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Worldwide estimates of incidence, prevalence and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas, 9th edition

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ABSTRACT

Aims: This article describes the methods, results and limitations of the International Diabetes Federation (IDF) Diabetes Atlas 9th edition estimates of worldwide numbers of cases of type 1 diabetes in children and adolescents.

Methods: Most information in the published literature is in the form of incidence rates derived from registers of newly-diagnosed cases. After systematic review of the published literature and recent conference abstracts, identified studies were quality graded. If no study was available, extrapolation was used to assign a country the rate from an adjacent country with similar characteristics. Estimates of incident cases were obtained by applying incidence rates to United Nations 2019 population estimates. Estimates of prevalent cases were derived from incidence rates after making allowance for higher mortality rates in less-developed countries.

Results: Incidence rates were available for 45% of countries (ranging from 6% in the sub-Saharan Africa region to 77% in the European region). Worldwide annual incidence estimates were 98,200 (128,900) new cases in the under 15 year (under 20 year) age-groups. Corresponding prevalence estimates were 600,900 (1,110,100) existing cases. Compared with

Abbreviations: AFR, International Diabetes Federation Africa Region; EUR, International Diabetes Federation Europe Region; GNI, Gross national income; IDF, International Diabetes Federation; IMR, Infant mortality rate; LMIC, Lower-middle-income country; LIC, Low-income country; HIC, High-income country; MENA, International Diabetes Federation Middle East and North Africa Region; NAC, International Diabetes Federation North America and Caribbean Region; SACA, International Diabetes Federation South and Central America Region; SEA, International Diabetes Federation South East Asia Region; SMR, Standardised mortality ratio; T1D, Type 1 diabetes; UMIC, Upper-middle-income country; UN, United Nations; WHO, World Health Organization; WP, International Diabetes Federation Western Pacific Region

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estimates in earlier Atlas editions, numbers have increased in most IDF regions, reflecting incidence rate increases, but prevalence estimates have decreased in sub-Saharan Africa because allowance has been made for increased mortality in those with diabetes.
Conclusions: Worldwide estimates of numbers of children and adolescents with type 1 diabetes continue to increase.

1. Introduction

Type 1 diabetes is one of the most common endocrine and metabolic conditions in childhood. In type 1 diabetes insulin therapy is life saving and lifelong. A person with type 1 diabetes needs to follow a structured self-management plan including insulin use and blood glucose monitoring, physical activity and a healthy diet [1]. In many countries, especially in economically disadvantaged families, access to self-care tools including self-management education as well as to insulin is limited. This leads to severe disability and early death. 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, chronic microvascular and macrovascular complications [2,3] and death [4].

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 [5,6].

Many children and adolescents find it difficult to cope emotionally with their condition. Diabetes causes them embarrassment, results in discrimination and limits social relationships. It may impact on school performance and family functioning. Many schools and nurseries are reluctant to receive children with diabetes [7].

Pharmaco-technological and psycho-social aspects of therapy are equally important. The glycaemic results achieved by an emphasis upon a pharmaco-technological paradigm are frequently disappointing in children and adolescents [8]. At the same time, manufacturers must pay more attention to patients' special needs and convenience.

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% [9]. There is some indication that incidence is increasing more steeply in some of the low prevalence countries in Europe and also that in some high incidence European countries the increasing incidence trend is levelling off [10].

The International Diabetes Federation (IDF) Diabetes Atlas provides an authoritative source of evidence for health professionals, academics and policy-makers on the impact of diabetes [11]. Worldwide, regional and national estimates are produced for incidence and prevalence of type 1 diabetes (T1D) in children and adolescents. Prevalence estimates for children under 15 years in the 7th and previous editions of the Atlas have been based largely on available published incidence rates, with an assumption of a prevalence to incidence ratio of 6.2 made for countries with no available age-specific incidence rates [12]. However, anecdotal and published evidence suggests that the resulting prevalence figures were unrealistically high in less developed countries where lack of access to insulin and facilities for T1D management results in high case mortality [13,14,15].

