Epidemiological Perspectives on Type 1 Diabetes in Childhood and Adolescence in Germany

20 years of the Baden-Württemberg Diabetes Incidence Registry (DIARY)

STEFAN EHEHALT, MD[1]
KLAUS DIETZ, PHD[2]
ANDRE M. WILLASCH, MD[3]
ANDREAS NEU, MD[1]
FOR THE BADEN-WÜRTTEMBERG DIABETES INCIDENCE REGISTRY (DIARY) GROUP*

OBJECTIVE — To predict the frequency of type 1 diabetes in childhood and adolescence (<15 years of age) in Germany for the next 20 years.

RESEARCH DESIGN AND METHODS — Data on diabetes onset has been collected by means of a registry in the federal German state of Baden-Württemberg (documentation period, 1987–2006; $n = 5{,}108$; completeness of data 98.1%).

RESULTS — The current incidence rate (2000–2006) is 19.4 per 100,000 per year (95% CI 18.6–20.2). The annual incidence rate can be expressed as a square of a linear function of the calendar year X [$y = (3.05 + 0.0778 \times \{X–1986\})^2$; $r^2 = 0.90$]. The highest increase per year was observed in the age-groups comprising 2- and 3-year-olds (12 and 13% per year, respectively). The incidence rate for the year 2026 is estimated to be 37.9 per 100,000 per year (95% CI 33.3–42.9).

CONCLUSIONS — The increase that we found in younger children is characteristic of a left shift toward an earlier age.

Diabetes Care 33:338–340, 2010

We present the statistics over 20 years pertaining to the frequency of type 1 diabetes among children and adolescents in the third largest state of Germany, which we derived from the Baden-Württemberg incidence register. We developed a prediction model in order to predict the frequency of diabetes for the total group (0–14 years of age) for the next 20 years. These data are essential for health care planning. Additionally, they provide further insight into the epidemiology of the disease in our country over a 40-year period.

RESEARCH DESIGN AND METHODS

— Diabetes onset in children and adolescents aged <15 years was documented according to the EURODIAB criteria (1). Data deriving from surveys done during meetings of independent patient groups were used as a secondary data source. The completeness of data at source was 98.1% (Capture-mark-recapture method) (2,3).

To predict the total number of cases of diabetes onset in Baden-Württemberg up to the year 2026, we developed a model described as follows. The incidence rates followed a Poisson distribution. Thus, a square-root transformation of the data from the total period of observation was done. This square-root–converted incidence rate for each age was described as a linear function of the calendar year. The estimated values of the slopes and the intercepts were described by means of a polynomial with three parameters. We applied a cubic function for the slopes, and a fourth-degree polynomial for the intercepts.

RESULTS

— The current incidence rate (2000–2006) is 19.4 per 100,000 per year (95% CI 18.6–20.2). The annual incidence rate can be expressed as the square of a linear function of the calendar year X [$y = (3.05 + 0.0778 \times \{X–1986\})^2$, $r^2 = 0.90$]. Thus, the incidence rate for the year 2026 is estimated to be 37.9 per 100,000 per year (95% CI 33.3–42.9). Between 1987 and 2006 there were 5,108 children and adolescents who developed type 1 diabetes. In the following 20 years, this figure is expected to rise to 7,600.

The prediction model based on the Baden-Württemberg incidence register is as follows: [$b0 + b1 \times age + b3 \times (age - 8)^4 + (m0 + m1 \times age + m3 \times (age - 8)^3) \times year)^2$; $b0 = 2.11$, $b1 = 0.152$, $b3 = -0.00062$, $m0 = 0.132$, $m1 = -0.0069$, $m3 = 0.000124$; age 1–15, year 1–20 (year 1 = 1987, year 20 = 2006)].

The highest incidence rate was found among 10–14-year-olds (18.7 per 100,000 per year [95% CI 17.9–19.5]), followed by 5–9-year-olds (16.5 per 100,000 per year [15.7–17.2]) and 0–4-year-olds (10.7 per 100,000 per year [10.1–11.3]; $P < 0.0001$). The highest linear increase was observed in the age-groups of the 2- and 3-year-olds (12 and 13% per year, respectively, for the square roots of the incidences), while the lowest increase occurred in the 11-year-olds (3% per year). Taking into consideration that the newborn population will decrease in Germany, we can expect that, in terms of absolute numbers, the highest frequency of type 1 diabetes will be among children 5–9 years of age (Fig. 1, *left shift*).

