence rates increased in boys across age groups. For boys aged 10–14 years, the fitted B-spline (Fig. 1) and log-linear trends (Supplementary Fig. S3) were greater and largely parallel to those of boys aged 5–9 years across the entire observation period. Among 10–14-year-old girls, the log-linear trend was below that for 5–9-year-old girls, except for the first years within the period (Supplementary Fig. S3). The fitted B-spline curve indicated more pronounced fluctuations in the incidence in 10–14-year-old girls than in younger girls (Fig. 1). According to the joinpoint analysis, there were two joinpoints with three segmented trends for most subgroups defined by sex and age (Supplementary Fig. S4).

Table 1
Pediatric type 1 diabetes incidence by sex and age group in NRW, Germany, from 1 January 1996 to 31 December 2022.

Cohort, years	Number of cases	Person-years	Crude incidence per 100,000 person-years (95 % CI)	Standardized incidence per 100,000 person-years (95 % CI)	Annual percent change (95 % CI)
All					
0–4	3,997	22,484,756	17.8 (17.2; 18.3)	17.8 (17.2; 18.3)	2.7 (2.1; 3.2)
5–9	7,015	23,661,524	29.6 (29.0; 30.3)	29.7 (29.0; 30.3)	3.4 (2.9; 3.9)
10–14	7,682	24,837,826	30.9 (30.2; 31.6)	30.9 (30.2; 31.5)	2.9 (2.4; 3.4)
0–14	18,694	70,984,106	26.3 (26.0; 26.7)	26.1 (25.7; 26.5)	3.0 (2.7; 3.3)
Boys					
0–4	2,140	11,542,192	18.5 (17.8; 19.3)	–	2.8 (2.0; 3.6)
5–9	3,577	12,145,434	29.5 (28.5; 30.4)	–	3.5 (2.8; 4.2)
10–14	4,296	12,752,605	33.7 (32.7; 34.7)	–	3.3 (2.6; 4.0)
0–14	10,013	36,440,231	27.5 (26.9; 28.0)	27.2 (26.7; 27.8)	3.2 (2.8; 3.6)
Girls					
0–4	1,857	10,942,564	17.0 (16.2; 17.8)	–	2.5 (1.8; 3.2)
5–9	3,438	11,516,090	29.9 (28.9; 30.9)	–	3.2 (2.6; 3.9)
10–14	3,386	12,085,221	28.0 (27.1; 29.0)	–	2.5 (1.9; 3.1)
0–14	8,681	34,543,875	25.1 (24.6; 25.7)	24.9 (24.4; 25.5)	2.8 (2.3; 3.2)

The case numbers were corrected for the degree of underreporting [7]. The direct method of standardization was applied, using a standard population that included equal numbers in each subgroup defined by age and/or sex. The population data by sex and age for each year were obtained from the German Federal Statistical Office [20].

4. Summary

We showed that the general increasing trend in the incidence of pediatric T1D varies by sex and age. Our observation that the incidence increased with age in boys but was highest in girls in the 5–9-year age group is consistent with other studies [10–12], but there are also contradictory findings [13,14]. We are not aware of any reports from other countries that reported age-specific B-spline curves differentiated by sex. The overall incidence of T1D in children is higher in NRW than those in several other Western countries [11–16] but lower than that in Finland [10]. The overall T1D incidence reported for Germany in a recent meta-analysis was lower than the rates calculated in the present evaluation for the period 2013–2022 [2].

The evaluations were based on high-quality data from a population-based incidence registry, with correction for underreporting. However, the findings are limited because the incidence registry does not contain any information to estimate the generalizability to the whole of Germany and to explain the observed fluctuations. The different changes in the T1D incidence curves by age group among girls and boys may reflect concurrent changes in yet unidentified risk factors such as environmental influences and lifestyle changes [17], and puberty may also have a modifying effect [18]. The temporarily particularly high incidence from 2020 to 2022 may be related to the coronavirus disease 2019 pandemic, which is suspected to have accelerated the transition from presymptomatic autoimmunity to clinically manifest T1D in predisposed individuals [19]. Unfortunately, the data from the diabetes registry are not suitable for analyzing whether and, if so, which effects of the pandemic (e.g., virus infection, unfavorable dietary habits and lack of exercise during lockdown) were causal. In conclusion, there are as yet unexplained differences between the individual age groups of girls and boys with respect to fluctuations in the long-term T1D incidence curves.

5. Author Agreement

All authors have reviewed and approved the final version of the manuscript being submitted. The article is original work and has not received prior publication nor is it under consideration for publication elsewhere.

6. Ethics

The diabetes incidence registry is audited by the Commissioner for Data Protection and Freedom of Information of the Federal State of NRW (AZ 41.5.2.10–215/02) and the responsible Ethics Committee at Düsseldorf University (study number 1726).

Declaration of Generative AI and AI-assisted technologies in the writing process

AI and AI-assisted technologies were not employed in the writing process.