Since the 8th edition IDF Diabetes Atlas [11] worldwide estimates of incidence and prevalence of T1D in the under 15 year and under 20 year age-groups have been produced, and more realistic figures for prevalence have been provided than in previous Atlas editions by making allowance for the higher mortality rates in those with prevalent T1D.

The objective of this article is to describe the methods developed for the 8th edition estimates of prevalent cases and to provide more detail and analysis of the incidence and prevalence estimates for the 9th edition.

2. Material and methods

2.1. *Literature search*

For the 8th edition IDF Diabetes Atlas we revised our search for population-based studies on incidence/prevalence of T1D in children and adolescents, without language restrictions and updated it again for the 9th edition. The following databases were searched: PubMed, Zetoc (title search of conferences), Web of Science, Embase and Medline (see Supplementary Fig. 1). Studies published between January 1990 and December 2018 were included. Titles and abstracts were first screened to select articles for full-text review. Reference lists of articles were also checked for further studies. Search records were cross-referenced and duplicates removed.

Studies were graded for quality as follows:

A. Population-based studies with validated ascertainment level ≥90%
B. Studies of lesser quality for which rates could be calculated (excluding case-series and studies which were not population-based)

If more than one study was available for a country, the following criteria were applied to select the most suitable: more recent studies, covering a large part of the country, including the age ranges 0–14 and 15–19 years, providing age/sex-specific rates for 0–4, 5–9, 10–14 and 15–19 year age-groups, and quality grade A.

In several countries, two or more studies were judged equally suitable on these criteria and the results of these studies were combined by averaging age/sex-specific rates. All studies used in the 9th edition estimates for T1D in children and adolescents provided incidence rates rather than prevalence rates.

2.2. International Diabetes Federation

The IDF divides countries into seven Regions: Africa (AFR), Europe (EUR), Middle East and North Africa (MENA), North America and Caribbean (NAC), South and Central America (SACA), South-East Asia (SEA) and Western Pacific (WP). This regional division was used throughout this article.

2.3. World Bank income group

Countries were assigned an income group based on gross national income (GNI) per capita in 2018 as published in the June 2019 World Bank Income Classification [16]: low-income country (LIC) ≤$1025, lower-middle-income country (LMIC) $1026 to $3995, upper-middle-income country (UMIC) $3996 to $12,735; high-income country (HIC) >$12,735.

2.4. Incidence rates for children

If age- and sex-specific incidence rates were available the direct method of standardisation was used, with the standard population having equal populations in each 5-year age/sex subgroup. If age-specific rates were not provided separately for each sex then the same rates were assumed for males and females. For countries in which no published incidence figures were available, the 0–14 year standardised incidence rate from similar countries were used instead. The choice of country from which to extrapolate was based on study quality, geographical proximity, per capita income and ethnic background.

2.5. Incidence rates for older adolescents

Relatively few studies had incidence data available for the 15–19 year age-group, but the following ratio was calculated for each country with available data. There was seldom sufficient data for the ratio to be obtained separately for each sex.

$$Ratio = \frac{15-19\ year\ old\ incidence\ rate}{0-14\ year\ old\ incidence\ rate}$$

A representative ratio was then calculated for each of the seven IDF Regions. In Regions where more than one country supplied data the ratio was obtained by averaging. The regional ratios are displayed in Table 1. For each country, the relevant regional ratio was multiplied by the 0–14 year incidence rate to give an estimated rate for the 15–19 year age group.

2.6. Mortality in type 1 diabetes

A method for estimating mortality in patients with T1D in any given country was required to adjust the derivation of prevalence from incidence to allow for mortality. Morgan and colleagues [4] conducted a systematic review of mortality follow-up studies in population-based cohorts of patients with T1D diagnosed in childhood or adolescence. Most of the 13 studies they identified reported findings as a standardised mortality ratio (SMR). The number of deaths observed in the cohort was compared with the number of deaths expected given the cohort age-structure on the assumption that the cohort experienced national mortality rates during follow-up. Conventionally the ratio is multiplied by 100 for presentation purposes.

$$SMR = \frac{observed\ deaths}{expected\ deaths} * 100$$

The SMR describes how many times more likely someone with T1D is to die compared to someone in the general population.

