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Incidence and trends of childhood Type 1 diabetes worldwide 1990–1999

The DIAMOND Project Group

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Abstract

Aims To examine incidence and trends of Type 1 diabetes worldwide for the period 1990–1999.

Methods The incidence of Type 1 diabetes (per 100 000/year) was analysed in children aged ≤ 14 years from 114 populations in 112 centres in 57 countries. Trends in the incidence of Type 1 diabetes were analysed by fitting Poisson regression models to the dataset.

Results A total of 43 013 cases were diagnosed in the study populations of 84 million children. The age-adjusted incidence of Type 1 diabetes among 112 centres (114 populations) varied from 0.1 per 100 000/year in China and Venezuela to 40.9 per 100 000/year in Finland. The average annual increase in incidence calculated from 103 centres was 2.8% (95% CI 2.4–3.2%). During the years 1990–1994, this increase was 2.4% (95% CI 1.3–3.4%) and during the second study period of 1995–1999 it was slightly higher at 3.4% (95% CI 2.7–4.3%). The trends estimated for continents showed statistically significant increases all over the world (4.0% in Asia, 3.2% in Europe and 5.3% in North America), except in Central America and the West Indies where the trend was a decrease of 3.6%. Only among the European populations did the trend in incidence diminish with age.

Conclusions The rising incidence of Type 1 diabetes globally suggests the need for continuous monitoring of incidence by using standardized methods in order to plan or assess prevention strategies.

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Keywords epidemiology, geographical distribution, incidence, trend, Type 1 diabetes

Introduction

The World Health Organization began the Multinational Project for Childhood Diabetes (DIAMOND) in 1990 [1]. Since then, standardized incidence data on Type 1 diabetes have been collected within the WHO DIAMOND Project until the year 1999.

The report on incidence of childhood Type 1 diabetes from 1990 to 1994 showed even larger global variation in incidence among children ≤ 14 years of age than was reported previously in the 1970s and 1980s [2–7]. During the first half of the 1990s, the overall age-adjusted incidence of Type 1 diabetes varied from 0.1 in China and Venezuela to 37 per 100 000/year in Sardinia and in Finland, representing a variation of over 350-fold in the incidence in the 100 populations worldwide. The variation in the incidence of Type 1 diabetes seemed to reflect the global distribution of major ethnic populations which demonstrate a different degree of genetic susceptibility to diabetes. However, large differences in incidence have been reported from European populations living in relatively close proximity and in those who are genetically similar [8,9]. The rapid increase in the incidence of Type 1 diabetes has been almost a global phenomenon during the last decades [8,10].

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In this study we investigated the age- and sex-specific incidence of Type 1 diabetes and trends in incidence between 1990 and 1999 worldwide.

Materials and methods

The detailed plan and organizational structure of the WHO DIAMOND incidence study have been described in previous reports [1,2]. Each of the participating centres is headed by a local principal investigator, who is responsible for data collection and the day-to-day aspects of the fieldwork (see Appendix). To be eligible to participate in the WHO DIAMOND study [1], each centre must have a well-defined population-based registry where the incidence can be accurately ascertained. Every centre prepared its own local methods of operation for the incidence study by following the framework provided by the WHO DIAMOND incidence study. In the local methods of operation, centres described the population base, the design of the registry, sources of data, data management, data items, and the time schedule for data collection. This analysis includes 112 centres from 57 countries. Most European countries included in the DIAMOND study are members of the EURODIAB Study Group [6].

Incidence study population

The total number of children aged 14 years or under living in the countries collaborating in the WHO DIAMOND incidence study was 740 million in 1996. The denominator for the analyses which included the children ≤ 14 years of age who resided in the study areas averaged 84 million per year. The numerator comprises 43 013 children ≤ 14 years of age diagnosed with Type 1 diabetes between the years 1990 and 1999 in the study areas.

Classification and case definition

The 1985 WHO classification of diabetes and the diagnostic criteria [11] are the basis of the minimum set of criteria for the WHO DIAMOND incidence study. Eligible individuals began daily insulin injections before their 15th birthday and were resident in the area of registration at the time of the first insulin administration. Registries are either prospective, retrospective or a combination of both. Participating centres have submitted annual incidence data to the WHO DIAMOND data centre in Helsinki using standardized forms. Data on gender, ethnic group, date of birth, date of first insulin administration, source of data (primary, secondary), family history of diabetes (the diabetic status of siblings, parents and children of registered cases) are collected. All the cases included in the database must have data at least on gender, the date of birth and the date of first insulin administration.

