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IDF Diabetes Atlas

Diabetes in the young – a global view and worldwide estimates of numbers of children with type 1 diabetes

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ABSTRACT

This paper describes the methodology, results and limitations of the 2013 International Diabetes Federation (IDF) Atlas (6th edition) estimates of the worldwide numbers of prevalent cases of type 1 diabetes in children (<15 years). The majority of relevant information in the published literature is in the form of incidence rates derived from registers of newly diagnosed cases. Studies were graded on quality criteria and, if no information was available in the published literature, extrapolation was used to assign a country the rate from an adjacent country with similar characteristics. Prevalence rates were then derived from these incidence rates and applied to United Nations 2012 Revision population estimates for 2013 for each country to obtain estimates of the number of prevalent cases.

Data availability was highest for the countries in Europe (76%) and lowest for the countries in sub-Saharan Africa (8%). The prevalence estimates indicate that there are almost 500,000 children aged under 15 years with type 1 diabetes worldwide, the largest numbers being in Europe (129,000) and North America (108,700). Countries with the highest estimated numbers of new cases annually were the United States (13,000), India (10,900) and Brazil (5000). Compared with the prevalence estimates made in previous editions of the IDF Diabetes Atlas, the numbers have increased in most of the IDF Regions, often reflecting the incidence rate increases that have been well-documented in many countries.

Monogenic diabetes is increasingly being recognised among those with clinical features of type 1 or type 2 diabetes as genetic studies become available, but population-based data on incidence and prevalence show wide variation due to lack of standardisation in the studies. Similarly, studies on type 2 diabetes in childhood suggest increased incidence and prevalence in many countries, especially in Indigenous peoples and ethnic minorities, but detailed population-based studies remain limited.

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1. Introduction

The incidence of childhood onset diabetes is increasing in many countries. There are clear indications of geographic differences in trends but the overall annual increase is estimated at around 3% [1]. Some 79,000 children worldwide are estimated to develop type 1 diabetes annually. There is some indication that incidence is increasing more steeply in some of the low prevalence countries in Europe and that, in relative terms, increases in Europe are greatest in young children [2]. There is also evidence emerging from high-incidence European countries that the increasing incidence trend seems to be levelling off which may give hope for the future [3–6].

The cause of type 1 diabetes remains unknown. There is clear evidence of a genetic predisposition and strong, but circumstantial, evidence for environmental factors triggering an autoimmune destruction of the beta cells leading to absolute dependence on insulin treatment.

Living with type 1 diabetes remains a challenge for the child and the whole family even in countries with access to multiple daily injections or an insulin pump, glucose monitoring, diabetes education and expert medical care. Poor metabolic control may result in the acute complications of hypoglycaemia and ketoacidosis, poor growth and chronic microvascular and macrovascular complications. Children are more sensitive to a lack of insulin than adults and are at higher risk of a rapid and dramatic development of diabetic ketoacidosis. Episodes of severe hypoglycaemia or ketoacidosis, especially in young children, are risk factors for structural brain abnormalities and impaired cognitive function which may cause schooling difficulties and limit future career choices [7,8]. Even in developed countries there is still significant excess mortality among children and young adults with type 1 diabetes diagnosed in childhood. A recent study from 10 European countries showed that there were twice as many deaths as expected from national age/sex specific mortality rates [9]. Over a third of the deaths could be directly attributed to diabetes, and these were mainly from metabolic disturbances, diabetic ketoacidosis and hypoglycaemia. Little is known about the mortality of type 1 diabetes in childhood in many developing countries where the prevalence of childhood diabetes is very low. It is suspected that many remain undiagnosed with the deaths attributed to malaria, gastroenteritis or other infections [10], while many that are diagnosed die within a year [11,12].

A small proportion of children diagnosed with type 1 diabetes have been shown to have monogenic diabetes and not auto-immune mediated diabetes [13]. A correct diagnosis is important as some forms of monogenic diabetes can be successfully transitioned from insulin to oral sulphonylurea medication.

Type 2 diabetes is also increasing in the childhood age group in many parts of world, especially among indigenous populations and in ethnic minorities [14], but few population-based studies are available and therefore will not be considered in detail in this review.

2. Methodology

Systematic searches of bibliographic databases were performed to identify studies that provided incidence or prevalence rates of type 1 diabetes in children as follows:

- Medline was accessed using OvidSP restricted to human studies published since 1980 and using [exp registries OR exp incidence OR exp prevalence) AND exp diabetes mellitus, insulin-dependent AND exp with the/ep [Epidemiology] sub-heading. If a country was not indexed in Medline then it was included in the search as a text word.
- PubMed using the Boolean search terms (incidence OR prevalence) AND diabetes AND.
- Published abstracts from recent international meetings including those in the Web of Science database were also searched.
- The titles and abstracts of all articles were reviewed and those likely to provide incidence or prevalence rates were obtained. The reference lists of articles were also scanned to check for further relevant publications. No restrictions were placed on the language of published articles.

