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Incidence and trends of type 1 diabetes before and after 2000 in the Western Pacific Region: A systematic review and *meta*-analysis

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A B S T R A C T

Objectives: To undertake a systematic review of publications describing Type 1 diabetes (T1DM) incidence, trends over time and associated factors in the Western Pacific Region (WPR).
Methods: As per the PROSPERO-registered (CRD42019122646) protocol English (MEDLINE, Embase, Global Health) and Chinese data-bases (China National Knowledge Infrastructure, VIP, Wanfang) from onset to 31/12/2019 were searched for T1DM incidence in the WPR. Country level data extracted included annual crude incidence rates by sex, number of new cases per annum (p.a.) and cumulatively, and the population at-risk. A *meta*-analysis for T1DM incidence was performed (by region and narrow age-bands, where possible) with subgroup analyses by time and by region.
Findings: Forty-five population-based studies (21 from China), published 1973–2017, estimated T1DM incidence, mostly in youth, in 11 WPR countries. After 2000, mean annual T1DM incidence/100,000 person years aged 0–14 years ranged from 0.9 (95 % confidence intervals (CI), 0.6–1.3) in Fiji to 23.2 (95 % CI, 21.3–25.2) in Australia. The mean annual increase over time ranged from 2.8 % in Australia (1990–2002) to 14.2 % in Shanghai (1997–2011). T1DM incidence increased most in China (2.7-fold over 30-years) then Thailand (2-fold over 15-years). Most studies documented increasing incidence with age, though only two studies included people aged $\geq$ 20 years. Many, but not all studies reported significantly higher T1DM incidence in females vs. males.
Conclusion: T1DM incidence in the WPR is generally increasing, varying by age, sex, time and country. Results increase understanding of regional T1DM incidence and inform research and healthcare strategies.

1. Introduction

Globally the annual incidence rate of Type 1 diabetes mellitus (T1DM) varies widely, for instance with higher rates in Europe, North America, Australia and New Zealand, with lower observed rates in East Asia and Southeast Asia [1–4]. The widely-reported increasing incidence of T1DM is likely related to a combination of both genetic susceptibility and environmental factors [1,5–7], which are not fully elucidated, with some increases, particularly in lower income countries, due to improvements in registries, reporting and diagnosis. In people with T1DM, early diagnosis of risk and onset, regular blood (and/or interstitial fluid) glucose monitoring, proper daily insulin treatment and attention to lifestyle and other risk factors (such as hypertension, dyslipidaemia and smoking), can improve the quantity and quality of life by mitigating acute and chronic diabetes complications.

According to the International Diabetes Federation (IDF) atlas, in children aged under 15 years, the IDF Western Pacific Region (WPR) annual incidence estimates were 8,700 new cases in 2019 [1], 10,000 in 2015 [8], 5,300 in 2013 [9], and 4,900 in 2010 [10]. The incidence pattern varied by age group and country. It is noted that until 2021 the IDF Atlas did not report T1DM incidence in adults, which is not uncommon, and there are relatively little data compared to that in youth [1,11,12], with only data from two countries [13,14] being identified in this systematic review. There are clear geographical differences in

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incident T1DM trends and wide variations in the overall annual increase across countries [15]. European evidence shows that T1DM incidence in youth under the age of 15 years is increasing more steeply in some low prevalence countries and also that in some high incidence countries the increasing incidence trend is levelling off, but so far the evidence is not conclusive [16].

In the IDF-WPR, estimates for T1DM in children and adults were based on studies from 11 of 39 countries, regions or territories (in alphabetical order: Australia, China, Fiji, Hong Kong China, Japan, New Zealand, Papua New Guinea, Republic of Korea, Singapore, Thailand, and Taiwan) [1]. The IDF Atlas 10th edition evaluated one study, typically the most recent available for each country to estimate T1DM incidence [1], which mainly related to childhood-onset T1DM. The availability and systematic analysis of more publications, particularly from low incidence rate but very populous countries, such as China, is of considerable interest and value for healthcare planning, as there is a wide range of health outcomes for people with T1DM in the WPR.

Understanding the incidence pattern of T1DM is key as a baseline for future studies and to facilitate improvements in healthcare where needed and in planning relevant research. However, there is a relative lack of comprehensive and accurate data, even in the IDF atlas, of the annual incidence of T1DM in WPR countries. Whilst comprehensive work by James et al. in 2022 [3] provided a valuable overview of childhood diabetes in non-European-origin populations in the Western Pacific Region, our study is distinct in its specific focus on the temporal trends in T1DM incidence. Additionally, we have incorporated a substantial body of research from China, which has not been comprehensively covered in prior reviews. Thus, our study objectives were to systematically review studies of T1DM incidence in the WPR, and to compare patterns by age and sex between countries.