Completeness of registration was confirmed by estimating the degree of ascertainment using the capture–recapture method [12] in most centres. In some centres (see Fig. 1) this was not necessary as a result of complete coverage of the primary source. According to the WHO DIAMOND methods of operation, the primary data source consists of the cases of Type 1 diabetes who fulfil the criteria for registration and have been identified from hospital records, or from the records of paediatrician or family physician. Records of the local diabetes association, school health records or social insurance schemes have been used as a secondary (independent) source for cases.

Statistical methods

Incidence rates were calculated as the incidence per calendar year and 100 000 population at risk without adjustment for under-reporting. Age adjustment for the rates was carried out using the direct method with a standard population consisting of equal numbers of children in each of the three age groups (0–4, 5–9, 10–14 years of age). The 95% confidence intervals were estimated assuming the Poisson distribution of the cases. The incidence rates were divided into five groups, as in our earlier report: (i) very low, < 1 per 100 000/year; (ii) low, 1–4.99 per 100 000/year; (iii) intermediate, 5–9.99 per 100 000/year; (iv) high, 10–19.99 per 100 000/year, and (v) very high, ≥ 20 per 100 000/year [2].

Poisson regression models were used to analyse the incidence rates by centre, gender, age, and calendar year, and their interactions. Models were fitted using the S-PLUS.

Results

Incidence of Type 1 diabetes

During the period 1990–1999, the overall age-adjusted incidence of Type 1 diabetes in 112 centres (114 populations) varied from 0.1/100 000/year in China and Venezuela to 40.9 per 100 000/year in Finland (Table 1, Fig. 1). In most Asian populations the incidence was very low; 70% of them having an incidence of < 1 per 100 000/year. A marked exception among the Asian populations was Kuwait, with a very high incidence of 22 per 100 000/year. Among African populations, incidence was low or intermediate, ranging between 1 per 100 000/year and 9 per 100 000/year. The incidence among South American populations varied between very low to high, < 1 per 100 000/year to 10 per 100 000/year. In Central America and the West Indies, the range of variation was from 2 per 100 000/year to 17 per 100 000/year. The highest incidence rates were among European and North American populations varying from low, 4 per 100 000/year, to very high, 41 per 100 00/year, in Europe and from high, 11 per 100 000/year, to very high, 25 per 100 000/year, in North America. In Oceania, the incidence of Type 1 diabetes was also high or very high, ranging from 14 per 100 000/year to 22 per 100 000/year, reflecting difference in the ethnicity of populations within this region. There was also a marked within-country variation in the age-adjusted incidence in most of countries having data from at least two centres (Table 1).

Age and sex differences in incidence

The age-specific incidence rates were calculated for three age groups (0–4, 5–9 and 10–14 years) separately for boys and