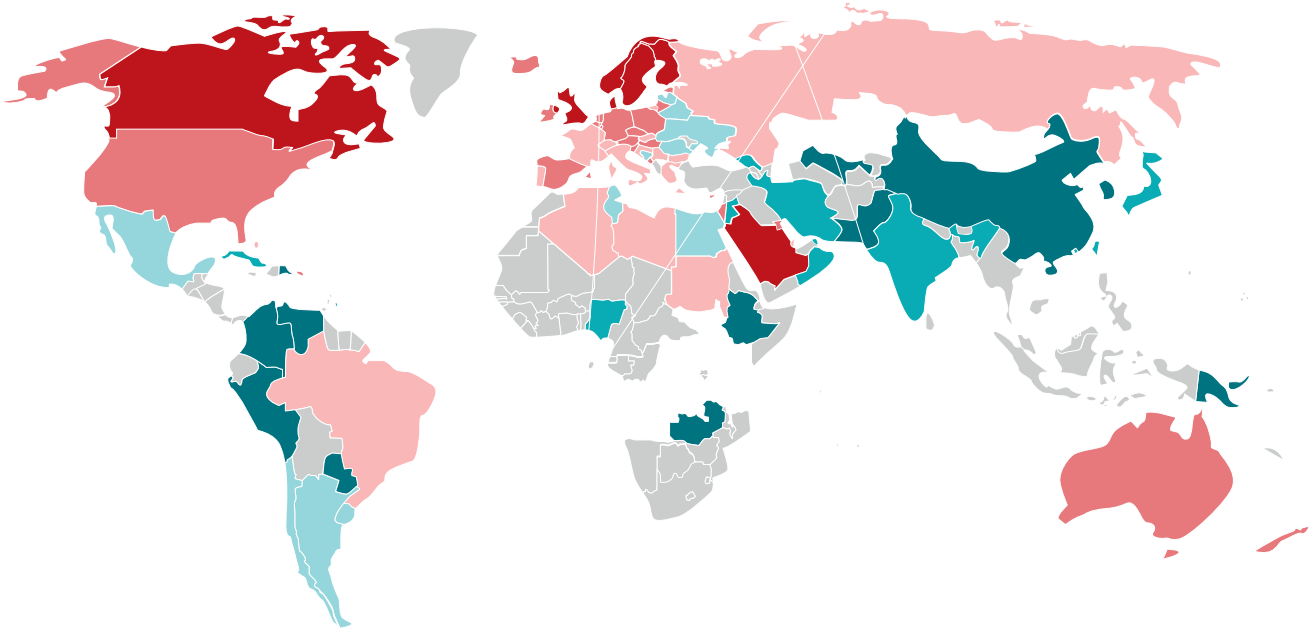
The following criteria were then applied, although not necessarily in the order shown, to select the most suitable study in a given country:

- More recent studies, preferably covering periods into the 1990s.
- Studies with widest coverage within the country.
- Studies providing rates for the target age range of 0–14 years.
- Studies providing sex-specific rates for the 0–4, 5–9 and 10–14 year age groups.

Where appropriate, the numerators and denominators of rates from two or more registers within a country were combined to obtain pooled rates.

The majority of studies found by the literature search provided incidence rates rather than prevalence rates. An estimate of the number of cases in each country was obtained by multiplying the United Nations 2012 Revision population estimates for 2013 [15] in each of six age/sex subgroups (males or females aged 0–4, 5–9 or 10–14 years) by the corresponding estimated prevalence rate. Prevalence rates in each age group were obtained by averaging cumulative incidence rates for the five individual years in the age group. For example, the prevalence in the 5–9 age group was obtained as an average of:

Prevalence (age 5) = 5* (0–4 year incidence rate) + 0.5*(5–9 year incidence rate).
Prevalence (age 6) = 5* (0–4 year incidence rate) + 1.5*(5–9 year incidence rate).
Prevalence (age 7) = 5* (0–4 year incidence rate) + 2.5*(5–9 year incidence rate).
Prevalence (age 8) = 5* (0–4 year incidence rate) + 3.5*(5–9 year incidence rate).



Prevalence (age 9) = 5* (0–4 year incidence rate) + 4.5*(5–9 year incidence rate).

In a few countries that reported age-specific rates pooled for boys and girls, the rates were taken to apply to both boys and girls.

The incidence rate is not uniform in the 0–14 year age group but rather it tends to be lower in young ages and increases to a peak usually in the 10–14 year age group. For countries in which age-specific rates were not available, a single multiplier to convert incidence rates to prevalence rates was derived as the median multiplier for countries for which age- and sex-specific incidence rates were available. Equal-sized populations in each age-sex subgroup were assumed in this calculation. The resulting prevalence to incidence ratio of 6.2 was therefore employed to convert incidence rates to prevalence rates in all countries in which age-specific incidence rates were unavailable. Using an assumption that the mean age at onset of diabetes occurring before the 15th birthday was 8.5 years, a similar conversion factor of 6.5 was derived in the second edition of the IDF Diabetes Atlas, as the mean duration of diabetes in the 0–14 year age range.

This method of estimating prevalence from incidence assumes that the effects of mortality are minimal. In developed countries, which tend to have high quality incidence data, mortality rates amongst children with diabetes are low and any adjustment for mortality is unlikely to have much impact. In less-developed countries, which often have poorly estimated incidence rates based on small numbers, the application of an adjustment for mortality could not be done. In the few countries that had published prevalence rates, these were lower than the 6.2 factor and so this may reflect some adjustment for mortality, or a pattern of older average age of onset. Further incidence and prevalence studies are needed to clarify the situation as mortality may be much higher than estimated.

For countries that had no incidence or prevalence rates available the choice of country to use for extrapolation was based on proximity, the state of economic development measured by the gross domestic product per capita and the ethnic composition as assessed from the Central Intelligence Agency World Factbook 2013 [16]. The choice was also influenced by the quality rating of the studies in the various countries.

The quality of estimates was assessed using the following simple rating system:

A. Studies that were based on registers that were population based with validated ascertainment levels of 90% or more.
B. Other studies in which population denominators were given to enable rates to be calculated (so excluding case-series and studies which used non population-based denominators).

3. Results

3.1. *Worldwide estimates of type 1 diabetes*

The following characteristics of the 88 studies reported in the literature which were used to produce the estimates are summarised in Table 1: first author and year of publication, geographical coverage, calendar period, incidence rate (age-standardised if sufficient information provided), number of cases, estimated completeness of ascertainment; and a

Table 1 – Data sources for childhood type 1 diabetes rates.