CRediT authorship contribution statement

Anna Stahl-Pehe: Writing – review & editing, Writing – original draft, Conceptualization. **Christina Baechle:** Writing – review & editing. **Stefanie Lanzinger:** Writing – review & editing. **Michael S. Urschitz:** Writing – review & editing, Data curation. **Reinhard W. Holl:** Writing – review & editing. **Joachim Rosenbauer:** Writing – review & editing, Supervision, Formal analysis, Data curation, Conceptualization.

Funding

The German Diabetes Center receives institutional funding from the

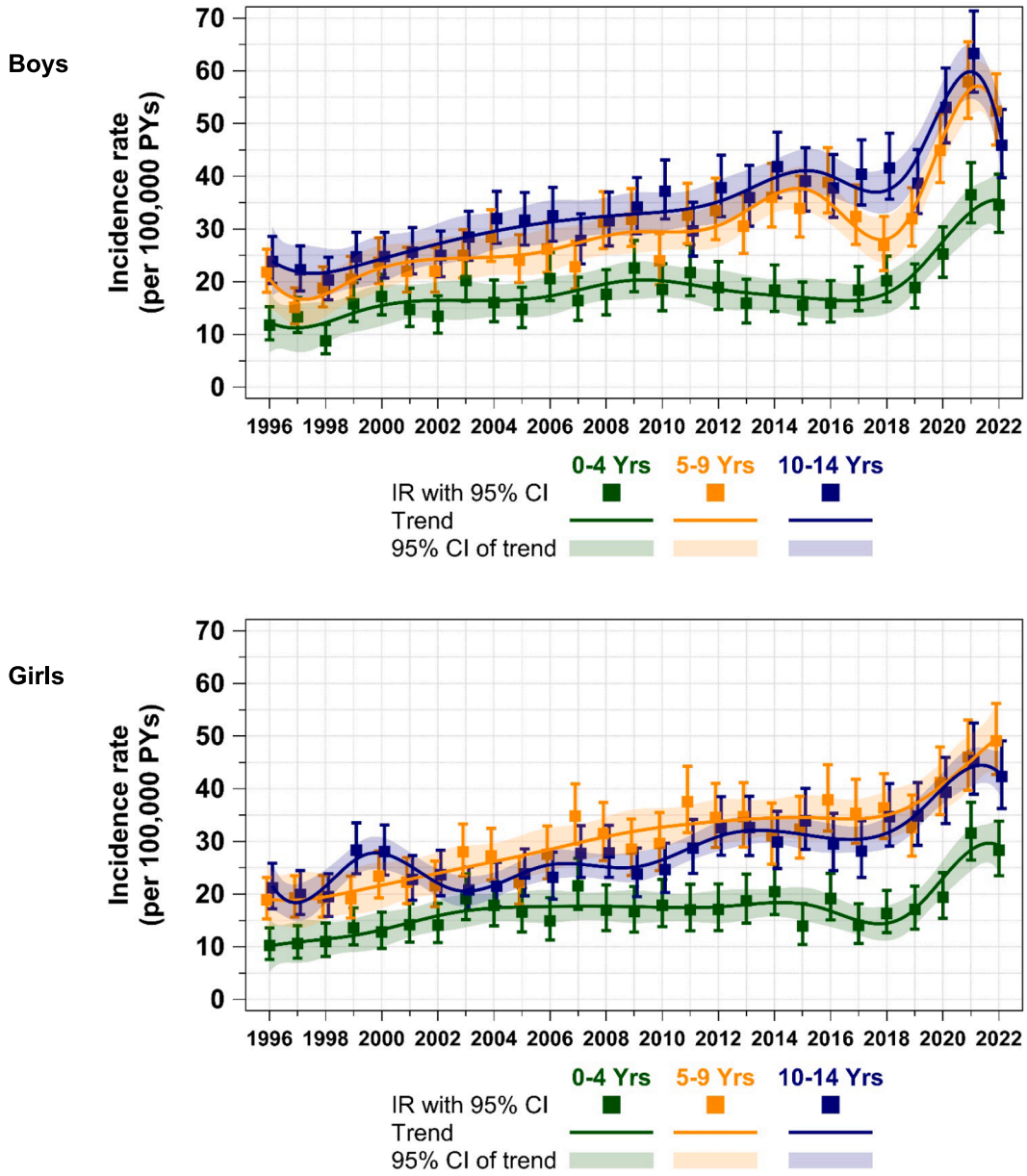


Fig. 1. Annual incidence rates and B-spline trends of T1D in NRW, Germany, by sex for different age groups, estimated on the basis of case numbers corrected for the degree of underreporting.

German Federal Ministry of Health (BMG) and the Ministry of Culture and Science of the State of North Rhine-Westphalia (MKW NRW). The DPV initiative is supported by the German Center for Diabetes Research (DZD), the Robert-Koch-Institute (RKI) and the German Diabetes Association (DDG). There was no external funding for this report.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank all reporting physicians for their cooperation with the NRW Diabetes Registry and their contribution to the hospital-based German Paediatric Surveillance Unit and the Diabetes Prospective Follow-up Register.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2025.111996.