2. Methods

2.1. Search strategy and selection criteria

English-language databases searched were: Global Health, MEDLINE and Embase. Chinese-language databases searched were: China National Knowledge Infrastructure (CNKI), VIP, Wanfang data published until 31st December 2019. Search terms were based on three categories: 1) the population of interest i.e. children, adolescents and adults; 2) the variable of interest i.e. Type 1 diabetes; 3) the outcome of interest i.e. incidence, population at risk. Full search terms are provided in Supplementary Table 1. We included studies reporting incidence or trends or prevalence of T1DM in the WPR and in individual countries. Study types were epidemiology studies with cross-sectional or cohort designs which reported T1DM incidence. The criteria for T1DM diagnosis used had to comply with those of the World Health Organization (1985 or 1999) or the American Diabetes Association (1997 or 2011).

We excluded studies that were: 1) reviews, viewpoints or commentaries; 2) did not report relevant denominators from which total or age /

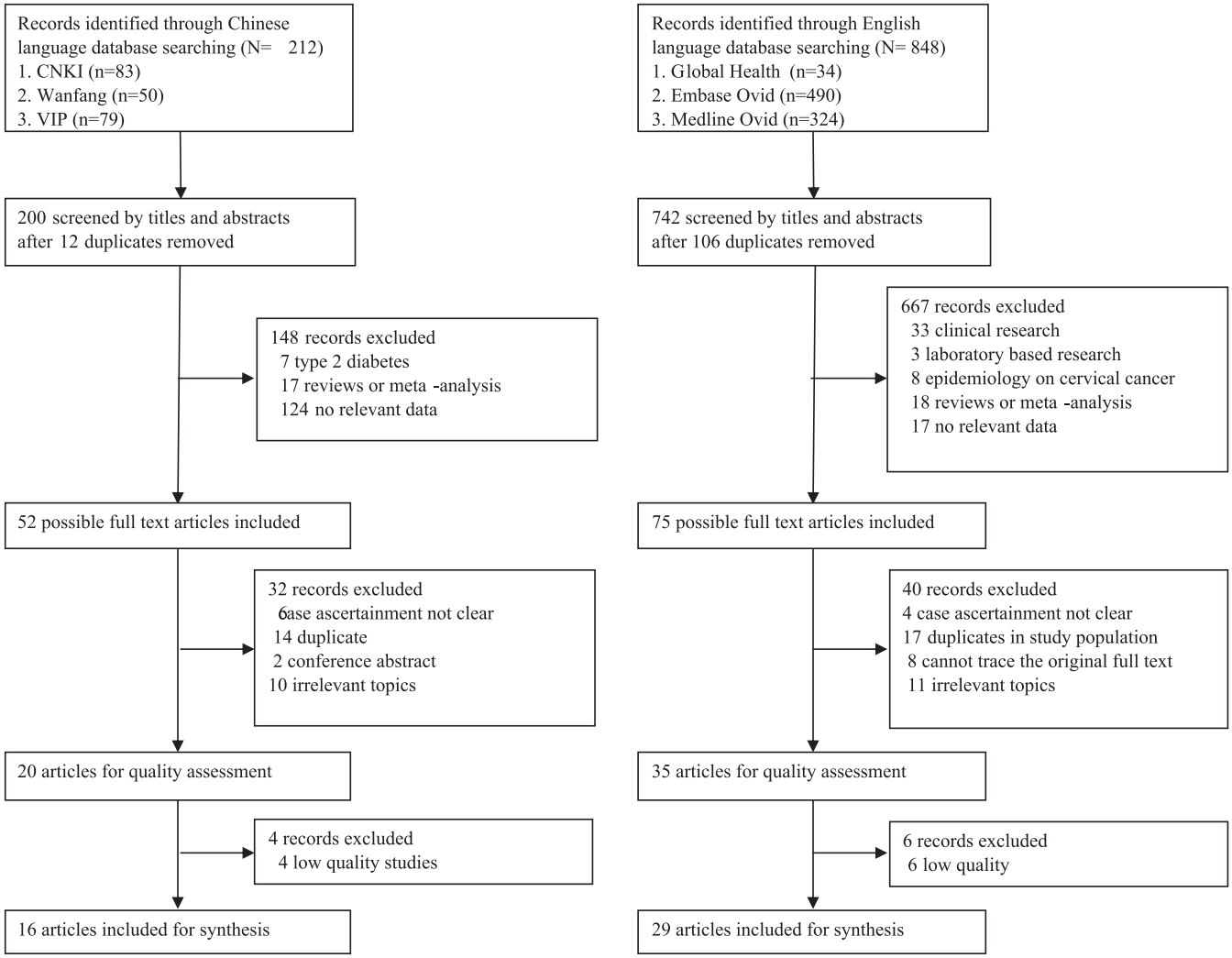

Fig. 1. Flow diagram for selection of studies.