Country	Period	Region represented by the study	Cases	Completeness (%)	Quality
AFR					
Ethiopia [17]	1995–2008	Gondar, Jimma	65	NA	B
Nigeria [18]	1990	Anambra	14	NA	B
United Republic of Tanzania [19]	1982–1991	Dar es Salaam	36	100	A
Zambia [20]	pre 1989	Copperbelt	37	90	B
EUR					
Austria [21]	2004–2008	Whole country	1159	97	A
Belarus [22]	1997–2002	Gomel, Minsk	~375	100	A
Belgium [21]	2004–2008	Antwerp	129	95	A
Bosnia and Herzegovina [23]	1998–2010	Republic of Srpska	320	100	A
Bulgaria [1]	1990–1999	Varma, West Bulgaria	924	99–100	A
Croatia [24]	1995–2003	Whole country	692	97	A
Cyprus [25]	2000–2009	Whole country	208	~100	A
Czech Republic [21]	2004–2008	Whole country	1443	97	A
Denmark [21]	2004–2008	Whole country	1286	99	A
Estonia [26]	1999–2006	Whole country	310	98	A
Finland [5]	2000–2005	Whole country	3186	NA	B
France [27]	1998–2004	Aquitaine	430	NA	B
Georgia [28]	1998–1999	Whole country	115	NA	B
Germany [21]	2004–2008	Baden-Württemberg, North Rhine-Westphalia, Saxony	5099	94–100	A
Greece [29]	1995–1999	Attica	279	100	A
Hungary [30]	2004–2009	18 counties	1227	100	A
Iceland [29]	1994–1998	Whole country	47	100	A
Ireland [31]	1997	Whole country	140	91	A
Israel [32]	2006–2007	Whole country	559	NA	B
Italy [33]	1990–2003	Turin, Liguria, Pavia, Modena, Trento, Firenze-Prato, Marche, Lazio, Umbria, Abruzzo, Campania, Sardinia	5180	91–99	A
Latvia [29]	1994–1998	Whole country	196	100	A
Lithuania [21]	2004–2008	Whole country	400	100	A
Luxembourg [21]	2004–2008	Whole country	81	100	A
Macedonia [21]	2004–2008	Whole country	139	100	A
Malta [34]	2006–2010	Whole country	81	NA	B
Montenegro [21]	2004–208	Whole country	111	100	A
Netherlands [35]	1996–1999	Whole country	1264	NA	B
Norway [21]	2004–208	Whole country	1504	92	A
Poland [36]	2004	Lodzkie, Malopolskie, Podlasie, Pomorskie, Silesia, Warmia-Mazury, Podkarpackie	NA	NA	B
Portugal [29]	1994–1998	Algarve, Madeira	74	85–100	A/B
Romania [37]	2000–2004	Whole country	1141	NA	B
Russian Federation [38]	1996–2005	Moscow	2031	94	A
Serbia [39]	2000–2004	Belgrade	171	NA	B
Slovakia [2]	1999–2003	Whole country	718	100	A
Slovenia [21]	2004–2008	Whole country	211	100	A
Spain [21,40–47]	1995–2011	Catalonia, Castlla y Leon, Castilla La Mancha, Madrid, Andalusia, Almeria, Galicia, Aragon, Canaries, Navarro	~1500	83–100	A/B
Sweden [3]	2005–2007	Whole country	2039	96–99	A
Switzerland [21]	2004–2008	Whole country	780	91	A
Ukraine [48]	1985–1992	Whole country	NA	NA	B
United Kingdom [21]	2004–2008	Leeds, Oxford, N. Ireland	2169	99	A
Uzbekistan [49]	2000	Whole country	NA	NA	B
MENA					
Algeria [1]	1990–99	Oran	223	NA	B
Egypt [50]	pre 1992	Alexandria, Damahour	NA	NA	B
Islamic Republic of Iran [51]	1991–1996	Fars	298	100	A
Jordan [52]	1992–1996	Whole country	275	96	A
Kuwait [1]	1992–1999	Whole country	531	79–96	B
Libya [53]	1991–2000	Benghazi	276	100	A
Oman [54]	1993–1994	Whole country	31	96	A

Table 1 (*Continued*)

Country	Period	Region represented by the study	Cases	Completeness (%)	Quality
Pakistan [1]	1990–1999	Karachi	104	51	B
Qatar [55]	1992–1996	Whole country	80	NA	B
Saudi Arabia [56]	2004–2009	Al-Madinah	419	NA	B
Sudan [57]	1991–1995	Khartoum	534	97	A
Tunisia [1]	1990–1999	Beja, Gafsa, Kairoan, Monastir	297	NA	B
NAC					
Antigua and Barbuda [58]	1989–1993	Antigua	4	100	A
Bahamas [59]	2001–2002	Whole country	9	NA	B
Barbados [1,60]	1990–1993	Whole country	5	NA	B
Canada [61–63]	1990–2010	Edmonton, Manitoba, Calgary, Prince Edward Island, Quebec, Newfoundland & Labrador	~1200	75–100	A/B
Dominica [1,60]	1990–1993	Whole country	5	NA	B
Mexico [64]	2010	Whole country	698	NA	B
United States of America [65]	2002–2003	Ohio, South Carolina, Washington, Amerindian reservations, California & Hawaii	1574	87–99	A/B
US Virgin Islands [1]	1990–1996	Whole country	22	NA	B
SACA					
Argentina [1]	1990–1999	Avellaneda, Cordoba, Corrientes, Tierra del Fuego	141	88–100	A/B
Brazil [66]	1986–2006	Sao Paulo	176	93	A
Chile [67]	2000–2005	Santiago	603	100	A
Colombia [1]	1990–1999	Cali: Santafe de Bogota	76	NA; 97	A/B
Cuba [1]	1990–1999	Whole country	572	25–100	B
Dominican Republic [1]	1995–1999	Whole country	34	39–67	B
Paraguay [1]	1990–1999	Whole country	168	NA	B
Peru [1]	1990–1994	Lima	53	35–100	B
Puerto Rico [1]	1990–1999	Whole country	1625	90–97	A
Uruguay [1]	1992	Montevideo	26	97	A
Venezuela [1]	1990–1994	Caracas	43	NA	B
SEA					
India [68]	2008	Karnal	82	NA	B
Mauritius [1]	1990–1994	Whole country	21	35–100	B
WP					
Australia [69]	2000–2006	Whole country	6350	97	A
China [1]	1990–1996	22 regions	500	69–100	A/B
Hong Kong SAR [70]	1992–1996	Whole country	120	NA	B
Japan [71]	1998–2001	Whole country	~1800	NA	B
New Zealand [72]	1999–2000	Whole country	298	95	A
Papua New Guinea [73]	1996–2000	Whole country	8	NA	B
Republic of Korea [1]	1990–1991	Seoul	61	NA	B
Singapore [74]	1992–1994	Whole country	40	92	A
Taiwan [75]	1992–1996	Whole country	170	NA	B
Thailand [76]	1996–2005	North East	340	NA	B