Using a negative binomial regression, Morgan and colleagues [4] fitted the following relationship between SMR and a country's infant mortality rate (IMR).

$$SMR = 1.6532 * 1.0688^{IMR}$$

IMR figures were obtained from the World Health Organization (WHO) Global Health Observatory data repository [17]. For countries not included in the repository, the Central

Table 1 – Estimated incident (newly-diagnosed) cases of type 1 diabetes per annum and prevalent (existing) cases in the 0-14 and 0-19 year age-groups by IDF Region after adjustment for mortality.

Region	Number of Countries with Incidence rates available (%)	Total Population (1000s)		Ratio of incidence rates in 15–19 year olds compared to 0–14 year olds	Incident Cases per annum (1000s)		Prevalent Cases (1000s)	
		0–14 year	0–19 year		0–14 year	0–19 year	0–14 year	0–19 year
AFR	3/47 (6%)	455,072	570,177	7.0	4.3	10.3	9.4	25.8
EUR	44/57 (77%)	166,664	217,968	0.7	25.1	31.1	162.6	296.5
MENA	12/21 (57%)	237,086	301,469	1.7	14.4	20.8	82.9	149.4
NAC	8/24 (33%)	107,354	143,931	0.5	18.7	21.9	121.4	224.9
SACA	12/19 (63%)	119,459	160,798	0.7	9.9	12.3	68.4	127.2
SEA	4/7 (57%)	429,779	576,715	1.2	17.1	21.3	101.7	184.1
WP	11/36 (31%)	462,520	611,028	1.1	8.8	11.2	54.4	102.2
World	**94/211 (45%)**	**1,977,936**	**2,582,088**		**98.2**	**128.9**	**600.9**	**1110.1**

Intelligence Agency World Factbook [18] or IndexMundi [19] were used.

2.7. Numbers of incident and prevalent cases

The number of incident (new) cases per year was estimated for each country by multiplying the United Nations population estimates for 2019 [20] in each of eight age/sex subgroups (males or females aged 0–4, 5–9, 10–14 or 15–19 years) by the corresponding incidence rate.

The number of prevalent (existing) cases was calculated by incrementally cumulating incident cases by year of age having subtracted the number of deaths predicted annually from the fitted SMR used as a multiplier on the national mortality rates. The method is described fully in the Supplementary text.

Numbers of incident and prevalent cases for each country were then summed by IDF Region and by World Bank income group to give regional and global numbers of incident and prevalent T1D cases in the relevant age groups (0–14 years or 0–19 years).

3. Results

3.1. Search summary

The 67 publications selected from the literature search gave incidence estimates for 94 countries as summarised in Supplementary Table 2. The table shows the geographical coverage, time period, age range, number of cases, estimated completeness of ascertainment and a quality category for each study. Fig. 1 shows a map of rates for 0–14 year olds, directly standardised where possible, with countries shaded according to their rate. The extrapolation of rates to countries without incidence data (the unshaded countries in Fig. 1) is summarised in Supplementary Table 3.

3.2. Incidence rates for older adolescents

Of the selected publications, only 19 had data on incidence rates of T1D aged 15 or older. This was too small a number of studies for meaningful extrapolation to neighbouring countries (the approach used in the 0–14 year age-group). Instead, 28 publications were selected to contribute towards ratio estimates for each IDF Region. Sixteen of these studies were from the EUR Region, three from the AFR Region, one from SACA Region and two from each of the remaining four Regions. Table 1 shows the ratios obtained for each Region calculated as the average of ratios for studies from the Region with available data. The ratio of 7.0 for the AFR Region was considerably larger than the ratio for any other Region, indicative of a markedly higher incidence in the 15–19 age-group relative to the 0–14 age-group in this Region.

