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Trends and cyclical variation in the incidence of childhood type 1 diabetes in 26 European centres in the 25 year period 1989–2013: a multicentre prospective registration study

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Abstract
Aims/hypothesis Against a background of a near-universally increasing incidence of childhood type 1 diabetes, recent reports from some countries suggest a slowing in this increase. Occasional reports also describe cyclical variations in incidence, with periodicities of between 4 and 6 years.

Methods Age/sex-standardised incidence rates for the 0- to 14-year-old age group are reported for 26 European centres (representing 22 countries) that have registered newly diagnosed individuals in geographically defined regions for up to 25 years during the period 1989–2013. Poisson regression was used to estimate rates of increase and test for cyclical patterns. Joinpoint regression software was used to fit segmented log-linear relationships to incidence trends.

Results Significant increases in incidence were noted in all but two small centres, with a maximum rate of increase of 6.6% per annum in a Polish centre. Several centres in high-incidence countries showed reducing rates of increase in more recent years. Despite this, a pooled analysis across all centres revealed a 3.4% (95% CI 2.8%, 3.9%) per annum increase in incidence rate, although there was some suggestion of a reduced rate of increase in the 2004–2008 period. Rates of increase were similar in boys and girls in the 0- to 4-year-old age group (3.7% and 3.7% per annum, respectively) and in the 5- to 9-year-old age group (3.4% and 3.7% per annum, respectively), but were higher in boys than girls in the 10- to 14-year-old age group (3.3% and 2.6% per annum, respectively). Significant 4 year periodicity was detected in four centres, with three centres showing that the most recent peak in fitted rates occurred in 2012.

Conclusions/interpretation Despite reductions in the rate of increase in some high-risk countries, the pooled estimate across centres continues to show a 3.4% increase per annum in incidence rate, suggesting a doubling in incidence rate within approximately 20 years in Europe. Although four centres showed support for a cyclical pattern of incidence with a 4 year periodicity, no plausible explanation for this can be given.

Keywords Cyclical variation · Epidemiology · Incidence · Temporal change · Type 1 diabetes mellitus

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Introduction

The increasing incidence of childhood type 1 diabetes has been well documented both in Europe, with an estimated annual increase of 3.9% (95% CI 3.6%, 4.2%) during the period 1989–2003 [1], and worldwide, with an estimated annual increase of 2.8% (95% CI 2.4%, 3.2%) in the period 1990–1999 [2]. Recent reports have, however, suggested a slowing or stabilisation in the rate of increase.

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Research in context

What is already known about this subject?

- Most countries in Europe have reported increasing incidence rates of type 1 diabetes in children
- In some countries with high incidence, rates have levelled off
- Studies have reported a cyclical variation in incidence with periodicities of between 4 and 6 years

What is the key question?

- Are the incidence rates of childhood type 1 diabetes in Europe continuing to increase?

What are the new findings?

- Based on the analysis of over 84,000 children registered in 22 European countries in a 25 year period from 1989 to 2013, incidence rates are still increasing in all childhood age groups in most countries, with no clear signs of levelling off
- A significant 4 year cycle in incidence was observed in only four of 26 contributing centres

How might this impact on clinical practice in the foreseeable future?

- With slower progress in disease prevention than hoped for, the increasing number of children being diagnosed has important implications for those involved in the planning and delivery of healthcare, and in preventing and treating the complications of type 1 diabetes

In the USA, pooled data from five centres for children and adolescents under 20 years of age indicated a 1.8% (95% CI 1.0%, 2.6%) annual increase during 2002–2012 after adjustment for age, sex and race or ethnic group [3], and a similar rate of increase of 1.3% (95% CI 0.0%, 2.5%) has been reported for the Canadian province of British Columbia in the period 2002–2013 [4]. In Australia, a non-significant annual increase of 0.4% (95% CI −0.1%, 0.9%) was reported in the under-15-year-old population during the period 2000–2011, although a significant increase of 1.2% (95% CI 0.4%, 2.1%) was observed in the 10- to 14-year-old age group [5]. Within Europe, no increase was found in Sweden during the period 2005–2007 despite a prolonged period of uniform increase during the previous 15 years [6]. Very similar levelling incidence rates, beginning at about the same time and with longer periods of observation, were subsequently reported in two other high-incidence Scandinavian countries, Finland [7] and Norway [8]. In contrast, a report from Zhejiang province in the low-incidence region of China described a very rapid 12.0% (95% CI 7.6%, 16.6%) increase in annual incidence rate among those aged under 20 years during the period 2007–2013 [9].