A: Studies from the country in question that were based on population-based registers with validated.
B: Other studies from the country in question, provided population denominators were given to enable rates to be calculated (excludes case-series studies).

classification of the source as either A or B using the criteria described in Section 2. The rates in these publications are mapped in Fig. 1 after directly standardising, where possible, to a population with equal numbers in each of the six age/sex categories (boys 0–4, 5–9, 10–14 years, and girls 0–4, 5–9, 10–14 years).

3.2. *Incidence and prevalence*

Table 2 contains information on population size in the 0–14 age group together with incidence and estimated numbers of prevalent cases in 2013, organised by IDF Region. It is estimated that on an annual basis some 79,000 children aged 14 years and under develop type 1 diabetes worldwide. Of the estimated total of approximately 500,000 prevalent cases of type 1 diabetes in childhood, more than a quarter come from the Europe (EUR) Region, where reliable, up-to-date estimates of incidence were available for the majority of countries. More than a fifth are from North America and Caribbean (NAC) Region. Only some 6% of children with type 1 diabetes come from the Western Pacific (WP) Region, despite it having the largest childhood population.

Table 2 – Estimates of prevalent cases and new cases per year for type 1 diabetes among children aged under 15 year in 2013 by IDF Region.

IDF Region	Number of countries	Number of countries with incidence or prevalence rates available (%)	Population of children (0–14 years) (1000s)	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)
AFR	48	4 (8%)	382,967.1	6.4	39.2
EUR	54	41 (76%)	158,565.1	20.0	129.0
MENA	22	12 (55%)	208,710.8	10.7	64.3
NAC	26	8 (31%)	108,922.7	16.7	108.7
SACA	20	11 (55%)	125,199.6	7.3	45.6
SEA	7	2 (29%)	426,705.1	12.6	77.9
WP	39	10 (26%)	461,643.0	5.3	32.5
World	216	88 (41%)	1,872,713.4	79.0	497.1

3.3. *Regional estimates of type 1 diabetes*

For each country within each IDF Region, Table 3 shows the population size in the 0–14 age group together with estimated numbers of new cases per year and the estimated numbers of prevalent cases in 2013. Where extrapolation was necessary the source country of the extrapolated rate is given. Table 4 shows the top 10 countries in terms of reported incidence rates for type 1 diabetes in children and in terms of estimated prevalent cases in the under 15-year age-group.

3.3.1. *Africa*

The need for extrapolation of rates of childhood type 1 diabetes was particularly evident in the sub-Saharan Africa (AFR) Region. Published rates were found for only four of the countries in this Region, and some of the studies were out-of-date, of poor quality and based on small numbers. Consequently imperfect estimates of rates from Ethiopia, Nigeria, Tanzania and Zambia have had to be used for widespread extrapolations because of the dearth of published studies. Mortality among children with diabetes is likely to be high in parts of this region. The limited published data available on mortality rates, and unpublished data on prevalence rates, suggest mortality rates are very high in some countries. Therefore it is very likely that actual prevalence numbers are substantially lower than the estimates in this publication.

On the other hand, incidence studies in lower-income countries in Africa and other regions may underestimate true incidence as new cases are frequently missed and die undiagnosed. Tropical and malnutrition diabetes may account for a proportion of cases in this Region, but reliable data are lacking. For these reasons the validity of the estimates of numbers of children with type 1 diabetes in this Region are questionable and must therefore be treated with considerable caution.

3.3.2. *Middle East and North Africa*

In contrast to the situation in sub-Saharan Africa, reliable data are available for childhood type 1 diabetes rates for more than half the countries in the Middle East and North Africa (MENA) Region. By far the largest contributions to the total number of estimated childhood type 1 cases for this region come from Saudi Arabia and Egypt whose estimates jointly account for nearly half of the Region's total. The incidence of type 1 diabetes in Saudi Arabia (31.4 per 100,000 population) and Kuwait (22.3 per 100,000 population) are particularly high and both feature in the top 10 country list. By contrast, in Pakistan the rate is less than 1 per 100,000 population, although this estimate was from a study with a poor ascertainment rate and gives a substantially lower incidence rate than some more recent studies from neighbouring countries. Therefore it is possible that the incidence in Pakistan is an underestimate.

3.3.3. *Europe*

Compared with other regions, the Europe (EUR) Region has by far the most complete and reliable data on the rates of childhood type 1 diabetes with three quarters of countries having registries many of which are either nationwide or cover several different parts of the country. Where extrapolation of incidence rates was necessary it was usually for countries with small populations, and therefore any error associated with the extrapolation will have little impact on the estimate of this Region's total. The Scandinavian countries, Finland, Sweden and Norway, occupy the first three places in the top 10 list of countries by incidence rate. The countries making the largest contribution to the total number of childhood type 1 diabetes cases were United Kingdom, Germany and the Russian Federation reflecting to some degree the large childhood populations in these countries. It is worth noting that the estimates for the Russian Federation were based on a study from Moscow which may not be representative of such a large country and much lower rates were reported in an earlier study in Siberia.