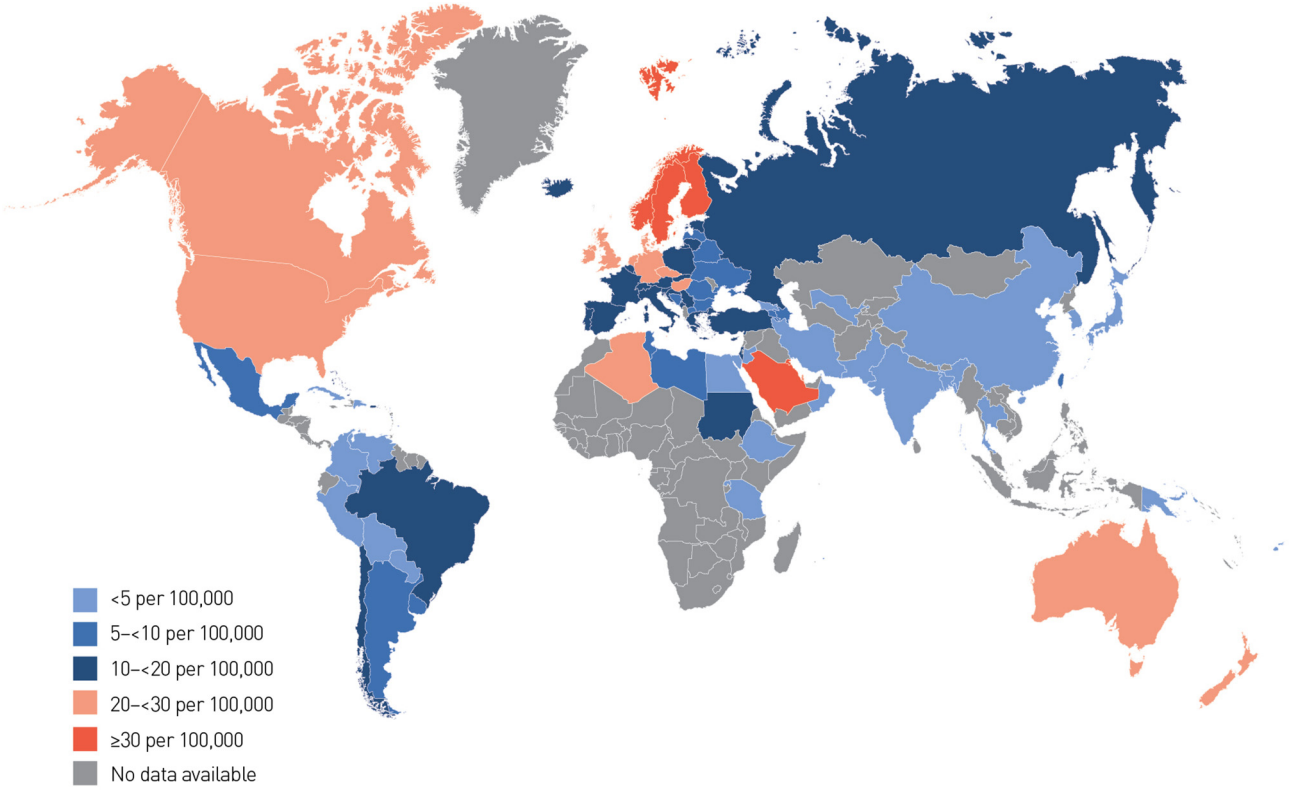

Fig. 1 – Map of age-sex standardised incidence rates (per 100,000) from publications of type 1 diabetes in children aged under 15 years.

3.3. *Worldwide estimates of type 1 diabetes*

Table 1 also summarises, by IDF Region, the number and percentage of countries with incidence data available, the total population and estimates of both incident and prevalent type 1 diabetes cases for both the 0–14 year and 0–19 year age-groups. It is estimated that 98,200 children under 15 years develop T1D worldwide annually, with this figure increasing to nearly 128,900 under 20 years. There are an estimated 600,900 children under 15 years living with type 1 diabetes worldwide, with this figure almost doubling to 1,110,100 for under 20 years.