CONCLUSIONS

— The frequency of type 1 diabetes is rising in almost every

From the [1]University Children's Hospital, Tuebingen, Germany; the [2]Department of Medical Biometry, Eberhard-Karls-University, Tuebingen, Germany; and the [3]Hospital for Children and Adolescents, Goethe University, Frankfurt, Germany.
Corresponding author: Andreas Neu, andreas.neu@med.uni-tuebingen.de.
Received 12 August 2009 and accepted 27 October 2009. Published ahead of print at http://care.diabetesjournals.org on 10 November 2009. DOI: 10.2337/dc09-1503.
*A complete list of the Baden-Württemberg Diabetes Incidence Registry (DIARY) Group members can be found in the ACKNOWLEDGMENTS.

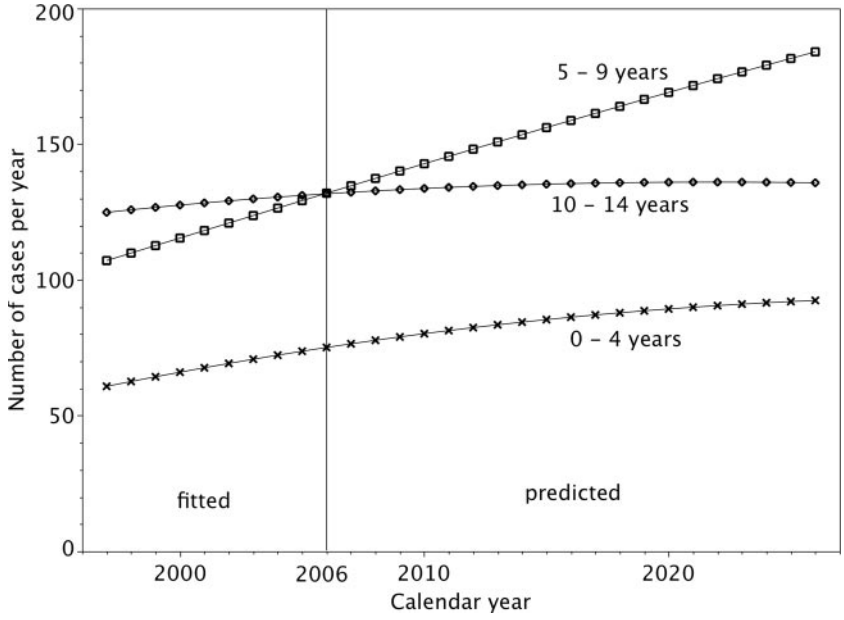

Figure 1—*Fitted number of documented cases (1997–2006) and prediction of new cases (2007–2026) according to age-groups.*

national population (4–6). On the one hand, the considerable variation (>350-fold) in the global incidence rates seems to be rather steady (6). On the other hand, there are differences in the incidence rates across Europe and even within various regions in an individual country, despite their close proximity and an essentially common genetic pool (4,7). This demonstrates the interplay between genes and environment.

Our study showed that children born at the present time face a significantly higher risk of developing type 1 diabetes than those born in the 1980s and 1990s. In comparison to observations made in previous years, this risk increases further with age progression. During the last 20 years in Baden-Württemberg there were ~5,100 children and adolescents who developed type 1 diabetes. Our predictions show that this figure will rise to 7,600 within the next 20 years. As immigration is not included in the population data, the predicted number of new cases might be an underestimation. In Finland, a country with the highest incidence rate (IR) in the world, it is estimated that the rate will reach 80 per 100,000 per year by 2010 (8). Calculations for Germany show that a similar IR would be expected after ~50 years (i.e., in 2062). As there is a uniform pattern over the last 20 years, our calculations are based on the assumption that the incidence trend will continue also in the forthcoming years.

The question that arises in view of the rapid increase in the incidence rates among children and adolescents is whether type 1 diabetes will also be more frequent in the total population or whether the onset will occur at an earlier age (left shift). The results of the analysis of our registry point toward a left shift: during the observational period we found that the onset was most frequent among 10–14-year-olds; however, the average increase in the IR among 2- and 3-year-olds (+12 and +13%) is higher than the IR for 11-year-olds (+3%). Although the most distinct increase in the IR was among the 0–4-years-olds, our predictions show that it will be the 5–9-year-olds who will develop type 1 diabetes, mainly as a result of the substantial decline in the birth rate in Germany (Fig. 1). A left shift has also been observed in other countries like Belgium and Sweden (9,10).