3.3.4. *North America Caribbean*

Although no published rates were available for childhood type 1 diabetes in many of the smaller Caribbean islands in the North America and Caribbean (NAC) Region, it was usually possible to extrapolate rates from an island in close proximity, although such rates were often based on very small numbers of cases. Highest rates were observed in Canada and the USA, both of which feature in the list of top 10 incidence rate countries. The USA estimate, which accounts for more than three-quarters of the region's total, and to a lesser extent the estimate for Canada predominate. The USA estimate of 13,000 makes the largest national contribution to the global total number of cases of childhood diabetes diagnosed each year.

Table 3 – Estimates of prevalent cases and new cases per year for type 1 diabetes among children aged under 15 year in 2013 by country within each IDF Region.

Country/ territory	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)	Country/ territory	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)	Country/ territory	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)	Country/ territory	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)	Country/ territory	Number of newly-diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)
AFR			**EUR**			**MENA**			**SACA**			**WP**		
Angola	0.1	0.5	Albania	0.04	0.2	Afghanistan	0.2	1.1	Argentina	0.7	4.3	Australia	1.0	6.3
Benin	0.1	0.8	Andorra	0.00	0.02	Algeria	0.9	4.7	Bolivia	0.02	0.1	Brunei Darussalam	0.00	0.00
Botswana	0.01	0.03	Austria	0.2	1.5	Armenia	0.05	0.3	Brazil	5.0	31.1	Cambodia	0.03	0.2
Burkina Faso	0.2	1.4	Azerbaijan	0.03	0.2	Bahrain	0.01	0.04	Chile	0.2	1.4	China	1.4	7.7
Burundi	0.04	0.3	Belarus	0.1	0.5	Egypt	2.0	12.7	Colombia	0.2	1.1	Cook Islands	0.00	0.00
Cameroon	0.3	1.7	Belgium	0.3	1.9	Iraq	0.5	3.1	Costa Rica	0.01	0.1	Dem. People's Rep. of Korea	0.1	0.4
Cape Verde	0.00	0.03	Bosnia & Herzegovina	0.05	0.4	Islamic Republic of Iran	0.7	3.9	Cuba	0.04	0.3	Fed. States of Micronesia	0.00	0.00
Central African Republic	0.1	0.3	Bulgaria	0.1	0.6	Jordan	0.1	0.4	Dominican Republic	0.02	0.1	Fiji	0.00	0.01
Chad	0.2	1.1	Channel Islands	0.01	0.04	Kuwait	0.2	1.1	Ecuador	0.1	0.4	French Polynesia	0.00	0.00
Comoros	0.00	0.02	Croatia	0.1	0.4	Lebanon	0.03	0.2	El Salvador	0.1	0.7	Guam	0.00	0.00
Côte d'Ivoire	0.2	1.5	Cyprus	0.03	0.2	Libya	0.2	0.8	French Guiana	0.00	0.00	Hong Kong SAR	0.02	0.1
Dem. Rep. of Congo	0.2	1.5	Czech Republic	0.3	1.9	Morocco	0.8	4.9	Guatemala	0.4	2.4	Indonesia	0.4	2.7
Djibouti	0.03	0.2	Denmark	0.2	1.5	State of Palestine	0.1	0.3	Honduras	0.2	1.1	Japan	0.4	2.6
Equatorial Guinea	0.01	0.1	Estonia	0.04	0.3	Oman	0.02	0.1	Nicaragua	0.1	0.8	Kiribati	0.00	0.00
Eritrea	0.01	0.1	Finland	0.5	3.7	Pakistan	0.3	1.6	Panama	0.01	0.1	Lao People's Dem. Rep.	0.01	0.1
Ethiopia	0.1	0.6	France	1.4	9.8	Qatar	0.03	0.2	Paraguay	0.02	0.1	Macau SAR	0.00	0.01
Gabon	0.02	0.1	Georgia	0.04	0.2	Saudi Arabia	2.6	14.9	Peru	0.04	0.3	Malaysia	0.05	0.3
Gambia	0.02	0.2	Germany	2.4	16.5	Sudan	1.6	9.8	Puerto Rico	0.1	0.7	Marshall Islands	0.00	0.00
Ghana	0.3	1.8	Greece	0.2	1.3	Syrian Arab Republic	0.2	1.5	Uruguay	0.1	0.4	Mongolia	0.00	0.03
Guinea	0.1	0.9	Hungary	0.3	1.8	Tunisia	0.2	1.0	Venezuela	0.01	0.1	Myanmar	0.1	0.5
Guinea-Bissau	0.02	0.1	Iceland	0.01	0.1	United Arab Emirates	0.04	0.2				Nauru	0.00	0.00
Kenya	0.2	1.0	Ireland	0.2	1.1	Yemen	0.2	1.5				New Caledonia	0.00	0.00
Lesotho	0.01	0.04	Israel	0.3	1.9					**SEA**		New Zealand	0.2	1.0
Liberia	0.1	0.3	Italy	1.0	6.9				Bangladesh	1.4	8.7	Niue	0.00	0.00
Madagascar	0.1	0.8	Kazakhstan	0.1	0.3		**NAC**		Bhutan	0.00	0.01	Palau	0.00	0.00
Malawi	0.1	0.4	Kyrgyzstan	0.02	0.1	Anguilla	0.00	0.00	India	10.9	67.7	Papua New Guinea	0.00	0.02
Mali	0.2	1.3	Latvia	0.02	0.1	Antigua and Barbuda	0.00	0.00	Maldives	0.00	0.02	Philippines	1.3	7.9
Mauritania	0.05	0.3	Liechtenstein	0.00	0.00	Aruba	0.00	0.00	Mauritius	0.00	0.02	Republic of Korea	0.1	0.5
Mozambique	0.1	0.7	Lithuania	0.1	0.4	Bahamas	0.01	0.05	Nepal	0.1	0.4	Samoa	0.00	0.00
Namibia	0.01	0.04	Luxembourg	0.02	0.1	Barbados	0.00	0.01	Sri Lanka	0.2	1.0	Singapore	0.02	0.1
Niger	0.3	1.6	Macedonia	0.02	0.2	Belize	0.01	0.04				Solomon Islands	0.00	0.00
Nigeria	2.2	13.8	Malta	0.01	0.1	Bermuda	0.00	0.00		Taiwan	0.1	0.8		