3.4. *Regional estimates of type 1 diabetes*

In addition to estimates of incident and prevalent cases by IDF Region presented in Table 1, Fig. 2 additionally includes estimated annual numbers of deaths among those with T1D. Over a quarter of the prevalent cases in both age groups are in the EUR Region. The second largest in both age groups is the NAC Region, contributing a further 20% to the global total prevalent cases. The AFR Region contributes the smallest portion of around 2% in both age groups, despite having one of the largest populations. The WP Region has the largest population in both age groups but contributed only approximately 9% of prevalent cases in each age group. Supplementary Table 4 shows, by IDF Region, each country's estimate of incident and prevalent cases for age-groups 0–14 years and 0–19 years.

3.4.1. *Africa Region*

Supplementary Table 2 shows that 6% of countries (three out of 47) in the AFR Region had incidence data for the 0–14 year age-group available, by far the lowest percentage of all the Regions. Although only one of the three was assigned to quality category A, all three did also provide data for the 15–19 year age-group. Thus, extrapolation was necessary for most countries in this Region. As can be seen from Supplementary Table 3, studies from both inside the AFR Region (Ethiopia, Rwanda and Tanzania) and from other Regions (Sudan and Mauritius) were used. Despite its low incidence rate, the AFR Region stands out in terms of the numbers of estimated deaths in those with T1D, in both age groups (Fig. 2). This is largely a reflection of the high infant mortality rates in the Region resulting in large predicted SMRs.

3.4.2. *Europe Region*

The highest coverage of studies with good quality data is found in the EUR Region, with over three quarters of countries reporting incidence rates for type 1 diabetes and 60% of the publications classified as quality grade A. Most countries without incidence data have small populations. This Region also had 16 publications covering the 15–19 year age group, the largest number for any Region. Estimates for the EUR Region are therefore likely to be the most reliable of all the Regions. The Nordic countries of Finland, Sweden and Norway are in the top five of countries worldwide ranked by incidence rate in the 0–14 year age group, and the United Kingdom, Ireland and Denmark also appear in the top 10.