There have also been reports in the literature of a cyclical variation in year-to-year incidence rates. The earliest report was from the Yorkshire regional registry in England during the period 1978–1990, which described a marked epidemic pattern with peaks at 4 year intervals [10]. A subsequent brief report from a neighbouring area of north-east England in the period 1990–2007 described a 6 year cyclical pattern with an amplitude of ±25% [11], but there is no established register in the region and no support for the claim of high ascertainment.

A sinusoidal cyclical pattern with peaks observed every 5 years and an amplitude of ±14% has also been reported from Western Australia for the period 1985–2010 [12], and was subsequently replicated in an Australia-wide analysis during the period 2000–2011 [5]. A report from five regions of Poland during the period 1989–2012 using Fourier series methods found a 5.33 year periodicity in rates, with an amplitude of ±8% [13].

To help clarify the recent trends in European incidence rates, an analysis of EURODIAB registry data from over 84,000 children in 26 European centres representing 22 countries is presented for the 25 year period 1989–2013, with separate estimates of incidence rate increases derived in each of five subperiods. This dataset also provides an excellent opportunity to investigate the claims of cyclical variation in incidence rates.

Methods

The establishment of the registries and case definition used has previously been described [14]. Type 1 diabetes was defined on the basis of a clinical diagnosis made by a physician, omitting cases that were secondary to other conditions (e.g. cystic fibrosis or high-dose corticosteroid treatment). Registries attempt to capture prospectively all newly diagnosed individuals in a geographically defined region. Primary and secondary sources of ascertainment were recorded for each child, and these were used to estimate completeness by capture–recapture methodology. The completeness

findings for 1989–2008 have previously been reported as being considerably in excess of 90% in most of the registries (as reported by ESM Table 2 from the 20 year report) [15]. The geographical coverage of the 26 registries is shown in Fig. 1 and represents 23% of the estimated European childhood population in 2011 (excluding Belarus, Ukraine and the Russian Federation). Ethics approval was obtained by individual centres where required.

Incidence rates were obtained by dividing the numbers of registered children by annual population estimates. Standardisation of rates was obtained by the direct method with a standard population comprising equal numbers in each of six subgroups defined by age group (0–4 years, 5–9 years and 10–14 years) and sex. Standard errors for the directly standardised rates were also calculated [16]. Trends in annual incidence rates in each country were investigated in the 25 year period using Poisson regression incorporating an adjustment for age group and sex. Comparisons of trends between age groups and sexes were obtained within each country by incorporating interactions into the Poisson regression model. The Joinpoint regression analysis program version 4.2 (Statistical Methodology and Applications Branch and Data Modeling Branch, National Cancer Institute, Bethesda, MD, USA) was used to fit segmented regression lines to the logarithmically transformed directly standardised incidence rates, taking account of their standard errors. Pooled estimates of rates of increase across all 26 centres were obtained using a mixed

effects Poisson regression model with centre treated as a random effect and age and sex as fixed effects.

Motivated by reports in the literature of 4, 5 and 6 year cycles in incidence rate, sine and cosine terms representing such cycles were added to Poisson regression models for annual age-/sex-specific incidence rates, along with terms for age group and sex as well as the segmented log-linear trends with year as identified by the Joinpoint analysis. The sine and cosine terms are similar to those described for the study of seasonal variation in month-to-month counts [17] but were adapted for the detection of cyclical variation in yearly rates.

Statistical analyses were performed in SPSS version 24 (IBM Corp, Armonk, NY, USA) and Stata release 14 (StataCorp, College Station, TX, USA). Unless otherwise stated, hypothesis testing was performed at the 5% significance level ($p < 0.05$).