References

[1] International Diabetes Federation. IDF Diabetes Atlas 10th edition 2021. 2021. Available from: http://www.diabetesatlas.org.
[2] Ruiz-Grao MC, Díez-Fernández A, Mesas AE, Martínez-Vizcaíno V, Sequí-Domínguez I, Sebastián-Valles F, et al. Trends in the Incidence of type 1 diabetes in European children and adolescents from 1994 to 2022: a systematic review and meta-analysis. Pediatr Diabetes 2024;2024:1–13.
[3] University Medical Center of the Johannes Gutenberg University Mainz. The German Paediatric Surveillance Unit ESPED: Methods. 2024. Available from: https://www.unimedizin-mainz.de/esped/methods/methods.html?L=1.
[4] Hofer SE, Schwandt A, Holl RW, Austrian GD. Standardized documentation in pediatric diabetology: experience from Austria and Germany. J Diabetes Sci Technol 2016;10:1042–9.
[5] Stahl-Pehe A, Baechle C, Lanzinger S, Urschitz MS, Reinauer C, Kamrath C, et al. Trends in the incidence of type 1 diabetes and type 2 diabetes in children and

adolescents in North Rhine-Westphalia, Germany, from 2002 to 2022. Diabetes Metab 2024;50:101567.
[6] Mayer-Davis EJ, Kahkoska AR, Jefferies C, Dabelea D, Balde N, Gong CX, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Definition, epidemiology, and classification of diabetes in children and adolescents. Pediatr Diabetes 2018;19 (Suppl 27):7–19.
[7] Bruno G, LaPorte RE, Merletti F, Biggeri A, McCarty D, Pagano G. National diabetes programs. Application of capture-recapture to count diabetes? Diabetes Care 1994; 17:548–56.
[8] Cameron AC, Trivedi PK. Regression Analysis of Count Data. 2 ed. Cambridge: Cambridge University Press; 2014.
[9] Eilers PHC, Marx BD. Flexible smoothing with *B*-splines and penalties. Stat Sci 1996;11(89–121):33.
[10] Parviainen A, But A, Siljander H, Knip M. Decreased incidence of type 1 diabetes in Young Finnish Children. Diabetes Care 2020;43:2953–8.
[11] Raicevic M, Samardzic M, Soldatovic I, Curovic Popovic N, Vukovic R. Trends in nationwide incidence of pediatric type 1 diabetes in Montenegro during the last 30 years. Front Endocrinol (Lausanne) 2022;13:991533.
[12] Hayes L, Cheetham T, Muirhead C, Hopper N, Reid J, Lamb W, et al. Type 1 diabetes in North East England and North Cumbria: patterns and time trends in 0-14-year-olds from 2012 to 2020. Front Public Health 2023;11:1193403.
[13] Goni Iriarte MJ, Brugos Larumbe A, Guillen Grima F, Sainz de Los Terreros Errea A, Chueca Guendulain MJ, Forga Llenas L. Incidence of type 1 diabetes in Navarra, 2009-2020. Evidence of a stabilization. Endocrinol Diabetes Nutr (Engl Ed). 2023; 70:80-7.
[14] Zhang S, Mittinty M, Davis EA, Cameron E, Haynes A. Childhood-onset type 1 diabetes in Western Australia: an update on incidence and temporal trends from 2001 to 2022. Diabet Med 2023;40:e15148.
[15] Nagl K, Waldhör T, Hofer SE, Blauensteiner N, Fritsch M, Fröhlich-Reiterer E, et al. Ongoing increase in incidence of diabetes in Austrian children and adolescents (1989–2021): results from a nationwide registry. Pediatr Diabetes 2023;2023:1–7.
[16] Gesuita R, Rabbone I, Marconi V, De Sanctis L, Marino M, Tiberi V, et al. Trends and cyclic variation in the incidence of childhood type 1 diabetes in two Italian regions over 33 years and during the COVID-19 pandemic. Diabetes Obes Metab 2023;25:1698–703.
[17] Norris JM, Johnson RK, Stene LC. Type 1 diabetes-early life origins and changing epidemiology. Lancet Diabetes Endocrinol 2020;8:226–38.
[18] Peltonen EJ, Veijola R, Ilonen J, Knip M, Niinikoski H, Toppari J, et al. What is the role of puberty in the development of islet autoimmunity and progression to type 1 diabetes? Eur J Epidemiol 2023;38:689–97.
[19] Bombaci B, Passanisi S, Sorrenti L, Salzano G, Lombardo F. Examining the associations between COVID-19 infection and pediatric type 1 diabetes. Expert Rev Clin Immunol 2023;19:489–97.
[20] German Federal Statistical Office. GENESIS-Online Population Table 12411-0006. 2023. Available from: https://www-genesis.destatis.de/genesis/online?operation=table&code=12411-0006&bypass=true&levelindex=1&levelid=1644998637276#abreadcrumb.