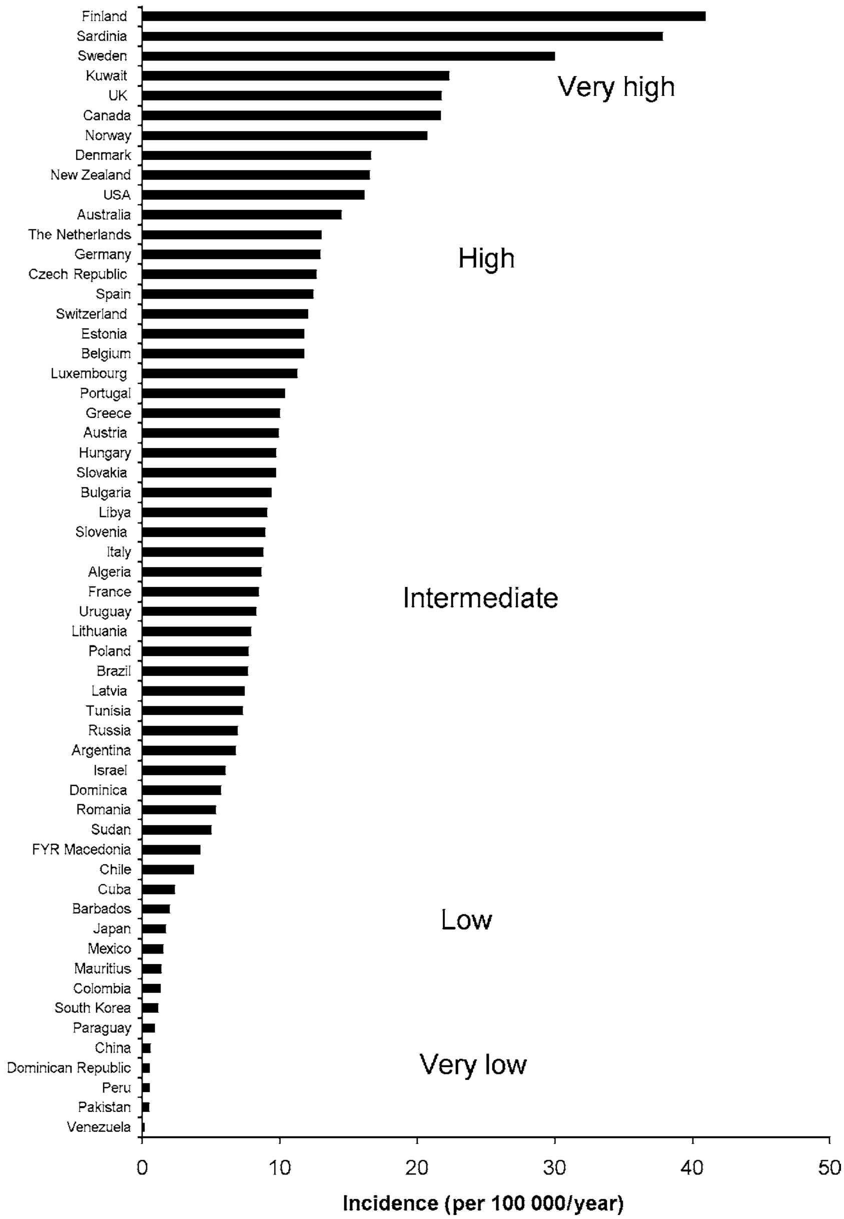

Figure 1 Age-standardized incidence of Type 1 diabetes in children under 14 years of age (per 100 000 per year). Countries are arranged in descending order according to the incidence.

girls On the whole, there were no marked differences in age-group specific incidence between the genders. The differences in incidence rates between age groups were statistically significant ($P < 0.001$) in almost all countries. In general, the incidence increased with age (Table 2). In the pooled data, the 5–9-year olds had 1.62 (1.57–1.66) times higher risk, and the 10–14-year olds 1.94 (1.89–1.98) times higher risk than that of the 0–4-year olds. The effect of age on the incidence did not differ between the genders. The exceptions were two countries of very high incidence, namely Finland and Sweden, and two countries with intermediate incidence, i.e. Romania and Lithuania. In all these countries, the age-specific incidence rates increased from 0 to 4 years to 10–14 years among boys, whereas among girls incidence increased only from the age group 0–4 years to the ages 5–9 years.

The global trend in the incidence of Type 1 diabetes

The mean annual increase in incidence calculated from 103 centres (submitted data for 3 years or more) was 2.8% (95% CI 2.4–3.2%; Table 3). In the first 5-year study from 1990 to 1994, the average annual increase was 2.4% (1.3–3.4%). During the second study period from 1995 to 1999, the annual increase was higher at 3.4% (2.7–4.3%), but the difference in the trend between periods was not statistically significant.

The trend in incidence did not differ significantly between genders, except in Kuwait, Bulgaria, and Cuba. In Kuwait, the annual increase was 2.9% (–2.4 to 8.6%) in boys and 11.2% (5.4–17.4%) in girls, in Bulgaria there was an increase of 7.5% (4.2–10.8%) in boys and an increase of 2.4% (–0.9 to 5.9%)

Table 1 Age-standardized incidence of Type 1 diabetes in children aged 14 years or under (per 100 000/year)