sex specific prevalence and T1DM incidence could be estimated; and 3) where case definition was not clear or inconsistently applied. The study selection followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17] and the selection process is displayed in Fig. 1, distribution of number of studies in Western Pacific Region is displayed in Fig. 2

DW, JH, XH and JS independently reviewed the titles and abstracts in the Chinese and English databases. Disagreements on any records were discussed and clarified by DW. The final decision for article inclusion in the systematic review was made by DW.

2.2. Data analysis

A data extraction spreadsheet was used to collect information on the characteristics of each included study (Supplementary Tables 2–3). It included three parts: 1) information about the study, namely: reference, year of publication, country, period of study, data source of the population, age group (0–4, 5–9, 10–14, 15–19 years), statistical analyses used; 2) information about T1DM incidence, namely: mean annual crude incidence rate by country, sex, confidence intervals, number of T1DM cases per year, number of cumulative T1DM cases, and population at risk. 3) Additional information, namely: case definition. All data were categorised by the IDF regions and study periods for further analysis. Four authors (DW, JH, XH and JS) extracted the information from included studies. When several articles from the same study had reported the same endpoint, we included only the article providing the most recent results, covering a large part of the country, including the age ranges 0–14 years, and providing age/sex-specific rates for 0–4, 5–9, 10–14 and 15–19-year age-groups. Studies involving individuals aged 20–80 years were retained in the analysis. These studies were included in the analysis but were not considered in the subgroup analysis for the 0–19 year age group.

An adapted version of GRADE guidelines [18] was used to assess the quality of the included studies, focusing on the following aspects: study design, quality of control group, sample size, analysis method, bias, confounding factors and geographical spread (Supplementary Table 4). The GRADE guidelines were translated from English into Chinese for assessing the Chinese language studies. Studies were assessed according to the checklist by three authors (JH, XH and JS). Any disagreement was resolved through discussion with DW. The overall score for each study was calculated after assessing each criterion listed above.

For each study included in the *meta*-analysis, the mean annual incidence rate (MAIR) was computed using the following formula: 1). For studies providing cumulative number of patients and persons at risk per year), the following formular was used: MAIR = Mean annual crude incidence = (cumulative number of patients)/(Persons at risk per year *Study years)*100,000; 2). For studies reporting persons at risk per year was derived when cumulative cases were provided, but not persons at