Results

Ascertainment rates remained in excess of 90% for most centres, although data were not available for all of these (see electronic supplementary material [ESM] Table 1). Table 1 shows the total numbers of children registered during the 25 year period 1989–2013 in each of the 26 centres, and the age- and sex-standardised incidence rates (with standard errors) in the 5 year subperiods 1989–1993, 1994–1998, 1999–
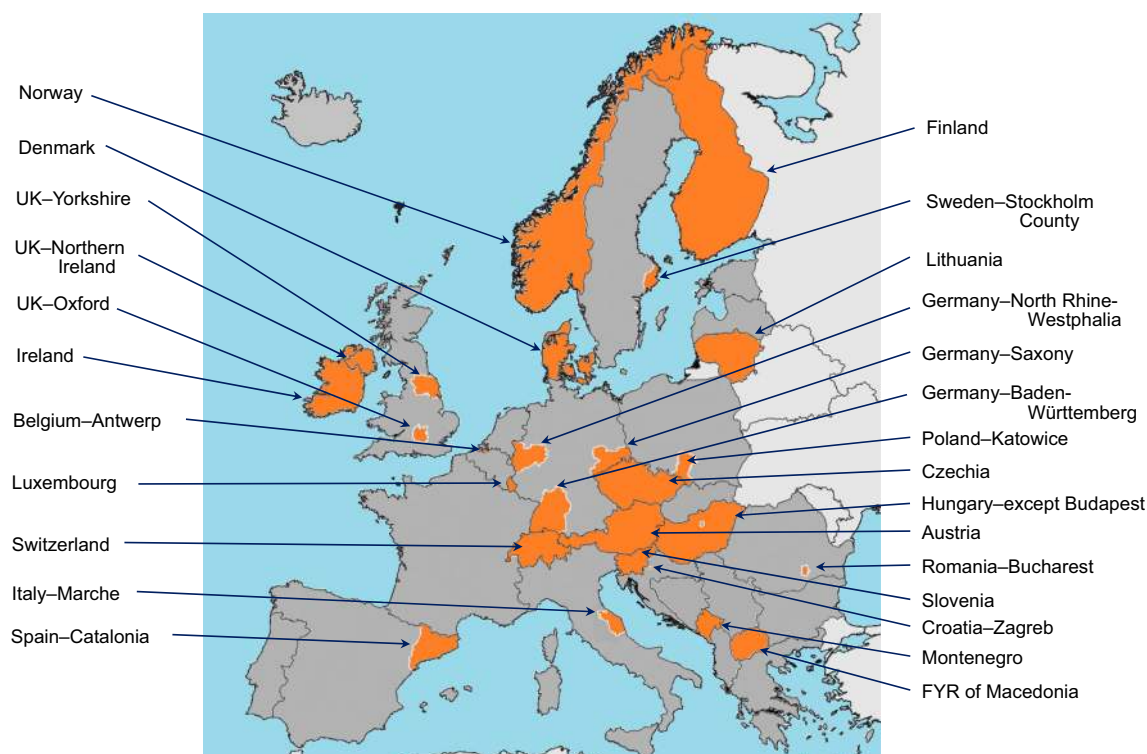

Fig. 1 Map of 26 participating EURODIAB centres (whole nations unless a region is specified). Administrative boundaries: ©EuroGeographics 2018; adapted with permission. FYR, Former Yugoslav Republic

Table 1 Incidence rates per 100,000 person-years (with standard errors) standardised for age group and sex in 5 year periods for 26 EURODIAB centres