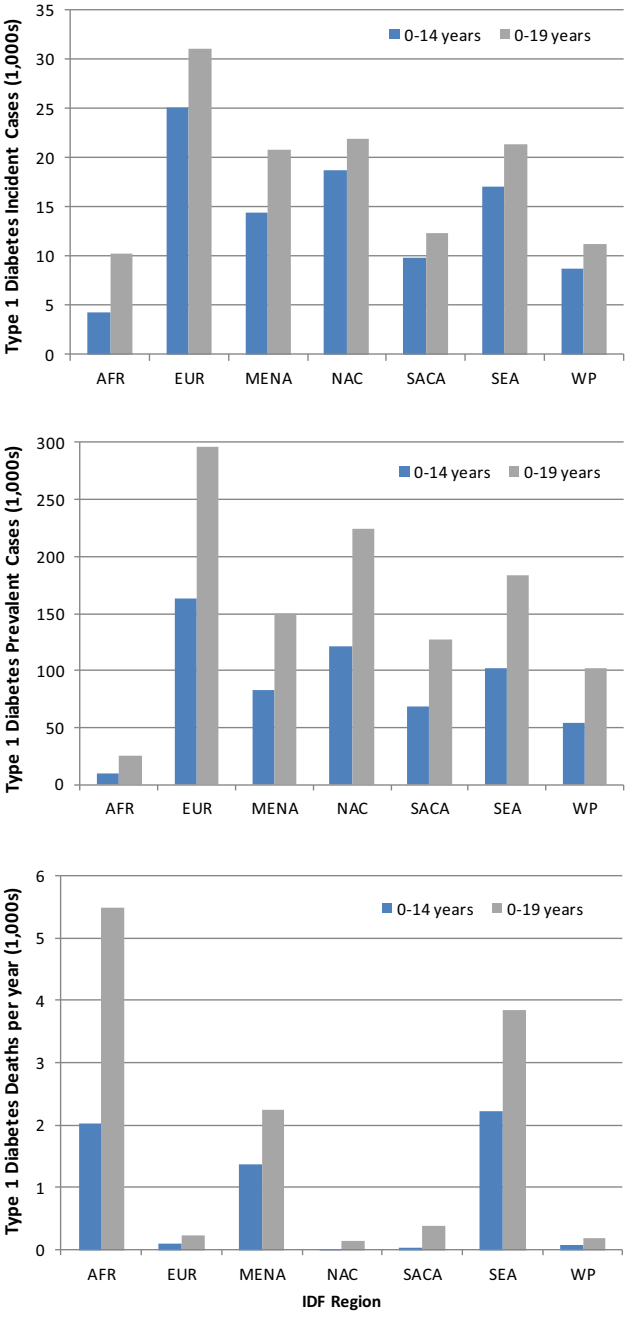

Fig. 2 – Comparison of type 1 diabetes incident and prevalent cases and deaths by IDF Region for 0–14 year and 0–19 year age-groups.

The United Kingdom (3500) and the Russian Federation (3200) have the largest numbers of new cases annually in the 0–14 year age-group in the Region. While this Region has the highest incidence rates and largest numbers of incident and prevalent cases, there are few deaths among those with T1D.

3.4.3. *Middle East and North Africa Region*

In contrast to the neighbouring AFR Region, the MENA Region has incidence data covering over half the countries in the

Region. It has three countries, Kuwait, Saudi Arabia and Qatar, in the top 10 ranked by incidence rate in the 0–14 year age group. The highest number of new cases each year in this age-group are for Algeria (3100), Saudi Arabia (2500) and Morocco (2400). The MENA Region has the third largest estimated number of deaths in those with T1D.

3.4.4. *North America and Caribbean Region*

Although studies were available for only eight out of the 24 countries in the NACA Region, most of the countries without published incidence rates are small, and together represent only 5% of the population in the Region. The United States ranks in second position worldwide for annual number of incident cases in the 0–14 age groups (14,700) accounting for almost 79% of the incident cases in the Region with Mexico (2100) and Canada (1800) accounting for most of the remainder. Despite the NAC Region having the second largest number of cases of all the Regions it had the smallest number of estimated deaths in those with T1D.

3.4.5. *South and Central America Region*

Published rates were available in the literature for 12 (63%) of the 19 countries in the SACA Region making it second only to the EUR Region for the availability of incidence data. Historically, this Region has reported low incidence rates, but a recent article shows a marked increase in rates in Brazil [21], which has by far the largest annual number of incident cases (7300 for the 0–14 year age-group), making up almost three quarters of the total for the Region. The estimated number of deaths in those with T1D in the SACA Region is small.

3.4.6. *South East Asia Region*

Four of the seven countries in the SEA Region had incidence data all quality grade B (India, Bangladesh, Maldives, Mauritius), and only Bangladesh had data on the 15–19 year age-group. Indian incidence rates are based in just one area and may therefore not reflect the diversity of the country, so estimates should be treated with caution. India has by far the largest population and so dominates the estimated case numbers in this Region with 15,900 incident cases in the 0–14 year age group, 93% of the total for the SEA Region. Worldwide, India ranks first in the countries of the world, for number of incident cases in the 0–14 and 0–19 year age groups. The SEA Region was notable for the large estimated numbers of deaths in those with T1D.

3.4.7. *Western Pacific Region*

Incidence rates data were available for 11 (31%) of the 36 countries in the WP Region, the second lowest of all the Regions. Apart from Australia and New Zealand, the rest of the countries in the Region tend to have low incidence rates. China was used to calculate the ratio between 15 and 19 year old and 0–14 year old incidence rates as it was the only country with data available in the older age-group. As Australia and New Zealand have large populations of European descent, the EUR Region ratio was used for these two countries. China dominates the figures for the Region accounting for over 50% of the population in the 0–14 year age-group and, with 4800 incident cases per year, contributes 55% of the estimated new cases in that age-group. Estimated numbers of deaths in those with T1D in the WP Region are small.