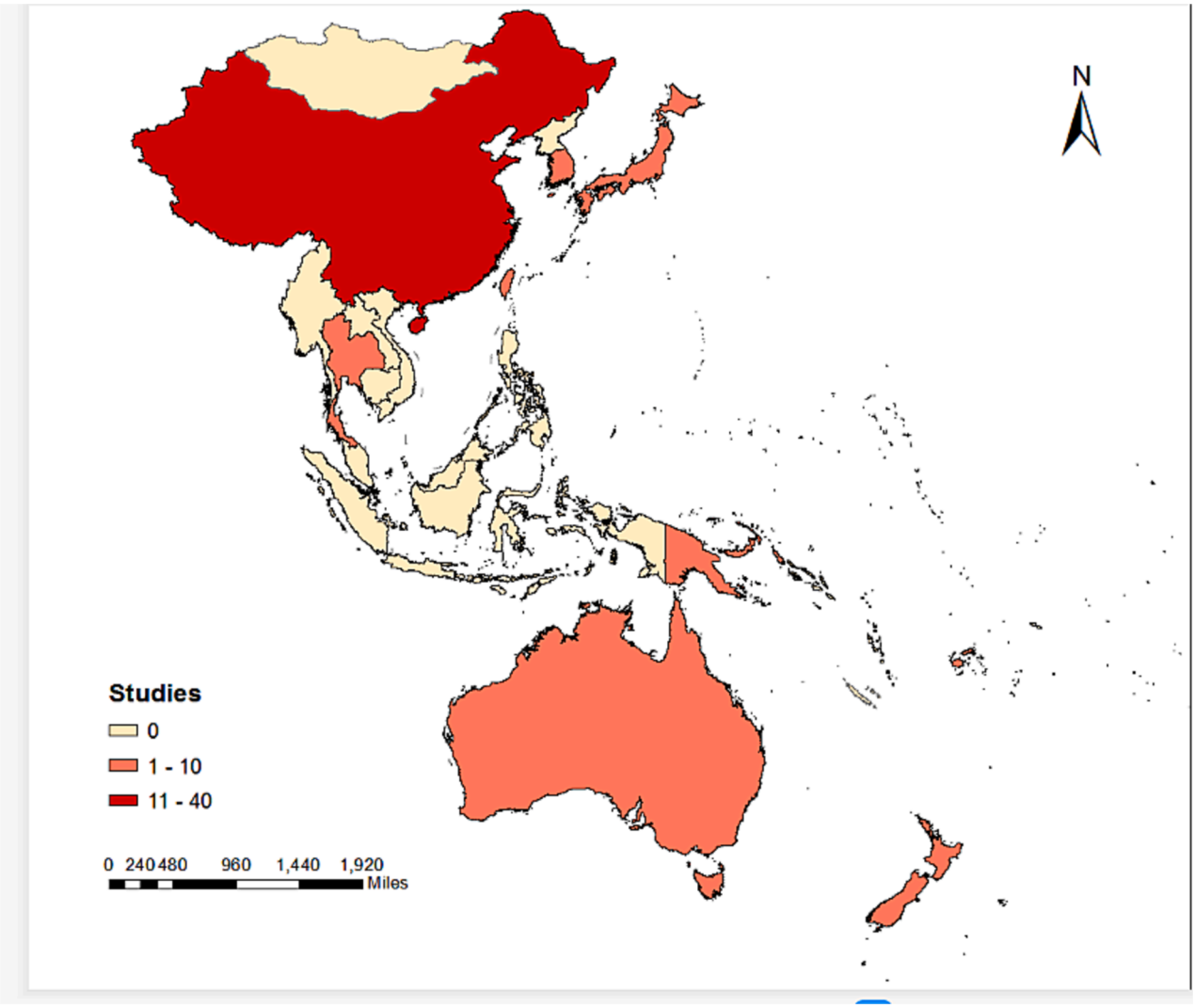

Fig. 2. Distribution of number of studies in Western Pacific Region.

risk per year, the following formular was used: Persons at risk per year = (cumulative number of patients*100000) / (Mean annual crude incidence*Study years); 3). For studies in which the number of Cumulative Cases was derived when persons at risk per year were provided, but not cumulative cases, the following formular was used: Number of cumulative cases = (Persons at risk * (Mean annual crude incidence*Study years)) / 100,000; 4). For studies reporting estimating persons at risk per year when Confidence Intervals (CI) are provided, the following formular was used: Persons at risk per year = (Mean annual crude incidence)/ [(Mean annual crude incidence - lower CI of Mean annual crude incidence)/1.96]^2. Please refer to Table 1 for the calculated values.

A *meta*-analysis (by region and narrow age bands, where possible) for T1DM incidence (mean annual crude incidence) was performed, with reporting of pooled estimates and 95 % CIs. The degree of heterogeneity among the included studies was evaluated using the I^2 statistic, a measure of variation attributed to between-study differences. As significant heterogeneity in the data was expected a random-effects (DerSimonian-Laird method) *meta*-analyses was performed to estimate the overall incidence of T1DM. The pooled WPR incidence rate was not estimated due to variations in study timeframes and the lack of data for many countries and regions.

The overall *meta*-incidence rate was derived by synthesising the results from all included studies using a random-effects model. The random-effects model considers variance within studies and between-studies.

Meta-Incidence Stratification: 1). region-specific *meta*-incidence: For stratification by region, studies were grouped based on geographical locations (e.g., East Asia, Pacific islands). A *meta*-analysis was performed separately for each region by pooling the incidence rates specific to that region using the same methods mentioned earlier for overall *meta*-incidence. 2). age band-specific *meta*-incidence: Stratification by age band involved grouping studies based on different age ranges (e.g., 0–4, 5–9 years). A *meta*-analysis was conducted within each age band to compute the *meta*-incidence rates specific to each category. 3). sex-specific *meta*-incidence: Stratification by sex involved separating studies based on male or female sex. A *meta*-analysis was performed separately for each sex category, combining incidence rates specific to each sex.

After obtaining stratified *meta*-incidence rates for regions, age bands, and sexes, these estimates were compared and combined into subgroup *meta*-analyses. The combined estimates for different subgroups were derived using similar *meta*-analytic methods as employed for the overall *meta*-incidence.