Table 3 (*Continued*)

Country/ territory	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)	Country/ territory	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)	Country/ territory	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)	Country/ territory	Number of newly diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)	Country/ territory	Number of newly-diagnosed children per year (1000s)	Number of children with type 1 diabetes (1000s)
Republic of Congo	0.02	0.1	Moldova	0.03	0.2	British Virgin Islands	0.00	0.00				Thailand	0.1	0.5
Réunion	0.00	0.02	Monaco	0.00	0.00	Canada	1.5	9.3				Timor L'Este	0.00	0.02
Rwanda	0.05	0.3	Montenegro	0.02	0.1	Cayman Islands	0.00	0.00				Tokelau	0.00	0.00
São Tome and Principe	0.00	0.01	Netherlands	0.5	3.6	Dominica	0.00	0.01				Tonga	0.00	0.00
Senegal	0.2	1.1	Norway	0.3	1.9	Grenada	0.00	0.00				Tuvalu	0.00	0.00
Seychelles	0.00	0.00	Poland	1.0	6.4	Guadeloupe	0.01	0.04				Vanuatu	0.00	0.00
Sierra Leone	0.1	0.5	Portugal	0.2	1.5	Guyana	0.00	0.00				Viet Nam	0.1	0.8
Somalia	0.01	0.1	Romania	0.2	1.1	Haiti	0.02	0.1						
South Africa	0.1	0.8	Russian Federation	2.6	16.0	Jamaica	0.02	0.1						
Swaziland	0.00	0.02	San Marino	0.00	0.00	Martinique	0.00	0.01						
Togo	0.1	0.5	Serbia	0.2	1.3	Mexico	2.2	13.4						
Uganda	0.2	1.0	Slovakia	0.1	0.7	St Kitts & Nevis	0.00	0.00						
United Rep. of Tanzania	0.2	0.7	Slovenia	0.04	0.3	St Lucia	0.00	0.01						
Western Sahara	0.01	0.1	Spain	1.5	9.2	St Vincent & the Grenadines	0.00	0.00						
Zambia	0.1	0.3	Sweden	0.7	4.2	Suriname	0.00	0.00						
Zimbabwe	0.04	0.3	Switzerland	0.2	1.1	Trinidad and Tobago	0.01	0.03						
			Tajikistan	0.04	0.2	United States of America	13.0	85.6						
			Turkey	0.6	3.8	US Virgin Islands	0.00	0.02						
			Turkmenistan	0.02	0.1									
			Ukraine	0.5	3.3									
			United Kingdom	3.1	19.2									
			Uzbekistan	0.1	0.6									

Table 4 – Top 10 countries for published type 1 diabetes incidence rate (a) and estimated prevalent cases (b) in the under 15-year age-group.

Rank	Country	(a) Incidence rate (per 100,000 population aged under 15 year)	Rank	Country	(b) Estimated new cases (1000s)
1	Finland	57.6	1	United States of America	13.0
2	Sweden	43.1	2	India	10.9
3	Norway	32.8	3	Brazil	5.0
4	Saudi Arabia	31.4	4	United Kingdom	3.1
5	United Kingdom	28.2	5	Russian Federation	2.6
6	Canada	25.9	6	Saudi Arabia	2.6
7	Denmark	25.1	7	Germany	2.4
8	United States of America	23.7	8	Nigeria	2.2
9	Australia	22.5	9	Mexico	2.2
10	Kuwait	22.3	10	Egypt	2.0

3.3.5. *South and Central America*

Although the incidence of childhood type 1 diabetes in the South and Central America (SACA) Region is generally low, there are some sharp contrasts between the rates in neighbouring countries. In this Region a strong inverse ecological correlation has been reported between a country's incidence rate and the proportion of its population that is Amerindian (indigenous) [77]. This has influenced the selection of countries used for extrapolation, but the choice can still make a considerable difference to the resulting estimate. Such estimates must therefore be interpreted with caution. The Brazilian estimate of 31,100 prevalent cases accounts for about 70% of the Region's total.

3.3.6. *South-East Asia*

India and Mauritius are the only two out of the seven countries in the South-East Asia (SEA) Region that have published rates for type 1 diabetes in childhood and therefore extrapolation of rates was necessary. The rate from China, although outside the Region, was used for some extrapolations, but the rate for India was more frequently used and it therefore plays a pivotal role in the estimates for this Region. Four sources of rates for India were available, two from urban Chennai [78,79], one from Karnataka [80] and the most recent from Haryana [68]. The first of the studies from Chennai was a small study giving a prevalence of 0.26 cases per 1000 person years, and applying a 6.2 conversion factor gave an equivalent incidence rate of 4.2 per 100,000 person years. The second larger study from the same centre suggested an incidence rate twice as high as the first study, but the rate had a large correction factor applied for under-ascertainment. The Karnataka study gave a much lower incidence rate of only 0.3 per 100,000 person years in the under 25-year age-group. The Haryana study gave a prevalence of 0.18 per 1000 person years, equivalent to an incidence rate of 3.0 per 100,000 on applying a 6.2 conversion factor. Given the wide variation in rates, and taking account of the rates reported from other countries in the area, the decision was made to use the rate for the most recent study from Haryana. The large childhood population in India and the widespread use of the Indian rate for extrapolation in this Region means that this decision has important consequences not only for the total in the Region but also for the worldwide estimate, both of which would be considerably altered had a different rate been used. Diabetes-associated mortality and tropical or malnutrition diabetes are also likely to play important roles in this Region, but unfortunately there is inadequate information to address these issues. These points reinforce the need for much more detailed data on childhood diabetes in the South-East Asia Region.