			Incidence					Annual change of incidence	
Region Country and area	Study period	Estimate of ascertainment %	Boys	Girls	Total	(95% CI)	Boys/girls	%	(95% CI)
Africa								3.0	(0.3; 5.8)
Algeria								11.6	(5.5; 18.0)
Oran*	1990–1999		7.7	9.6	8.6	(7.6; 9.8)	0.8		
Libya								–0.9	(–5.6; 4.0)
Benghazi	1991–1999		7.8	10.3	9.0	(8.0; 10.2)	0.8		
Mauritius	1990–1994	35–100	1.2	1.4	1.3	(0.8; 2.0)	0.9	–2.2	(–27.8; 32.3)
Sudan									
Gezira	1990	100	5.6	4.4	5.0	(3.8; 6.5)	1.3		
Tunisia								0.7	(–3.5; 5.2)
Beja*	1990–1999		8.4	6.9	7.7	(6.1; 9.6)	1.2		
Gafsa*	1990–1999		9.5	7.5	8.5	(6.9; 10.3)	1.3		
Kairoan*	1991–1993		7.3	7.8	7.6	(5.6; 10.0)	0.9		
Monastir*	1990–1999		6.6	5.1	5.8	(4.6; 7.3)	1.3		
Asia								4.0	(1.8; 6.2)
China								–0.1	(–5.7; 5.8)
Beijing*	1990–1994		0.7	1.1	0.9	(0.7; 1.1)	0.6†		
Chang Chun	1990–1994	86–100	0.6	1.1	0.8	(0.5; 1.3)	0.6		
Changsha	1990–1994	100	0.2	0.2	0.2	(0.2; 0.4)	1.3		
Dalian	1990–1994	100	1.1	1.2	1.2	(0.7; 1.7)	0.9		
Guilin	1991–1994	100	0.6	1.0	0.8	(0.2; 2.0)	0.6		
Hainan	1990–1994	100	0.1	0.2	0.2	(0.1; 0.2)	0.5		
Harbin	1990–1996	100	0.6	0.6	0.6	(0.4; 0.8)	1.0		
Hong-Kong*	1990–1995		0.6	1.9	1.3	(0.8; 1.9)	0.3†		
Huhehot	1990–1994	100	1.1	0.7	0.9	(0.5; 1.5)	1.5		
Jilin	1990–1994	100	0.4	0.8	0.6	(0.4; 0.9)	0.5		
Jinan	1990–1995	100	0.5	0.4	0.4	(0.3; 0.6)	1.1		
Lanzhou	1991–1994	100	0.4	0.2	0.3	(0.1; 0.5)	1.9		
Nanjing	1990–1995	100	0.5	1.2	0.9	(0.6; 1.2)	0.5		
Nanning	1990–1994	100	0.3	0.7	0.5	(0.3; 0.8)	0.4		
Shanghai	1990–1994	69–100	0.7	0.7	0.7	(0.5; 0.9)	0.9		
Shenyang	1990–1994	100	0.4	0.5	0.5	(0.3; 0.7)	0.9		
Sichuan	1990–1994	80–100	1.8	2.7	2.3	(1.4; 3.3)	0.7		
Tie Ling	1990–1994	100	0.2	0.1	0.2	(0.1; 0.3)	1.0		
Wuhan	1990–1994	100	5.2	3.8	4.5	(2.8; 7.0)	1.5		
Wulumuqi	1990–1994	100	0.9	0.8	0.8	(0.3; 1.7)	1.2		
Zhengzhou	1991–1994	86–100	0.2	1.0	0.6	(0.3; 1.1)	0.2		
Zunyi	1990–1995	100	0.0	0.1	0.1	(0.0; 0.2)	0.6		
Israel‡	1990–1993	100	5.5	6.6	6.0	(5.4; 6.7)	0.8†	7.6	(–2.0; 18.1)
Japan								–3.5	(–15.7; 10.6)
Chiba*	1990–1993		1.2	1.6	1.4	(1.1; 1.8)	0.8		
Hokkaido	1990–1993	100	2.2	2.1	2.2	(1.7; 2.6)	1.0		
Okinawa	1990–1993	77–100	1.0	1.8	1.4	(0.8; 2.2)	0.6		
Kuwait	1992–1999	79–96	21.7	22.9	22.3	(20.5; 24.2)	1.0	7.0	(3.0; 11.1)
Pakistan								–5.6	(–11.2; 0.3)
Karachi	1990–1999	51	0.4	0.5	0.5	(0.3; 0.5)	0.8		
Russia								6.6	(3.0; 10.3)
Novosibirsk	1990–1999	87–100	6.8	7.1	6.9	(6.3; 7.6)	1.0		
South Korea									
Seoul*	1990–1991		1.1	1.2	1.1	(0.9; 1.5)	0.9		
Europe								3.2	(2.7; 3.6)
Austria‡	1990–1999	99–100	10.3	9.5	9.9	(9.4; 10.4)	1.1	2.1	(–0.4; 4.8)
Belgium‡								1.5	(–3.4; 6.7)
Antwerpen	1990–1999	90–100	10.7	12.8	11.7	(10.2; 13.5)	0.8		
Bulgaria								5.1	(2.8; 7.5)
Varna	1990–1999	100	7.9	8.3	8.1	(7.4; 9.0)	1.0		
West-Bulgaria	1990–1999	99–100	11.6	9.8	10.7	(9.8; 11.6)	1.2†		
Czech Republic‡	1995–1999		12.6	12.7	12.7	(11.9; 13.5)	1.0	9.6	(5.2; 14.2)