Since the global incidence of TIDM has changed over the years and the WHO DIAMOND Project [15] collected data worldwide until the year 1999, we stratified the studies by study period (before Dec 31, 2000 versus after 2000) to make comparisons more robust and to obtain contemporary incidence data.

Subgroup analyses by year of data completion (before and including 2000, and after 2000); by region (Australia and New Zealand, East Asia, South-East Asia, Fiji and Papua New Guinea (PNG)). We classified studies as pre-2000 if the study ended before 31st December 2000, or 2002 irrespective of the publication date. This is because most studies that were conducted before 2000 ended by 31st December 2000 and four studies [19–22] with a long period of follow-up ended by 31st December 2002. For example, the Haynes *et al* study [19] was conducted between 1985 and 2002 (baseline) and 2016 (follow-up), the Kou *et al* study [20] was conducted between 1985 and 2003, and data were available between 1985–2000. For studies conducted after 2000, we estimated and compared the annual incidence of T1DM by country, age, sex, and study period. For studies exploring sex/age differences and time trends in incidence, we narratively synthesised data and summarised results by whether males or females had the higher incidence, by whether a trend or sinusoidal pattern was observed, and by whether a peak incidence by age group existed. For regional subgroup analysis, we classified studies as European-origin countries (Australia and New Zealand), Eastern Asian nations or territories (China, Hong Kong SAR, Taiwan, Japan, and South Korea), non-Chinese-origin South-East Asian (Thailand) and Western Pacific Island countries (Papua New Guinea (PNG), and Fiji).

Sensitivity analyses were undertaken after removal of all low-quality studies. The protocol of this study is registered with PROSPERO, number CRD42019122646. R software (version 3.5.2; https://www.r-project.org/) was used for data analyses.

2.3. Role of the funding source

The funder of the study, the IDF, had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

3. Results

The English search identified 848 records; 106 duplicates were removed and 742 titles and abstracts were screened; 75 were retained for full text review, and 35 were retained for quality assessment. The Chinese search identified 212 records; 12 duplicates were removed and 200 titles and abstracts were screened; 52 were retained for full text review, and 20 were retained for quality assessment. In total 29 English and 16 Chinese language studies, covering 11 WPR countries conducted between 1973 and 2017, were included (Fig. 1).

The number of studies conducted by decade were: before 2000 (26 studies), after 2000 (10 studies) and study period across 2000 (nine studies, six of which can be divided into two periods by 2000). Before 2000, the follow-up period ranged from 1973 to 92 in Matsuura's Japanese study [23] to 1999–2002 in the Chong *et al* Australian study [22]. After 2000, the follow-up period ranged from 2001 to 2003 in the Kou *et al* China-Liaoning study [20] to 2002–2017 in the Haynes Australian study [12]. Most studies (n = 21) were conducted in China (Table 1). Australia contributed six studies [11,12,19,21,22,24], Japan four studies [23,25–27], Hong Kong SAR [28–30] and Thailand [31–33] three studies each, Korea [14,34] and New Zealand [35,36] two studies each, while Taiwan [37], Singapore [38], Fiji [39], PNG [40] had one study each (Table 1).

Of the 45 studies 44 (97.8 %) were population-based studies; 34 studies had at least two sources of case ascertainment, either in the registry system or in populations under surveillance; four studies (two in Korea [14,34], one each in Taiwan [37], and Japan [23]) reported incidence from a registry with one source of case ascertainment; two studies reported incidence from one source of case ascertainment (two in Thailand). Only one (Fiji) [39] study was hospital-based, with well-defined populations and one study source was case ascertainment. Forty-three studies reported over 90 % case ascertainment. All 45 studies estimated incidence on the basis of a census-based denominator of people at risk. Only two studies (one in China [13] and one in Korea[14]) reported disease incidence by age group for the full age range (0–80 years). Twenty-one studies (45.7 %) reported the incidence by narrow age bands for 0–14 year old children. Only 13 studies (seven in China, five in Australia, and one in New Zealand) reported data for age and sex specific rates by narrow age bands (Supplementary Table 3), with a primary focus on individuals within the 0–14 years age group and emphasising the sex-specific aspect. Data from studies included in the *meta*-analyses were heterogeneous ($p < 0{\cdot}0001$). There were only two studies which reported incident T1DM in those aged over 19 years at onset. Lack of information in adult-onset T1DM is an important issue as many people do not present until their adult years. In relatively low T1DM incidence countries, in the years 2010–2013 in China, 65.3 % of new onset cases was in people aged $\geq$ 20 years [13] and in 2013 in Korea, 54.9 % cases were aged 30 years or older [14].