3.3.7. *Western Pacific*

With the exception of Australia and New Zealand, the rates of childhood type 1 diabetes in the Western Pacific (WP) Region appear uniformly low. Few of the Pacific islands had published data and the rate for Papua New Guinea had to be extrapolated far into the Pacific Ocean, although any error induced in the Region's total by this extrapolation is likely to be small because of the generally low rates and small populations involved. The rate for Thailand was used extensively for extrapolation in the Indochina peninsula. Despite its very low incidence, China accounts for almost a quarter of the region's total estimate of prevalent cases. The Western Pacific Region makes the smallest contribution of all to the world total of type 1 diabetes even though it has the largest childhood population.

4. Discussion

The global distribution of childhood type 1 diabetes clearly indicates large area-to-area variations. This variability may partly be due to different distributions of risk genes for the disease as well as different distributions of environmental exposures, but part of the apparent variability both between countries and regions may also be due to methodological problems:

- The available incidence data sometimes covers only one small part of a large country. For example, in India incidence data were extrapolated from a study in Haryana and in the Russian Federation from a study in Moscow. Obviously there may be considerable variability within such large countries in both the distribution of risk genes and environmental exposures such as climate and lifestyle-related factors.
- For some countries where extrapolation of incidence rates was necessary the choice had to be made between countries whose reported rates were very different, possibly on occasions because they were based on small datasets. Where possible characteristics of the countries were taken into account in making the choice.

- The need for extrapolation was most evident in the African continent, particularly in sub-Saharan Africa. Here rates from undesirably small, dated and unreliable datasets have had to be used in extrapolations because of the lack of published studies.
- Another problem was the need to make extrapolations involving isolated island populations such as in Polynesia where both genetic predisposition and lifestyle habits may be very different. The danger inherent in such extrapolations is clear from recent publications of island populations that have very different rates compared with their mainland neighbours: Crete has a lower rate than mainland Greece [81], Newfoundland has a higher rate than other parts of Canada [63] and Sardinia has a higher rate than peninsular Italy [33].
- Of the reports on childhood type 1 diabetes rates used in this edition, only one-third relate to periods since 2000 with all but a few of the remainder relating to periods starting in the 1990s. Given that a rising incidence has been documented in many countries, it is likely that this will result in the underestimation of numbers, particularly for those countries whose estimates rely on rates from older reports.
- Many cases in sub-Saharan Africa, and quite possibly also in some countries in South-East Asia and the Americas likely die undiagnosed. Rwiza et al. [10] showed that in Tanzania diagnosis of diabetes was very frequently missed at first (only 39.4% correct), with diagnostic rates increasing steadily at each level of the health system. Even on admission to the ward the diagnosis was only accurate in 77.1% of cases. This and numerous other anecdotal reports show that diabetes (particularly diabetic ketoacidosis) is frequently misdiagnosed as malaria, gastroenteritis, typhoid, pnuemonia, meningitis, HIV/AIDS, malnutrition and other disorders. The authors believe that many die undiagnosed, particularly in rural areas. This will affect some incidence studies, potentially leading to an underestimate of true incidence.
- There is a lack of data on mortality rates among children already diagnosed with diabetes in most populations. In less developed countries, in which mortality could have a significant impact, the disease rates were often based on such small numbers of cases or on extrapolation so that the application of an adjustment to incidence data to allow for mortality was not thought to be justified.
- In sub-Saharan Africa mortality among children with diabetes has frequently been reported to be high [11,12,82–86]. Most of these papers are from leading centres in these countries and so it is likely that mortality rates are even higher overall. Reasons for the high mortality are – misdiagnosis as another condition, lack of access to or unaffordability of insulin, blood glucose monitoring and diabetes education; limited health professional experience with type 1 diabetes in children; distance from clinics; and other factors. Programmatic data from the International Diabetes Federation Life for a Child Programme suggest that the prevalences calculated are far higher than actual numbers in many countries, particularly when support is first commenced. Therefore it is very likely that actual prevalence numbers in sub-Saharan Africa are substantially lower than the estimates in this publication. Further studies are needed to gather reliable information for improving the estimates in these regions.

4.1. *Time trends*

In addition to the geographical variation in the incidence of childhood type 1 diabetes there are also well-documented secular trends over time, which may also differ from country to country and from region to region within a country and even from one time period to the next [21]. Such time trends have not explicitly been incorporated in these estimates since reliable data are available for only a very small number of countries, but these trends are of considerable importance for healthcare planning. Only a few studies have looked at time trends in those aged over 15 years [87–90]. The evidence so far is not conclusive, but there are indications that rates are not increasing in these older age groups and instead of a shift towards diagnosis at younger ages.