| Centre | Years | Cases | Period | | | | | | | | | |
| | | | 1989–1993 | | 1994–1998 | | 1999–2003 | | 2004–2008 | | 2009–2013 | |
			Rate	SE	Rate	SE	Rate	SE	Rate	SE	Rate	SE
Austria–whole nation	1989–2013	4594	9.0	0.4	9.8	0.4	13.2	0.4	17.3	0.5	19.7	0.6
Belgium–Antwerp	1989–2013	610	10.9	1.2	13.0	1.3	16.4	1.4	16.3	1.4	18.1	1.5
Croatia–Zagreb	1995–2013	364	–		11.1	1.5	14.8	1.6	19.4	1.8	18.8	1.8
Czechia–whole nation	1989–2013	6528	8.5	0.3	11.5	0.4	17.1	0.5	19.3	0.5	21.8	0.5
Denmark–whole nation[a]	1989–2013	4148	17.0	1.2	16.3	1.2	22.5	0.7	25.2	0.7	27.0	0.7
Finland–whole nation	1989–2011	11,132	38.2	0.9	46.7	1.0	54.5	1.1	63.3	1.2	60.9	1.5
Germany–Baden-Württemberg	1989–2013	6931	11.0	0.4	13.0	0.4	15.4	0.4	22.0	0.5	23.1	0.6
Germany–North Rhine-Westphalia[b]	1989–2013	10,202	13.3	0.8	16.2	0.9	20.9	0.4	24.0	0.4	26.9	0.5
Germany–Saxony	1998–2013	1463	–		11.6	1.5	15.6	0.8	20.1	1.0	22.8	1.0
Hungary–except Budapest	1989–2013	4283	9.0	0.3	10.7	0.4	12.4	0.4	18.3	0.6	20.0	0.6
Ireland–whole nation	2008–2013	1566	–		–		–		27.5	1.7	27.5	0.8
Italy–Marche	1989–2013	579	9.6	1.0	11.9	1.1	12.6	1.2	12.6	1.1	11.6	1.1
Lithuania–whole nation	1989–2013	1862	7.3	0.4	8.2	0.5	10.3	0.6	14.2	0.7	19.9	0.9
Luxembourg–whole nation	1989–2013	312	11.4	1.9	12.3	1.8	15.7	2.0	18.4	2.1	18.6	2.0
Macedonia (FYR)–whole nation	1989–2013	584	3.2	0.4	3.9	0.4	6.0	0.5	7.2	0.6	7.7	0.7
Montenegro–whole nation	1996–2013	362	–		10.1	1.5	14.7	1.5	17.4	1.7	18.5	1.8
Norway–whole nation	1989–2013	6348	22.7	0.8	24.6	0.8	29.6	0.8	33.1	0.9	33.6	0.9
Poland–Katowice	1989–2013	2360	5.2	0.3	7.9	0.4	13.0	0.6	16.5	0.7	20.1	0.8
Romania–Bucharest	1989–2013	714	4.7	0.5	5.6	0.5	9.7	0.8	12.3	1.0	13.4	1.0
Slovenia–whole nation	1989–2013	949	7.8	0.6	9.1	0.7	11.1	0.8	14.9	1.0	16.3	1.1
Spain–Catalonia	1989–2013	3447	12.4	0.5	13.6	0.5	13.1	0.5	12.1	0.5	16.1	0.5
Sweden–Stockholm County	1989–2013	2704	25.8	1.3	25.6	1.3	34.5	1.4	35.1	1.4	39.6	1.5
Switzerland–whole nation	1991–2013	3020	7.9	0.5	8.3	0.4	11.0	0.4	13.1	0.5	13.4	0.5
UK–Northern Ireland	1989–2013	2652	20.0	1.0	24.7	1.1	29.9	1.3	34.2	1.4	34.4	1.4
UK–Oxford	1989–2013	2920	17.2	0.8	21.7	0.9	24.0	1.0	25.2	1.0	22.8	0.9
UK–Yorkshire	1989–2011	3660	16.1	0.7	19.7	0.7	23.5	0.8	25.5	0.9	31.0	1.2

[a] Four counties only for 1989–1998

[b] Düsseldorf region only for 1989–1998

FYR, Former Yugoslav Republic

2003, 2004–2008 and 2009–2013. The age- and sex-specific incidence rates for each period used in the calculations are shown in ESM Table 2.

As illustrated in Fig. 2, the trends in age-standardised rates differed little between the sexes. Two of the centres (Denmark and Germany–North Rhine-Westphalia) expanded their geographical coverage in 1999, and the lines for these centres are therefore shown with a break at that point, although in both cases the degree of any discontinuity appears to be minimal. In a preliminary analysis, incidence rate increases were estimated using Poisson regression analysis assuming a constant rate of increase throughout the period.