Heterogeneity was high across all the studies before and after 2000, with I^2 estimated at 99.1 %, $P < 0.001$ (Supplementary 5). The overall

Table 1
The Characteristics of studies and mean annual incidence of type I diabetes in each study.

First Author	Publication Year	Country/ territories	Region	Study period	Study years	Agerange	Persons at risk per year	Number ofcumulative cases	Mean annual crude incidence per 100,000
Haynes A	2017	Australia	Western	2002–2017	16	0–14	65,887,987	16,463	25
Taplin CE	2005	Australia	New South Wales	1990–2002	13	0–14	1299322†	3260	19.30
Chong JW	2007	Australia	Victoria	1999–2002	4	0–14	3,831,904	745	19.44
Catanzarit L	2009	Australia	–	2000–2006	7	0–14	28,028,715	6350	22.66
Haynes A	2012	Australia	Western	1985–2012	32	0–14	13098801†	2499	19.10
Tran F	2014	Australia	New South Wales	2001–2008	8	10–18	819886†	1443	22.00
Haynes A	2015	Australia	–	2000–2011	12	0–14	49,015,342	11,575	23.60
Wang LM	1998	China	Heilongjiang	1989–1994	6	0–14	56497†	4	1.18
Shi LY	1998	China	Hubei	1989–1996	8	0–14	802,670	30	0.47
Yang HH	1999	China	Guangxi	1989–1996	8	0–14	783,378	28	0.45
Huang ZS	1999	China	Guangxi	1989–1998	10	0–14	1666667†	10	0.06***
Fu SH	1999	China	Hainan	1989–1995	8	0–14	2,284,238	53	0.29
Bu RF	1999	China	Jiangsu	1990–1997	8	0–14	416667†	18	0.54
Jiang JU	1999	China	Henan	1989–1996	8	0–14	333333†	16	0.60
Wang Kean	1999	China	Nationwide	1988–1996	9	0–14	19,411,256	833	0.56***
Zhu C	2000	China	Beijing	1988–1996	9	0–14	2,064,406	183	0.98
Zhu LY	2000	China	Hebei	1985–1997	13	0–14	653846†	51	0.60
Zhang HY	2001	China	Heilongjiang	1989–1997	9	0–14	1282051†	75	0.65
GCDA	2002	China	Guangdong	1990–1999	10	0–14	1,483,188	80	0.54
Yang XY	2004	China	Sichuan	1989–2000	12	0–14	702,584	45	0.53
Gong CX	2004	China	Beijing	1997–2000	4	0–14	1,749,867	71	1.01
Wang SS	2004	China	Guangxi	1997–1999	3	0–14	839,314	19	0.75
Zhang HY	2008	China	Harbin	1990–2000	11	0–14	1,286,154	103	0.73
Kou QH	2009	China	Liaoning	1985–2003	19	0–14	1302225†	240	0.97
Yuan SX	2009	China	Shenzhen	1999–2006	8	0–14	661,454	39	0.74
Zhao ZH	2014	China	Shanghai	1997–2011	15	0–14	1337634†	622	3.10
Wu HB	2015	China	Zhejiang	2007–2013	7	0–18	4795918†	611	1.82
Weng JP	2017	China	Nationwide	2010–2013	4	all age groups	135,408,192	5018	0.93
Ogle GD	2016	Fiji	–	2001–2012	12	0–14	254,312	28	0.92
WONG GWK	1994	Hong Kong SAR	–	2011–2019	8	0–14	235294†	32	1.70
Huen KF	2000	Hong Kong SAR	–	1984–1996	13	0–14	1,229,400	218	1.36
Huen KF	2009	Hong Kong SAR	–	1997–2007	11	0–18	1,431,800	335	2.13
Kitagawa T	1994	Japan	Hokkaido	2011–2014	10	0–14	1,220,000	253‡	2.07
Kitagawa T	1994	Japan	Tokyo	2011–2015	10	0–14	2,000,000	330‡	1.65
Kitagawa T	1994	Japan	Kagoshima	2011–2016	10	0–14	390,000	69‡	1.78
Kitagawa T	1994	Japan	Osaka	2011–2017	7	0–17	1,550,000	250‡	2.3
Kitagawa T	1994	Japan	Kagoshima	2011–2018	5	0–14	390,000	25‡	1.3
Matsuura N	1998	Japan	Hokkaido	1973–1992	20	0–14	6,563,055	396	1.63
Kida K	2000	Japan	–	1986–1990	5	0–14	16800000†	1260	1.50
Onda Y	2016	Japan	–	2005–2010	6	0–14	3592592†	485	2.25
Kim JH	2015	Korea	–	2012–2014	3	0–14	22131661†	706	3.19
Kim JH	2015	Korea	–	1995–2000	6		–	–	1.36
Lee YB	2019	Korea	–	2007–2013	7	all agegroups	50,452,335	13968‡	3.95
Campbell-Stoke PL	2005	New Zealand	–	1999–2000	2	0–14	832,083	298	17.91
Derraikn JGB	2012	New Zealand	Auckland	1990–2009	20	0–14	5390244†	884	16.40
Ogle GD	2001	Papua NewGuinea	–	1996–2000	5	0–14	2,150,000	8	0.08
Unachak K	2001	Thailand	–	1996–2000	7	0–14	2,974,082	76	0.37
Tuchinda C	2002	Thailand	North	1991–1995	5	0–14	3629630†	49	0.27
Tuchinda C	2002	Thailand	Northeast	1991–1995	5	0–14	5,135,595	77	0.30
Tuchinda C	2002	Thailand	South	1991–1995	5	0–14	1,900,825	42	0.44
Tuchinda C	2002	Thailand	Central	1991–1995	5	0–14	2,148,553	23	0.21
Tuchinda C	2002	Thailand	Bangkok	1991–1995	5	0–14	48,909	4	1.64
Panamonta O	2011	Thailand	Northeastern	1991–1997	10	0–14	5,322,130	340	0.64
Lu CL	2014	Taiwan,China	–	2003–2008	6	0–14	4106918†	1306	5.30
Lee WW	1998	Singapore	–	1992–1994	3	0–12	11237023††	276.43‡	2.46