3.5. *World Bank income group estimates*

Fig. 3 shows the distribution of incident and prevalent cases and estimated annual numbers of deaths in countries aggregated by World Bank income groups. The number of incident and prevalent cases is largest in the high-income countries even though these countries only include about 10% of the world population in both the 0–14 and 0–19 year age-groups.

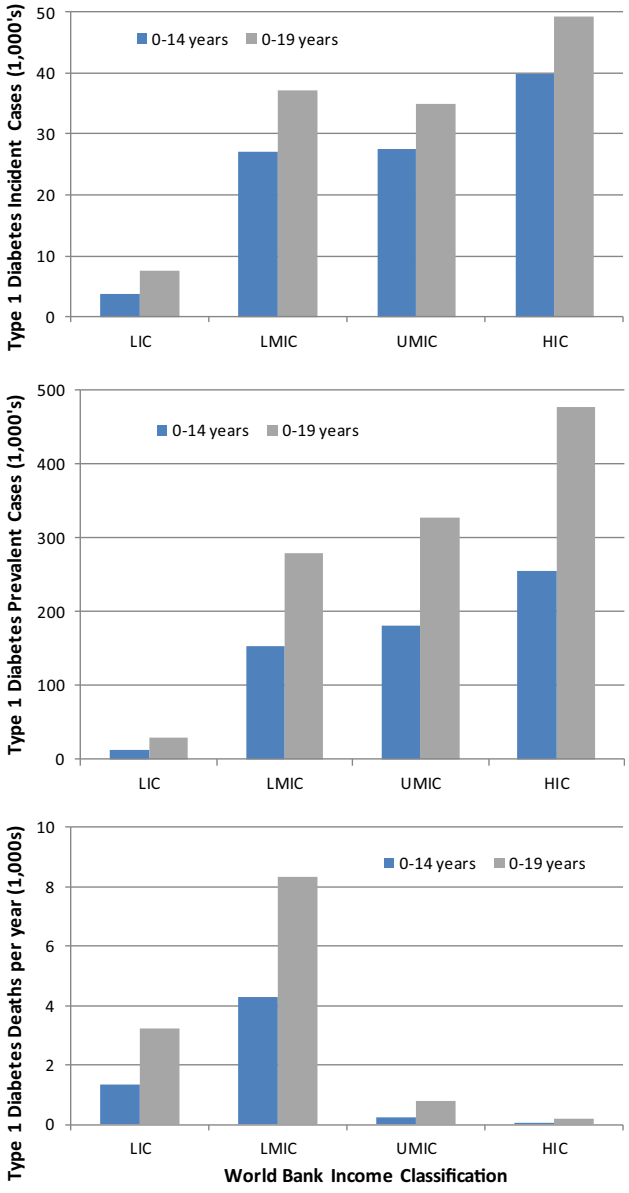

Fig. 3 – Comparison of Type 1 Diabetes incident and prevalent cases and deaths by World Bank Income Classification for 0–14 year and 0–19 year age-groups (LIC – low-income countries, LMIC – lower-middle-income countries, UMIC – upper-middle-income countries, HIC – high-income countries).

The lower-middle and upper-middle-income countries have roughly similar numbers of incident cases despite the former having a much larger percentage of the population (47%) than the latter (28%). However, the numbers of prevalent cases are notably smaller in the lower-middle-income countries reflecting their higher predicted mortality. The low-income countries, which account for 15% of the world population in these age-groups, had by far the smallest number of incident and prevalent cases. Most of the total estimated numbers of deaths in children and adolescents with T1D were in the low-income and lower-middle-income countries.

4. Discussion

Nationwide, population-based prospective registries provide the best data on the incidence of T1D in childhood and adolescence, particularly if high ascertainment rates are maintained, but such studies are typically only conducted in well-resourced countries. Smaller studies can show large year to year fluctuations in T1D incidence and, where available, several years of data were used to obtain more reliable estimates. Given the widely-reported increasing T1D incidence rates in childhood, the use of data published prior to 1990 has been discontinued in the 9th edition estimates and the most up-to-date data available for each country has been used, but many of the sources in Supplementary Table 2 give rates which relate only to the 1990s. No attempt has been made to adjust these rates to reflect increases in incidence in intervening years, and neither have adjustments been made to inflate rates from registries which are known to have incomplete ascertainment. The expense of maintaining high-quality registries is considerable, and in the future it seems likely that alternative sources of incidence rate estimates will be obtained from computerised clinical information systems and prescription or health insurance databases.