Figure 3 shows that the rate of increase was highest in the Poland–Katowice centre (6.6% per annum) and the lowest in the Spain–Catalonia centre (0.5% per annum). Except for the Ireland and Italy–Marche centres, all rates of increase were significantly greater than zero. A significant inverse relationship was found between the rate of increase in each centre and its directly standardised rate during the entire period (Spearman's rank correlation coefficient, $r_s = -0.45$, $p = 0.02$), indicating that the percentage increase in rate tended to be lower in centres with higher rates. A comparison of rates of increase between the sexes within each centre revealed differences in three centres, each showing a significantly higher rate of increase in boys than girls. A comparison of rates of increase between age groups within each centre revealed differences in nine centres, and in six of the nine the highest rate of increase was found in the 0- to 4-year-old age group. Full details are available in ESM Table 3.
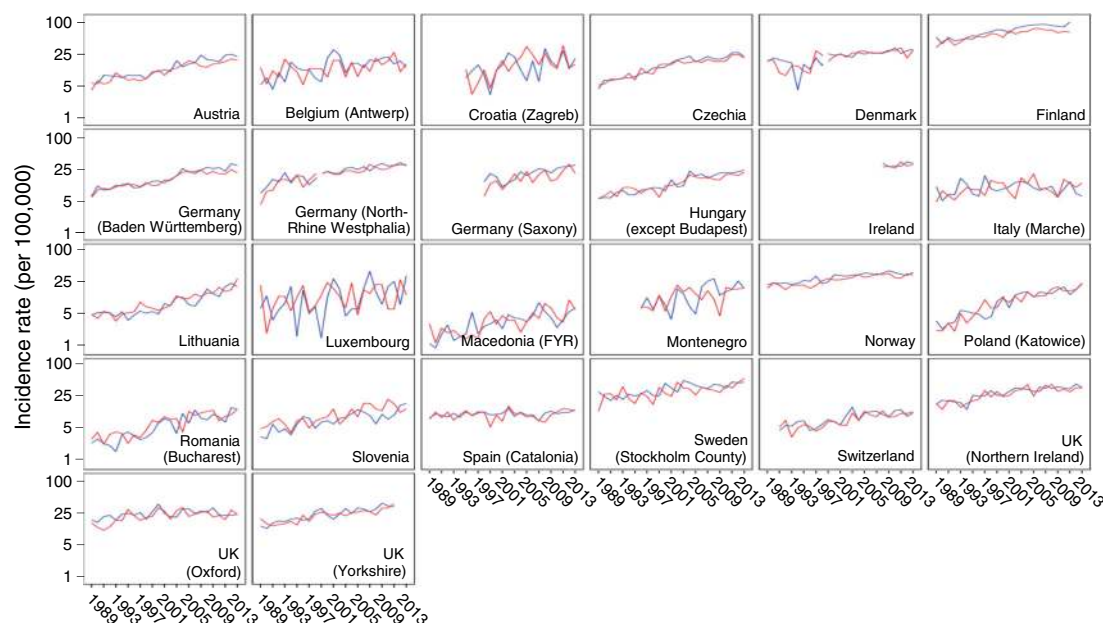
Fig. 2 Trends in age-standardised incidence rates, plotted on a logarithmic scale, by sex for type 1 diabetes in 26 European centres during 1989–2013. Blue lines, boys; red lines, girls. Breaks are shown for Denmark and Germany (North Rhine-Westphalia) between 1998 and 1999 because of increased coverage of these registers, but any discontinuities appear to be very minor. Macedonia (FYR), Former Yugoslav Republic of Macedonia

Mixed effects Poisson regression provided estimated rates of increase in the pooled data from the 26 centres, as shown in Table 2. Overall, the annual rate of increase was estimated to be 3.4% (95% CI 2.8%, 3.9%). Rates of increase were similar in boys and girls in the 0- to 4-year-old age group (3.7% and 3.7% per annum, respectively) and in the 5- to 9-year-old age group (3.4% and 3.7% per annum, respectively), but were higher in boys than girls in the 10- to 14-year-old age group (3.3% and 2.6% per annum, respectively). The estimates of overall rate of increase by period suggested a slowing in 2004–2008, but the rate of increase appeared to have almost returned to previous levels in the 2009–2013 period.

Fig. 3 Estimated rates of annual increase in type 1 diabetes in 26 European centres. Rates of increase in individual centres were derived from Poisson regression analyses with adjustment for age, sex, age × sex interaction and inclusion of a log-linear term for year in the model. The overall pooled estimate was derived from a Poisson regression with centre as a random effect. FYR, Former Yugoslav Republic; N., North
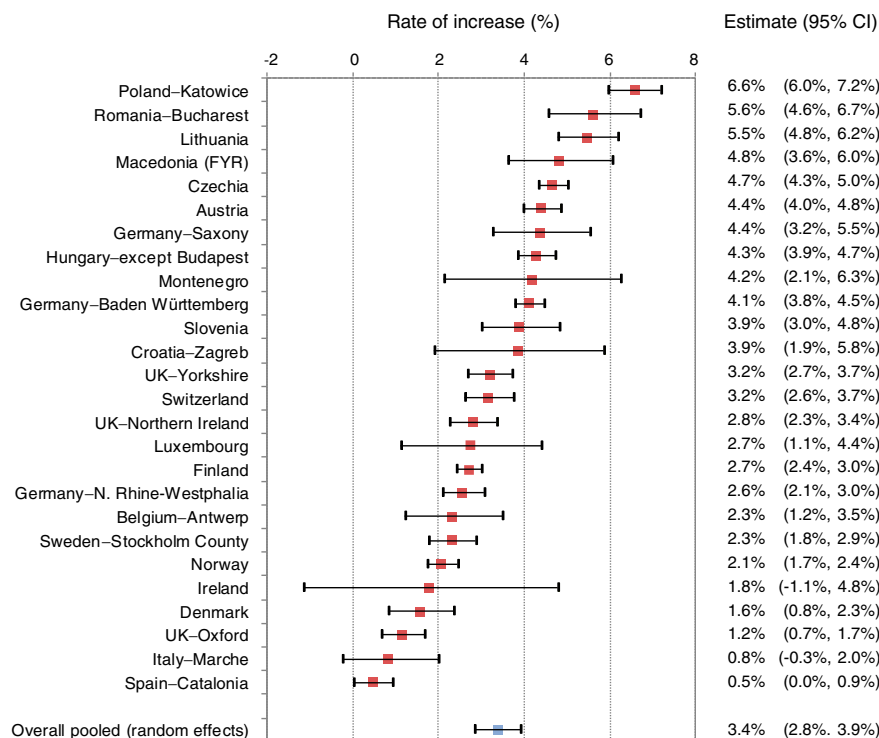