GCDA = Registration group of Guangzhou Children's Diabetes Association
† - Persons at risk per year = (Number of patients*100000) / (Mean annual crude incidence*Study years).
‡ - Number of cumulative cases = (Persons at risk * (Mean annual crude incidence*Study years)) / 100,000.
††- Persons at risk per year = (Mean annual crude incidence)/ [(Mean annual crude incidence - lower CI of Mean annual crude incidence)/1.96]^2.
*** - Mean annual crude incidence=((Number of patients) / (Persons at risk / Study years)*100000.

pooled incidence was not estimated in the whole WPR. The regional estimates showed that Australia and New Zealand had the highest pooled incidence at 19.54 (95 % CI, 17.75–21.41) per 100,000 person years, and the incidence in New Zealand Maori was 4.5 times lower than in European-origin children [35] (Table 2,Supplementary 5). However, East Asia had a pooled incidence rate of 1.27 (95 % CI, 0.97–1.60) per 100,000 child years (Table 2, Supplementary 5), and there were considerably lower rates in Southeast Asia (Thailand): 0.39 (95 % CI,0.26–0.55) per 100,000 person years, and Western Pacific islands countries Fiji 0.92 (95 % CI,0.62–1.3) [39] and PNG 0.08 (95 % CI,0.04–0.14) [40] per 100,000 person years (Fig. 3). In Fiji, the rate in Indo-Fijians was 9.3 times higher than the rate in Native Fijians [39]. Using the United Nations population projection, these rates would amount to approximately 5685 new cases in people aged 0–14 years in China in 2019.

We analysed the difference in T1DM incidence at both country and regional levels. We observed that both country-level and regional level estimates for T1DM incidence varied substantially across study periods. Thirty-five studies provided data before 2000, 25 of which were from East Asia (21 from China, three from Japan, one from Hong Kong SAR), five from Australia and New Zealand, three from Thailand, and one study each from Singapore and PNG (Table 1). Seventeen studies reported data after 2000, 11 of which were from East Asia (seven from China, two from Korea, one from Japan, one from Taiwan), five from Australia and New Zealand, and one study each from Thailand and Fiji (Fig. 3). At regional level, an increasing trend of T1DM incidence over time was observed. The incidence of T1DM aged 0–14 years increased across all regions from the period of 1973–2000 to 2001–2017 (ranging from a 30 % increase in the Australia & New Zealand Region to a 1.8-fold increase in the East Asia Region) (Fig. 3). There were insufficient data to determine changes in the incidence of T1DM in subjects with older age onset.