4.2. *Potential risk factors*

The causes of the changes over time are unknown and although migration might slowly change the genetic background within a population, the rapid changes in incidence rate reported to occur within comparatively short time spans are more likely due to changes in environmental risk factors. These environmental risk factors may initiate autoimmunity or accelerate and precipitate an already ongoing beta cell destruction [91]. Potential risk factors, such as early foetal events [92], viral infections during pregnancy and postnatally [93,94], and early exposure to cow's milk components and other nutritional factors [95] may initiate the autoimmune process. Since type 1 diabetes in childhood is associated with estimates of general wealth such as gross domestic product [96] it has been suggested that lifestyle habits related to wealth might be responsible for the changes in trend. Wealth is a well-known determinant of birth weight and childhood growth. Different estimates of child growth such as high birth weight, an increased height, weight, weight for height and body mass index (BMI) have repeatedly been shown to be risk factors for childhood type 1 diabetes [97–101]. Although autoimmune mechanisms are responsible for the beta cell destruction leading to type 1 diabetes, overload factors may accelerate this process [102–104]. Systematic reviews of observational (mainly case-control) studies have identified some protective factors (e.g. breast feeding [105], early vitamin D supplementation [106], atopic disease [107], pre-school day-care as a proxy measure of infections [108]) and some risk factors (e.g. older maternal age [109], Caesarean section delivery [110], low birth order [111]).

4.3. *Type 2 diabetes in youth*

Over the past 20–30 years type 2 diabetes in youth has increasingly been recognised in many countries around the world. The main driving forces for the emergence of type 2 diabetes in youth have been increasing rates of obesity and overweight, unhealthy eating habits and an increasingly sedentary lifestyle. The US TODAY Type 2 diabetes in youth

study [112] demonstrated early onset microvascular and macrovascular complications of diabetes, with undoubted major impacts on future quality of life, healthcare costs and productivity. The population-based US SEARCH for Diabetes in Youth study [113] revealed type 2 diabetes prevalence rates for adolescents 10–19 years of age to be 18 per 100,000 for non-Hispanic white, 46 for Hispanic white, 108 for African-Americans and 145 for US Navajo Indians. However, a recent systematic review of global trends in the incidence and prevalence of type 2 diabetes in children and adolescents revealed substantial methodological variations in the reported studies from around the world, resulting in a range of 0–330 per 100,000 person-years for incidence rates and 0–5300 per 100,000 population for prevalence rates [14]. Some of the variation was due to different age ranges of the study populations, different ethnicities, different geographical regions and different calendar times, but in addition different methodological characteristics were noted in the diagnostic criteria for diabetes, response rates to the surveys and ascertainment rates. Low incidence rates were found in European countries (0 per 100,000 person years in the Netherlands, 0.83 per 100,000 person years in the UK) and the highest in 0–14 year old Pima Indians in the USA (330 per 100,000 person years). As a generalisation, ethnic minorities have a higher incidence of youth onset type 2 diabetes than white individuals in almost all countries studied. This finding was especially marked in the indigenous peoples of the USA and Canada. Furthermore, female incidence rates tend to be higher and significantly higher incidence rates are seen in adolescence versus childhood. The trends in incidence over time have shown variations with reductions seen in Japanese school children and increases in Pima Indian children [114,115]. Accurate data on trends in the incidence, prevalence of type 2 diabetes in youth are needed in order to formulate realistic policies for healthcare management and for future primary and secondary prevention strategies.

5. Monogenic diabetes

Monogenic diabetes is caused by a defect in a single gene and can present clinically as either type 1 or type 2 diabetes [116]. At least 10 single gene mutations have been described, involving various transcription factors important for pancreatic development or for islet cell function. Monogenic diabetes which presents in the first 6 months of life is referred to as neonatal diabetes. It can be permanent or transient and it can be isolated or part of a broader syndrome [117]. The majority of neonatal diabetes is due to single gene mutations affecting the K-ATP channel (ABCC8 or KCNJ11) but many other monogenic mutations have also been described. Accurate diagnosis is important as some may respond to oral sulphonylurea treatment instead of needing insulin.

In the older child or young adult, monogenic diabetes is also known as Maturity Onset Diabetes in the Young (MODY). The criteria for the diagnosis of MODY include hyperglycaemia, an autosomal dominant inheritance, insulin independence occurring in individuals under the age of 25 years who are shown to be negative for anti-islet antibodies and with a fasting C-peptide level >0.8 ng/ml. Over 99% of monogenic diabetes in childhood with a known genetic aetiology result from mutations in hepatocyte nuclear factor HNF1A (formerly MODY 3), glucokinase GCK (formerly MODY 2) or HNF4A (formerly MODY 1) [118]. Individuals with GCK mutations are generally detected in childhood with incidental mild hyperglycaemia (<10 mmol/l), have HbA1c < 7.5% and require no therapy. Individuals with HNF1A or HNF4A are more likely to be diagnosed as having type 1 diabetes, but being sensitive to sulphonylureas they can often be successfully changed from insulin therapy to oral therapy.

The prevalence of monogenic diabetes was 1.1% of patients in the Norwegian nationwide population-based registry of childhood diabetes [119] while the population-based SEARCH for Diabetes in Youth Study in the US tested for the 3 most common mutations and found a prevalence of at least 1.2% of monogenic diabetes among those with physician-diagnosed diabetes [118]. In the SEARCH study the majority of those identified with monogenic diabetes had been diagnosed as having type 1 diabetes and had been treated with insulin. Following genetic diagnosis, many were able to treated with oral hypoglycaemic medication. On the other hand, confirming that monogenic diabetes can also masquerade as type 2 diabetes, a prospective national surveillance study of children < 18 years of age in Canada with non-type 1 diabetes observed a minimum incidence rate of 0.2 cases of monogenic diabetes per 100,000 children per year [120].

6. Conclusion

The incidence and prevalence rates for type 1 diabetes in the young appear to be slowly rising in most countries in the world, with the increases being most marked in the very young and in those countries experiencing rapid economic growth. However, much of the data for low- and middle-income countries are either missing, incomplete, non-representative or several decades old. Caution is needed in accepting or interpreting data on the burden of diabetes in the young when data from neighbouring regions or countries are used to extrapolate incidence and prevalence estimates. More standardised epidemiological data are needed to allow informed healthcare planning for diabetes in the young.

Conflict of interest

There are no conflicts of interest.

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