	Rate of increase (%)	Estimate (95% CI)
Poland–Katowice		6.6% (6.0%, 7.2%)
Romania–Bucharest		5.6% (4.6%, 6.7%)
Lithuania		5.5% (4.8%, 6.2%)
Macedonia (FYR)		4.8% (3.6%, 6.0%)
Czechia		4.7% (4.3%, 5.0%)
Austria		4.4% (4.0%, 4.8%)
Germany–Saxony		4.4% (3.2%, 5.5%)
Hungary–except Budapest		4.3% (3.9%, 4.7%)
Montenegro		4.2% (2.1%, 6.3%)
Germany–Baden Württemberg		4.1% (3.8%, 4.5%)
Slovenia		3.9% (3.0%, 4.8%)
Croatia–Zagreb		3.9% (1.9%, 5.8%)
UK–Yorkshire		3.2% (2.7%, 3.7%)
Switzerland		3.2% (2.6%, 3.7%)
UK–Northern Ireland		2.8% (2.3%, 3.4%)
Luxembourg		2.7% (1.1%, 4.4%)
Finland		2.7% (2.4%, 3.0%)
Germany–N. Rhine-Westphalia		2.6% (2.1%, 3.0%)
Belgium–Antwerp		2.3% (1.2%, 3.5%)
Sweden–Stockholm County		2.3% (1.8%, 2.9%)
Norway		2.1% (1.7%, 2.4%)
Ireland		1.8% (−1.1%, 4.8%)
Denmark		1.6% (0.8%, 2.3%)
UK–Oxford		1.2% (0.7%, 1.7%)
Italy–Marche		0.8% (−0.3%, 2.0%)
Spain–Catalonia		0.5% (0.0%, 0.9%)
Overall pooled (random effects)		3.4% (2.8%. 3.9%)

Table 2 Annual increases in incidence rate over a 25 year period pooled over centres as estimated by mixed effects Poisson regression in subgroups defined by age group, sex and time period

Subgroup	Annual increase (%)	(95% CI)
Boys		
0–4 years old	3.7	(3.0, 4.4)
5–9 years old	3.4	(2.7, 4.0)
10–14 years old	3.3	(2.8, 3.8)
0–14 years old	3.5	(2.9, 4.0)
Girls		
0–4 years old	3.7	(2.9, 4.5)
5–9 years old	3.7	(3.2, 4.2)
10–14 years old	2.6	(2.2, 3.0)
0–14 years old	3.3	(2.8, 3.8)
Period		
1989–1993	4.1	(2.7, 5.6)
1994–1998	3.2	(1.9, 4.5)
1999–2003	4.1	(3.1, 5.2)
2004–2008	1.1	(0.2, 2.1)
2009–2013	2.7	(1.7, 3.7)
1989–2013[a]	3.4	(2.8, 3.9)

[a] Overall time period

The fitted Joinpoint segmented regression analyses for each centre are presented in ESM Fig. 1. The best fit for 18 of the 26 centres throughout the period was a log-linear increase in the age-standardised rate. Six centres showed more rapid increases in an early period followed by lower rates of increase in a later period. In two Central European centres (Czechia and Poland–

Katowice), the change took place in 2002, at roughly the same time as in two UK centres (UK–Oxford in 2000 and UK–Northern Ireland in 2003). In two Scandinavian centres (Finland and Norway), the levelling off took place a little later, in the years 2005 and 2007, respectively. Only in a single centre (Lithuania) was an initially low rate of increase followed by a period after 1996 with a higher rate of increase. The final centre (Germany–Baden-Württemberg) showed a more complex pattern, with steady rates of increase in the early and late part of the 25 year period separated by a short period of more rapid increase in 2001–2004.