As well as the use of extrapolation of incidence from a country to its neighbours, which was particularly common in AFR Region where so few countries supplied data, the use of rates from regional studies to represent whole countries is an obvious weakness, especially in countries with heterogeneous and ethnically-diverse populations. Again, the availability of more publications with national coverage, particularly from less developed countries, would be the most satisfactory solution to this concern.

In the previous 8th edition of the IDF Diabetes Atlas, for the first time, attempts were made to adjust the method of obtaining prevalence from incidence to take account of the well-known excess mortality in children and adolescents with T1D. An important consequence of this is that prevalence estimates for children and adolescents are no longer comparable with those provided in earlier editions of the Atlas, the lack of comparability affecting particularly the less-developed countries where survival of those with T1D is poorest. The method that was used can be criticised on the basis that it requires considerable extrapolation of a relationship between excess mortality in those with T1D (as measured by the SMR) and infant mortality rate that was derived mainly from data in developed counties [4]. As more studies of mortality follow-up are published it may be possible to refine this relationship but it seems likely that the criticism will continue to be relevant until more high-quality mortality studies are published from lower-income countries.

It has been argued that infant mortality is dominated by neonatal mortality and the numbers of deaths in the first year of life are not falling as rapidly as in children aged 1–5 years [22,23]. Therefore the derivation of the formula for SMR (section 2.6) and prevalence calculations were repeated using UNICEF under-5 year mortality rates [24] instead of infant mortality rates. The changes in the total prevalent cases in the 0–14 or 0–19 year age groups were minimal in most Regions but prevalence figures for the AFR Region were reduced in both age groups.

The scarcity and poor quality of data means that estimates for the AFR Region in particular should be treated with some caution. In lower income countries, and in sub-Saharan Africa in particular, reported incidence rates may in reality be higher than perceived because of cases being missed and dying without a diagnosis of T1D ever being made [25,26]. Also some of the cases reported as type 1 may actually be another form of diabetes (type 2, atypical diabetes, or malnutrition-related diabetes) [15,27]. Unsurprisingly, the inclusion of the correction to adjust for mortality (introduced in the 8th edition estimates) has resulted in a reduction in the numbers of prevalent cases in the AFR Region, but the numbers of incident cases in the AFR Region have also reduced compared with those of previous editions because of the replacement of some older, less-reliable source studies with more recent ones. The calculated ratio of incidence rates in the 15–19 year age group to the 0–14 year age-group was notably higher in each of the three countries in the AFR Region that provided data than in other countries, perhaps indicative of a different pattern of incidence by age-group. Further data from this Region should help to refine this ratio.

Furthermore, there is evidence from Tanzania [13], Mali [14] and Rwanda [15] that numbers of known children and adolescents with T1D can rise quickly with interventions by local diabetes centres supported with insulin, test strips and other supplies by international aid programs such as Life for a Child [28] and Changing Diabetes in Children [29].

The analysis by World Bank income groups in Fig. 3 shows most starkly the disparity across the countries of the world in the distribution between the incidence of T1D and its associated mortality. Although the majority of T1D cases occur in the high-income and upper-middle-income countries, the majority of deaths are in the low-income and lower-middle-income countries. This key finding reinforces the need for improved access to insulin and blood glucose meters and test strips in lower income countries [30,31] and the training of healthcare workers in such countries to recognise and treat this condition. Three tiers of care (minimal, intermediate and comprehensive) have been defined by availability of insulin and blood glucose monitoring regimens, requirements for HbA1c testing, complications screening, diabetes education, and multidisciplinary care [32], and it is to be hoped that policy-makers will aspire to attain the highest levels of care possible given the resources available.

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Declaration of Competing Interest

The authors declare no conflict of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.107842.

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