Table 1 *Continued*

Region Country and area	Study period	Estimate of ascertainment %	Incidence				Boys/girls	Annual change of incidence	
			Boys	Girls	Total	(95% CI)		%	(95% CI)
Denmark‡								15	(–2.6; 5.7)
Four counties	1990–1999	83–100	17.1	16.2	16.6	(14.9; 18.4)	1.1		
Estonia*	1990–1999		12.6	10.9	11.7	(10.6; 13.0)	1.1	3.7	(0.1; 7.5)
Finland*	1990–1999		41.9	39.9	40.9	(39.6; 42.2)	1.1†	4.2	(3.1; 5.3)
France‡								4.8	(–0.5; 10.5)
Four regions	1990–1994	95–99	8.7	8.3	8.5	(7.9; 9.1)	1.1		
FYR Macedonia‡	1995–1999		4.9	3.5	4.2	(3.4; 5.2)	1.4	9.7	(–9.6; 33.2)
Germany‡								2.3	(0.8; 3.8)
Düsseldorf	1995–1999	97–98	14.8	16.1	15.4	(13.8; 17.2)	0.9		
Baden-Württemberg	1990–1999	91–100	12.7	12.6	12.6	(12.1; 13.2)	1.0		
Greece‡								0.9	(–2.0; 3.8)
Attica	1990–1999	100	11.0	9.0	10.0	(9.2; 10.9)	1.2†		
Hungary‡								2.6	(0.8; 4.5)
Eighteen counties	1990–1999	99–100	9.6	9.8	9.7	(9.2; 10.2)	1.0		
Italy								0.9§	(–0.9; 2.7)
Lazio‡*	1990–1999		8.9	8.6	8.8	(8.1; 9.4)	1.0		
Lombardia‡	1990–1995	100	7.2	6.5	6.9	(6.3; 7.5)	1.1		
Marche	1990–1999	100	10.5	9.7	10.1	(8.8; 11.6)	1.1		
Pavia	1990–1999	100	12.3	12.5	12.4	(9.7; 15.6)	1.0		
Sardinia‡	1990–1998	37–85	45.0	30.6	37.8	(35.5; 40.3)	1.5	1.4	(–1.1; 3.9)
Eastern Sicily‡	1990–1994	96–100	13.4	9.9	11.7	(9.8; 13.9)	1.3		
Turin	1990–1999	97–100	11.7	10.3	11.0	(9.8; 12.3)	1.1		
Latvia	1990–1999		7.8	7.0	7.4	(6.6; 8.3)	1.1	3.1	(–0.6; 6.8)
Lithuania	1990–1999	100	7.6	8.2	7.9	(7.3; 8.5)	0.9	2.5	(–0.2; 5.3)
Luxemburg‡	1990–1999	100	10.3	12.2	11.3	(9.0; 13.9)	0.8	–0.1	(–7.2; 8.1)
The Netherlands‡								3.4	(–4.0; 11.3)
Five regions	1990–1994	87–98	12.9	13.2	13.0	(11.7; 14.4)	1.0		
Norway‡								–0.9	(–3.2; 1.4)
Eight counties	1990–1999	91–100	21.6	19.9	20.8	(19.4; 22.1)	1.1		
Poland								7.6	(4.9; 10.4)
Cracow*	1990–1999	100	7.5	7.6	7.6	(7.0; 8.2)	1.0		
Upper Silesia‡	1995–1999		8.0	9.5	8.8	(7.9; 9.7)	0.8		
Wielkopolska	1990	100	4.1	6.0	5.0	(3.9; 6.4)	0.7		
Portugal								2.0	(–4.1; 8.4)
Algarve‡	1990–1994	74–100	16.3	12.9	14.6	(10.6; 19.6)	1.3		
Coimbra	1990–1999	100	10.1	9.1	9.6	(7.6; 12.2)	1.1		
Madeira Island‡	1990–1999	100	7.1	6.8	6.9	(5.0; 9.4)	1.1		
Portalegre‡	1990–1994	86–100	15.9	26.7	21.3	(13.3; 31.9)	0.6		
Romania‡								2.8	(–3.9; 10.0)
Bucharest	1990–1999	100	4.7	5.9	5.3	(4.7; 6.1)	0.8		
Slovakia	1990–1999	100	9.7	9.7	9.7	(9.2; 10.3)	1.0	6.3	(4.3; 8.5)
Slovenia‡	1990–1999	100	8.3	9.5	8.9	(8.0; 9.9)	0.9	3.3	(–0.5; 7.2)
Spain								–1.9	(–3.7; 0.0)
Catalonia	1990–1999	50–96	12.6	12.3	12.4	(11.7; 13.1)	1.0		
Sweden*	1990–1999	100	30.5	29.4	30.0	(29.1; 30.8)	1.0	3.6	(2.6; 4.7)
Switzerland‡	1995–1999		13.3	10.7	12.0	(11.2; 12.9)	1.2†	2.1	(–3.1; 7.5)
UK								4.0	(3.0; 5.0)
Scotland (Aberdeen)	1990–1999	100	26.8	25.9	26.4	(25.4; 27.4)	1.0		
Leicestershire‡	1990–1994	97–100	15.4	15.3	15.3	(12.9; 18.1)	1.0		
Northern Ireland‡	1990–1999	95–100	21.5	21.2	21.3	(19.9; 22.8)	1.0		
Oxford‡*	1990–1994		20.1	15.3	17.7	(16.2; 19.5)	1.3†		
Plymouth	1990–1999	96–100	17.1	20.8	19.0	(16.8; 21.2)	0.9		
Yorkshire‡	1990–1999	99	18.9	18.1	18.5	(17.5; 19.5)	1.0		
North America								5.3	(3.3; 7.3)
Canada								5.1	(1.9; 8.5)
Edmonton	1990–1996	75–96	23.0	23.6	23.3	(20.5; 26.4)	1.0		
Calgary	1990–1999	100	20.3	20.9	20.6	(18.5; 22.7)	1.0		
Prince Edward Island*	1990–1993	100	28.0	20.8	24.5	(16.4; 35.2)	1.3		