Poisson regression results provided most support for a 4 year periodicity, with four centres giving likelihood ratio tests that attained significance at the reduced $p < 0.01$ level (to allow for multiple testing) compared with none for a 5 year periodicity and two for a 6 year periodicity (tests of significance summarised in ESM Table 4). Plots of the observed age-standardised annual incidence rates and the fitted rates for 4 year cycles are shown in Fig. 4 for these four centres. One of the four centres showed its most recent peak in fitted incidence rate in 2011 (Switzerland, with an amplitude of ±10% superimposed on the log-linear increasing trend), while the three remaining centres showed the most recent peaks in 2012 (Germany–North Rhine-Westphalia with an amplitude of ±5%, Germany–Saxony with an amplitude of ±15% and UK–Oxford with an amplitude of ±9%).

Discussion

Our analyses of individual centre results confirmed the recent slowing of incidence rate increases in some high-incidence

Fig. 4 Observed (continuous blue line) and fitted (red dashed line) standardised incidence rates (per 100,000 person-years) obtained by Poisson regression in four centres that showed significant ($p < 0.01$) 4 year periodicity when superimposed on long-term Joinpoint segmented regression trends: (**a**) Germany–North Rhine-Westphalia; (**b**) Germany–Saxony; (**c**) Switzerland; (**d**) UK–Oxford
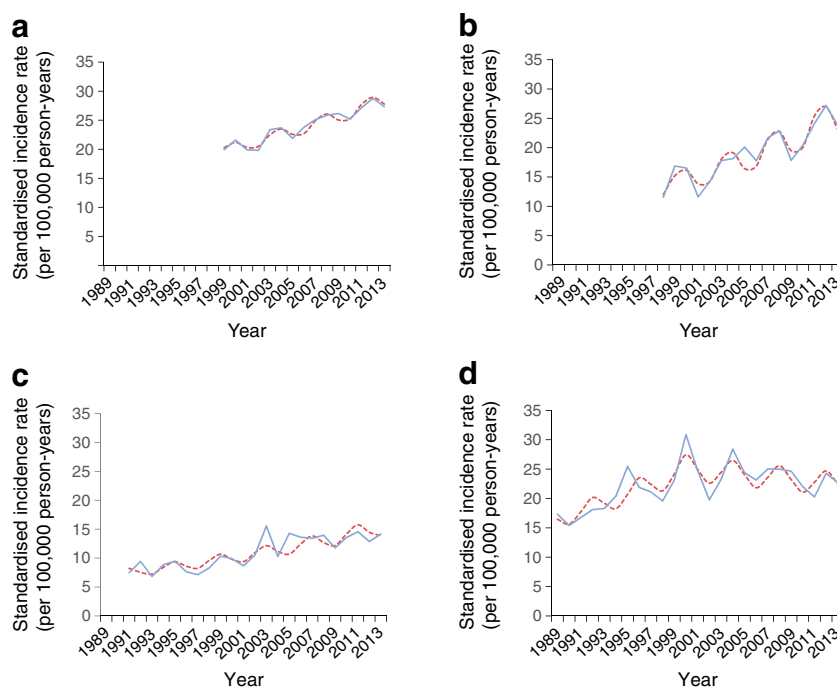
areas such as Finland [7] and Norway [8], but using only data from Stockholm County we were unable to detect the same pattern that had previously been reported from Sweden [6]. Two of the three centres from the UK, another country with high rates, also showed reducing rates of increase, although these seemed to have begun a few years earlier than in Scandinavia.

Our pooled estimates suggest that, despite some high-risk countries showing some slowing in the rate of increase in recent years, the overall pattern is still one of an approximately 3% per annum increase, although with a possible temporary slowing in the 2004–2008 period. As previously noted in our 15 year analysis, the rate of increase in girls aged 10–14 years is less marked than in other age/sex subgroups [1].

Our analysis shows that, in the majority of centres, a steady log-linear increase in rates with time provided a good description of the temporal changes, with only a few (mainly high-incidence) areas showing some evidence of non-uniformity. The cyclical pattern in incidence observed in four of our 26 centres is consistent with the earliest report of a 4 year cyclical incidence pattern [10], but subsequent reports have described 5 year or 6 year periodicities [11–13], for which we found little support in our data.