Based on our previous migration studies and taking into consideration the left shift in the frequency of disease occurrence, we concur with other authors that the earlier onset can be ascribed to environmental factors in individuals with a genetic predisposition (11–13). The steady and uniform rise suggests that the occurrence of type 1 diabetes can hardly be associated with short-term regional modifications but, instead, is a consequence of lasting changes to the environment on a global scale.

Acknowledgments— The Baden-Württemberg Diabetes Incidence Registry (DIARY) has been supported by the Foundation for the Diabetic Child (Stiftung "Das zuckerkranke Kind").

No potential conflicts of interest relevant to this article were reported.

Members of the Baden-Württemberg Diabetes Incidence Registry (DIARY) Group: S. Becker, A. Böckmann, U. Brand, C. Döring, R. Dürr, D. Ecker, F. Eickmeier, W.K. Ertelt, U. Faller, M. Fedorcak, L. Feldhahn, G. Fitzke, J. Grulich-Henn, M. Holder, D. Jantzen, M. Kelle, M. Krüger, B. Lippmann-Grob, U. Radlow, U. Rappen, A. Ruland, R. Sauter, G. Schädel, A. Schumacher, U. Schürmann, K.O. Schwab, F.K. Trefz, A. Veigel, M. Wabitsch, J. Wissert, M. Witsch.

References

1. Green A, Gale EAM, Patterson CC. Incidence of childhood-onset insulin-dependent diabetes mellitus: the EURODIAB ACE Study. Lancet 1992;339:905–909
2. Ehehalt S, Blumenstock G, Willasch AM, Hub R, Ranke MB, Neu A. Continuous rise in incidence of childhood type 1 diabetes in Germany. Diabet Med 2008;25:755–757
3. LaPorte RE, McCarty D, Bruno G, Tajima N, Baba S. Counting diabetes in the next millennium: application of capture-recapture technology. Diabetes Care 1993; 16:528–534
4. Green A, Patterson CC, on behalf of the EURODIAB TIGER Study Group. Trends in the incidence of childhood-onset diabetes in Europe 1989–1998. Diabetologia 2001;44:B3–B8
5. Onkamo P, Väänänen S, Karvonen M, Tuomilehto J. Worldwide increase in incidence of type I diabetes: the analysis of the data on published incidence trends. Diabetologia 1999;42:1395–1403
6. The DIAMOND Project Group. Incidence and trends of childhood type 1 diabetes worldwide 1990–1990. Diabet Med 2006; 23:857–866
7. Rytkönen M, Ranta J, Tuomilehto J, Karvonen M, the SPAT Study Group. The Finnish Childhood Diabetes Registry Group: Bayesian analysis of geographical variation in the incidence of type I diabetes in Finland. Diabetologia 2001; 44(Suppl. 3):B37–B44
8. Harjutsalo V, Sjöberg L, Tuomilehto J. Time trends in the incidence of type 1 diabetes in Finnish children: a cohort study. Lancet 2008;371:1777–1782
9. Pundziute-Lyckå A, Dahlquist G, Nyström L, Arnqvist H, Björk E, Blohmé G, Bolinder J, Eriksson JW, Sundkvist G, Ostman J, the Swedish Childhood Diabetes Study Group. The incidence of type I diabetes has not increased but shifted to a younger age at diagnosis in the 0–34 years group in Sweden 1983 to 1998. Diabetologia 2002;45:783–792
10. Weets I, De Leeuw IH, Du Caju MV, Rooman R, Keymeulen B, Mathieu C, Rottiers R, Daubresse JC, Rocour-Brumioul

D, Pipeleers DG, Gorus FK, the Belgian Diabetes Registry. The incidence of type 1 diabetes in the age group 0–39 years has not increased in Antwerp (Belgium) between 1989 and 2000: evidence for earlier disease manifestation. Diabetes Care 2002; 25:840–846
11. Ehehalt S, Popovic P, Muntoni S, Muntoni S, Willasch A, Hub R, Ranke MB, Neu A, the DIARY Group Baden-Wuerttemberg. Incidence of diabetes mellitus among children of Italian migrants substantiates the role of genetic factors in the pathogenesis of type 1 diabetes. Eur J Pediatr 2009;168:613–617
12. Gale EA. Spring harvest? Reflections on the rise of type 1 diabetes. Diabetologia 2005;48:2445–2450
13. Neu A, Willasch A, Ehehalt S, Kehrer M, Hub R, Ranke MB. Diabetes incidence in children of different nationalities: an epidemiological approach to the pathogenesis of diabetes. Diabetologia 2001;44 (Suppl. 3):B21–B26