Table 1 *Continued*

Region Country and area	Study period	Estimate of ascertainment %	Incidence Boys	Girls	Total	(95% CI)	Boys/girls	Annual change of incidence %	(95% CI)
USA								5.5	(3.0; 8.0)
Allegheny, PA	1990–1994	87–100	19.1	16.4	17.8	(15.5; 20.3)	1.2		
Chicago, IL									
African-American	1990–1999	51–100	15.2	19.4	17.3	(15.8; 18.7)	0.8†		
Hispanic	1990–1999	51–100	11.7	11.1	11.4	(10.1; 12.9)	1.1		
Others	1995–1999	> 75	19.0	17.5	18.3	(15.7; 22.2)	1.1		
Jefferson, AL*	1990–1995		14.1	15.1	14.6	(12.2; 18.2)	0.9		
South America								5.3	(2.8; 7.9)
Argentina								0.4	(–8.8; 10.5)
Avellaneda	1990–1996	88–100	5.3	7.2	6.3	(5.7; 11.1)	0.7		
Cordoba	1991–1992	88–92	6.2	7.9	7.0	(5.2; 9.3)	0.8		
Corrientes	1992–1999	90–100	4.7	8.5	6.6	(5.0; 8.7)	0.6		
Tierra del Fuego	1993–1996	100	14.2	6.3	10.3	(5.5; 18.5)	2.2		
Brazil								–16.0	(–48.6; 37.2)
Sao Paulo	1990–1992	70–95	6.9	9.1	8.0	(5.5; 11.1)	0.8		
Passo Fundo	1996–1999	100	5.4	8.7	7.0	(4.1; 11.9)	0.6		
Chile								7.5	(4.3; 10.9)
Santiago	1990–1999	100	3.6	3.9	3.7	(3.4; 4.0)	0.9		
Colombia									
Cali*	1995–1999		0.4	0.5	0.5	(0.3; 0.7)	0.8		
Bogota	1990	97	4.7	2.9	3.8	(2.9; 4.9)	1.6		
Paraguay*	1990–1999		1.0	0.8	0.9	(0.8; 1.0)	1.1	–0.5	(–5.7; 4.9)
Peru								12.1	(–7.5; 35.8)
Lima	1990–1994	35–100	0.4	0.6	0.5	(0.4; 0.64)	0.7		
Uruguay									
Montevideo	1992	97	8.3	8.2	8.3	(5.4; 11.7)	1.0		
Venezuela								–6.8	(–24.6; 15.3)
Caracas*	1990–1994		0.1	0.2	0.1	(0.1; 0.2)	0.7		
Central America and West Indies								–3.6	(–5.0; –2.2)
Barbados*	1990–1993		2.4	1.6	2.0	(0.6; 4.1)	1.5		
Cuba	1990–1999	25–100	2.1	2.5	2.3	(2.2; 2.5)	0.8	–10.8	(–13.4; –8.2)
Dominica	1990–1993		6.6	4.9	5.7	(2.4; 12.6)	1.3	–46.1	(–78.3; 34.0)
Dominican Republic	1995–1999	39–67	0.7	0.3	0.5	(0.4; 0.7)	2.3†	12.6	(–11.4; 43.0)
Mexico									
Veracruz	1990–1993	100			1.5	(0.7; 2.9)			
Puerto Rico (USA)	1990–1999	90–97	15.8	17.8	16.8	(16.0; 17.6)	0.9†	–1.0	(–2.7; 0.7)
Virgin Islands (USA)*	1990–1996			14.0	12.8	(8.1; 18.8)		7.1	(–13.2; 32.1)
Oceania								3.2	(–0.4; 6.9)
Australia								4.1	(–2.5; 11.1)
New South Wales	1990–1993	89–100	13.1	15.9	14.5	(13.5; 15.6)	0.8†		
New Zealand								2.8	(–1.4; 7.2)
Auckland	1990–1996	100	12.9	14.6	13.7	(12.0; 15.7)	0.9		
Canterbury	1990–1999	100	23.8	20.8	22.3	(19.1; 25.9)	1.1		

*One source.
†Statistically significant $P < 0.05$.
‡Also belongs to EURODIAB Ace Study.
§Without Sardinia.

in girls, and in Cuba a decrease of 7.4% (3.5–11.3%) in boys and a decrease of 13.9% (10.3–17.4%) in girls.