No clear rationale for periodicity has yet been proposed and, to the authors' knowledge, no climatological factor [18], viral infection [19] or other environmental exposure has yet been firmly established that exhibits such a cyclical pattern. Since autoimmunity and progressive beta cell destruction typically start long before the clinical diagnosis of type 1 diabetes, the periodicity in diagnosis could be indicative of cycles of infectious disease that accelerate the diagnosis rather than initiate the disease. Regular cycles of infectious diseases are well known from classic work done before population-wide vaccination for measles, an extremely contagious viral disease of childhood; this research showed that, in an otherwise stable population, epidemic cyclicity depends on community size [20].

It is also unclear why only a small proportion of the 26 centres showed this periodicity and, although we acknowledge that power may be limited in smaller centres, it was not apparent in many of the largest centres that might be expected to have had a high power to detect it. This could perhaps suggest that it may have more localised origins. What determines this localisation remains enigmatic, as cyclical patterns were absent in Austria, Czechia and Germany–Baden-Württemberg, three large registers each with neighbouring areas where pronounced cyclical patterns were noted. It is possible that not only the size of the population, but also its spatial structure (i.e. the size of the communities, and their mutual links) may play an important role in the ability of the hypothetical infectious accelerator to be transmitted [21].

To our knowledge, among autoimmune conditions, only incidence cycles in juvenile idiopathic arthritis have been correlated to cycles of serologically confirmed microbial agents—in a Canadian study, peak incidences of arthritis were concurrent with peaks of *Mycoplasma pneumoniae*, whereas no such phenomenon was noted for the incidence of seronegative (i.e. non-immune mediated) spondyloarthropathies [22]. The recent report of a twofold risk of type 1 diabetes diagnosed by the age of 30 years among those with laboratory-confirmed pandemic influenza A (H1N1) [23] may stimulate interest in less consistent patterns of incidence peaks in type 1 diabetes since localised seasonal influenza epidemics (as opposed to much rarer pandemics) can occur at irregular intervals [24].

Most of the participating registers have maintained their completeness of coverage at levels in excess of 90% in the most recent 5 year period, but these estimates of completeness rely on an assumption of independence in the primary and secondary sources that is very difficult to verify. As more sophisticated information systems for drug prescribing and clinical management become available, it seems likely that the traditional approach based on notification of individual new diagnoses will give way to more automated approaches that take advantage of these information systems.

Although it could be argued that the diagnosis of type 1 diabetes should ideally be confirmed by the presence of one or more specific autoimmune markers [25], this is seldom done in clinical practice, and we have therefore continued to use a pragmatic definition of type 1 diabetes based on clinical judgement. A UK study found that all but 8 (3%) of 256 clinically diagnosed cases of type 1 diabetes in individuals aged 20 years or younger were positive for one or more of four antibodies [26], but the case for routine antibody testing at diagnosis is not compelling [27]. Individuals diagnosed before 6 months of age now tend to be routinely investigated for monogenic forms of the disease [28], but the number of such cases is very small. Findings in the literature on whether or not type 2 diabetes is becoming more common in children and adolescents are inconsistent [29–31], but the distinction between the two types of diabetes is generally not difficult in the paediatric age group. Furthermore, European studies [30–33] confirm that the rate of type 2 diabetes is a small fraction of that of type 1 diabetes, and we do not therefore feel that misclassification of type 2 diabetes represents a serious challenge to the validity of our findings.

The use of mixed effects Poisson regression, in which age group and sex are considered as fixed effects but centre is treated as a random effect, gives similar estimates of the increase in incidence rate to the more conventional fixed effects analysis that we have used in previous analyses; however, confidence limits for the mixed effects model tend to be rather wider and should give a fairer reflection of uncertainty in the estimates of incidence rate increase. Taking into account the uncertainty associated with our overall incidence rate increase of 3.4% (95% CI 2.8%, 3.9%), we may expect to see a doubling in European incidence in between 18 and 25 years if the trends evident in the last 25 years are maintained.

The steadily increasing number of children being diagnosed with this chronic disease, which is associated with well-documented, life-long increases in morbidity and mortality, has important implications for those planning and delivering healthcare. The limited success in identifying either environmental causes or gene–environment interactions that could eventually lead to disease prevention means that efforts must continue to improve quality of care to help reduce long-term complications and diabetes-related deaths. Key to this is the improvement in glycaemic control that will be achieved not only by more sophisticated methods of insulin delivery, but also by an increased investment in services to support well-trained and dedicated care teams in sufficient numbers to meet the growing needs of this group of children and their families.

The EURODIAB childhood type 1 diabetes registers, with their wide, population-based coverage of European regions of differing incidence, and their high levels of case ascertainment, will continue to provide a valuable source of data for monitoring the future incidence of childhood type 1 diabetes.

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