In the pooled data, the increase was less in the older age groups: 4.0% (3.1–4.9%) in the 0–4-year age group, 3.0% (2.4–3.7%) in the 5–9-year age group and 2.1% (1.5–2.7%) in the 10–14-year age group. This decrease in the annual increase over the age groups was seen mainly in European populations.

The trend was also estimated by continents (Table 3). The statistically significant increasing trend was 4.0% (1.8–6.2%) in Asia, 3.2% (2.7–3.6%) in Europe and 5.3% (3.3–7.3%) in North America. In Central America and the West Indies, the trend was a significant decrease at 3.6% (2.2–5.0%). However, a decreasing trend in this area was seen only in Cuba where the decrease was 10.8% (Table 1). In general, the

Table 2 Poisson regression analyses of the incidence of Type 1 diabetes in age groups by sex (pooled analyses for all centres)

	Age group (years)	Risk ratio	95% CI
Boys*	0–4	1.00	
	5–9	1.52	(1.47; 1.58)
	10–14	1.94	(1.87; 2.01)
Girls*	0–4	1.00	
	5–9	1.72	(1.66; 1.79)
	10–14	1.93	(1.86; 2.01)
Total†	0–4	1.00	
	5–9	1.62	(1.57; 1.66)
	10–14	1.94	(1.89; 1.98)

*Adjusted for centre.
‡Adjusted for centre and sex.

increasing trend was strongest in the centres with very high incidence 3.7% (3.1–4.2%) and in centres with intermediate incidence 3.5% (2.8–4.2%). In the centres with low and very low incidence, there were no significant increases in incidence rates over time.

When Poisson regression models were fitted to the dataset (Table 4), the simplest model showed that there were statistically significant differences in incidence between centres and age groups, but not between genders (Table 4, lines 2, 4 and 3). The overall annual increase in incidence was statistically significant (line 5) and the effect of age and gender on the incidence was not similar in all centres (lines 6, 7 and 12). The trends in incidence varied between the age groups (line 11) and between centres (line 9).

Discussion

The rising incidence of Type 1 diabetes is a global phenomenon. The incidence of Type 1 diabetes has increased by 2.8% per year during the years 1990–1999 worldwide. Thus, the results of this study confirm the previously reported trend of 2.5–3.0% annual increase in incidence since the early 1970s [8,10]. The total population of children aged 14 years or under (740 million) from countries for which the incidence of Type 1 diabetes is estimated using a standardized study protocol covers 41% of the world's population aged 14 years or under. The global variation in incidence (> 350-fold) appears to be stable, although we were not able to estimate the global range for the whole 10-year study period, because incidence data from most low incidence countries were available for the first 5-year period only. There was also within-country variation in incidence in several countries. However, it has not been possible to investigate this variation further in this review.

The global increase in incidence of Type 1 diabetes may be partly explained by an improvement in case ascertainment. An underestimation is certainly inherent in all registration systems, but the problem was avoided in this study by measuring the degree of ascertainment on the basis of two or more data sources. In some countries collecting incidence data, secondary sources for ascertainment of cases are not available or are difficult to find. However, 81% of registries checked the degree of ascertainment using two independent data sources. Most of the information of the incidence of Type 1 diabetes is from regions with a high or intermediate incidence, mostly in Europe and North America, where several registries have been established since the mid-1980s or even before. The data from Asia, South America and Africa are still sparse. However, the incidence appears to be increasing in almost all populations worldwide and statistically significant increases were found in all continents except in South America, Central America and the West Indies. The latter was the only continent where there was a significantly decreasing trend in this study.

Unfortunately, information is lacking from many countries with very low gross domestic product and the largest child populations. These are mostly countries in Africa and South and East Asia, where infectious diseases are the greatest childhood killers. When one child in 10 dies before his/her fifth birthday, as happens in these countries today, it may be practically impossible to get reliable data on the incidence of diabetes among children. The symptoms of diabetes surely remain

Table 3 Annual increase (%) of incidence of Type 1 diabetes by age groups and by continents in children aged 14 or under in 1990–1999; the results of the Poisson regression analyses

	Total Age/ year*			0–4 years		5–9 years		10–14 years		
Continent	Trend %	95% CI	*P*	Trend %	95% CI	Trend %	95% CI	Trend %	95% CI	*P*
Africa	3.0	(0.3; 5.8)	0.029	0.9	(−5.6; 7.9)	9.2	(3.8; 14.9)	0.6	(−3.0; 4.3)	0.154
Asia	4.0	(1.8; 6.2)	<0.001	1.3	(−3.5; 6.2)	5.0	(1.4; 8.8)	5.1	(1.8; 8.5)	0.238
Europe	3.2	(2.7; 3.6)	<0.001	4.7	(3.9; 5.6)	3.4	(2.7; 4.0)	2.2	(1.6; 2.8)	<0.001
North America	5.3	(3.3; 7.3)	<0.001	6.9	(2.4; 11.5)	4.7	(1.4; 8.1)	5.1	(2.3; 8.1)	0.674
South America	5.3	(2.8; 7.9)	<0.001	6.5	(1.2; 12.0)	9.2	(4.7; 13.9)	1.7	(−2.0; 5.6)	0.071
Central America and West Indies	−3.6	(−5.0; −2.2)	<0.001	−3.6	(−6.7; 0.3)	−4.2	(−6.5; −1.9)	−3.2	(−5.3; 1.0)	0.881
Oceania	3.2	(−0.4; 6.9)	<0.001	11.1	(3.2; 19.6)	−0.6	(−6.4; 5.5)	2.1	(−3.3; 7.8)	0.042
All regions	2.8	(2.4; 3.2)	<0.001	4.0	(3.1; 4.9)	3.0	(2.4; 3.7)	2.1	(1.5; 2.7)	<0.001

*Interaction between age group and calendar year.

Table 4 Summary of the Poisson regression analyses of the incidence of Type 1 diabetes for data from 105 populations worldwide during the period 1990–1999

Model terms*		Suitability of fit		Test for last term		
		Deviance	d.f.	Deviance	d.f.	*P*-value
1	Constant	57767.7	4493			
2	(1) + population	8595.9	4389	49171.8	104	< 0.0001
3	(2) + sex	8594.0	4388	1.9	1	0.171
4	(3) + age	5713.4	4386	2880.6	2	< 0.0001
5	(4) + year	5472.1	4385	241.4	1	< 0.0001
6	(5) + population/sex	5279.6	4281	192.4	104	< 0.0001
7	(6) + population/age	4703.7	4073	576.0	208	< 0.0001
8	(7) + sex/age	4663.7	4071	40.0	2	< 0.0001
9	(8) + population/year	4325.4	3967	338.2	104	< 0.0001
10	(9) + sex/year	4323.3	3966	2.1	1	0.145
11	(10) + age/year	4303.9	3964	19.4	2	< 0.0001
12	(11) + population/sex/age	4070.6	3756	233.3	208	0.126
13	(12) + population/sex/year	3969.2	3652	101.4	104	0.565
14	(13) + population/age/year	3709.0	3444	260.1	208	0.011
15	(14) + sex/age/year	3704.3	3442	4.8	2	0.091
16	(15) + population/sex/age/year	3475.5	3234	228.7	208	0.154

*Population = centre; sex = gender; age = variable categorized into three groups 0–4, 5–9 and 10–14 years; year = calendar year.

unrecognized when children die, for example, from acute respiratory infections or diarrhoea. Thus, reliable estimation of the incidence of diabetes in these areas may be possible only after child mortality decreases.

The risk of Type 1 diabetes has been increasing since the 1950s and there are no signs that this trend is abating [8,10,13]. The results of this analysis confirm the widely believed assumption that the increase in the incidence of Type 1 diabetes has been very rapid, particularly in the youngest age groups in European populations [14–18]. Another widely adopted assumption that high incidence regions, except Finland, would have reached a plateau is not supported by our analysis. We found no significant differences in the trend of incidence levels over time between participating countries.

The constantly increasing incidence of Type 1 diabetes over such a short period of time (10 years) cannot be explained by shifts in genetic susceptibility alone. Hence, causative agents should be sought in the environment or in gene–environment interaction. There is already some evidence that rapid growth and obesity in early childhood increases the risk of Type 1 diabetes [19]. Further, psychological stress in families has been found to be associated with diabetes-associated autoantibodies in 1-year-old children [20]. Recent studies [21–24] have shown that environmental factors have a stronger effect on genetically non-susceptible individuals than those genetically susceptible to getting Type 1 diabetes. It might be timely to extend the study of the environmental agents to completely new areas of children's lifestyle, including social circumstances, stressful life events, and health behaviour in the widest sense.

In conclusion, the incidence of childhood Type 1 diabetes continues to rise and continuous monitoring, using updated diagnostic criteria and developed standardized methods, is required. In particular, it is important to differentiate between Type 1 and Type 2 diabetes, because the latter has become increasingly common in adolescents in some populations The fact that prevention strategies are presently in progress justifies ongoing surveillance of incidence: i.e. when these trials are performed on a population basis, surveillance will allow us to demonstrate their effectiveness.

Competing interests

None declared.

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