Before 2000, country level T1DM incidence in children aged 0—14 years ranged from 0.08 (95 % CI = 0.04–0.14) in Papua New Guinea to 18.44 (95 % CI = 16.67–20.30) per 100,000 person years in Australia (Fig. 3). After 2000, the country level T1DM incidence in children aged 0—14 years ranged from 0.92 (95 % CI,0.62–1.3) in Fiji to 23.17 (95 % CI,21.27–25.16) in Australia (Fig. 3). T1DM incidence increased by at least 25 % in all the WPR countries with available data, with the highest increase observed in China compared with studies conducted before 2000 (by 2.7-fold; Fig. 3), followed by Thailand (increased by 2-fold, Fig. 3). There were relatively few studies reporting T1DM incidence in Southeast Asia and Western Pacific island countries, and their incidences were much lower than the highest rates (in Australia and New Zealand), and even lower than in low incidence rate countries (East Asia countries).

T1DM incidence varied widely over time. The incidence increased with time in most WPR countries except for Fiji [39], PNG [40], and a Korean [14] study in adults. The highest average annual increase of 6.5–14.2 % was observed in China [13,20,41–43], followed by a 5.6 % annual increase in Korea [34], 5.3 % increase in Taiwan [37]; and strikingly, a Zhejiang China study [43] (2007–2013) demonstrated a significant average annual increase in children aged under five years of 33.6 %. A similar increasing trend was observed in a 20-year Japanese study (1973–1992) [23], but was not present in shorter Japanese studies (1980-1990 [25], 2005-2012 [27]). A 5-year cyclical variation in incidence was observed only in Australia. Notably, this pattern was characterised by five-year cycle peaks and troughs with a significant annual increase in T1DM incidence in one state of Western Australia. Almost identical peak and trough incidence years were found in other parts of Australia as those reported in Western Australia, but the 5-year cyclical pattern showed an annual decrease trend in the rest of Australia and for the country overall between 2002 and 2007 [11,12,19]. This pattern, characterised by cyclical variation with annual increases, was not found in other WPR countries. In contrast, an overall decrease in T1DM incidence was seen in adults aged ≥ 20 years in a Korean study spanning 2007 to 2013 [14].

Across subregions and countries, T1DM incidence usually increased with increasing age of youth. T1DM incidence rates were highest in children aged 10–14 years. However, this trend was not observed in Fiji

Table 2
The overall pooled incidence rate of T1DM in youth and adults per 100,000 population in the WPR†.

Sex	Age		Australia & New Zealand	East Asia*
Total	all age group	Studies	11 (0–18 years)	32 (all age groups)
		Incidence(95 %CI)	19.54 (17.75–21.41)	1.27 (0.97–1.60)
	0–14 years	Studies	10 (0–14 years)	30 (0–14 years)
		Incidence(95 %CI)	19.54 (17.75–21.41)	1.27(0.97–1.60)
	0–4 years	Studies	6	15
		Incidence(95 %CI)	14.03 (12.79–15.33)	0.72 (0.47–1.03)
	5–9 years	Studies	6	15
		Incidence(95 %CI)	23.27 (21.71–24.88)	1.33 (0.97–1.74)
	10–14 years	Studies	6	15
		Incidence(95 %CI)	26.97 (24.02–30.10)	1.92 (1.42–2.51)
Male	all age group	Studies	8	25
		Incidence(95 %CI)	20.69 (18.54–22.95)	1.07 (0.83–1.34)
	0–4 years	Studies	5 (Aus & NewZ)	7 (China)
		Incidence(95 %CI)	15.20(13.41–17.11)	0.28 (0.14–0.47)
	5–9 years	Studies	5 (Aus & NewZ)	7 (China)
		Incidence(95 %CI)	21.40(18.71–24.27)	0.58 (0.18–1.21)
	10–14 years	Studies	5 (Aus & NewZ)	7 (China)
		Incidence(95 %CI)	25.16(18.89–32.32)	1.18 (0.27–2.71)
Female	all age group	Studies	8	25
		Incidence(95 %CI)	21.14(19.84–22.49)	1.31 (0.98–1.69)
	0–4 years	Studies	5 (Aus & NewZ)	7 (China)
		Incidence(95 %CI)	13.20(11.50–15.03)	0.35(0.14–0.64)
	5–9 years	Studies	5 (Aus & NewZ)	7 (China)
		Incidence(95 %CI)	24.90(22.57–27.35)	0.87 (0.25–1.86)
	10–14 years	Studies	5 (Aus & NewZ)	7 (China)
		Incidence(95 %CI)	27.62(25.18–30.18)	1.35 (0.38–2.92)

* Countries or territories includes China, Hong Kong SAR, Taiwan, Korea, Japan, Singapore.
† A *meta*-analysis (by region and narrow age bands, where possible) for T1DM incidence (mean annual crude incidence) was performed, with reporting of pooled estimates and 95 % CIs. As significant heterogeneity in the data was expected a random-effects (DerSimonian-Laird method) *meta*-analyses was performed to estimate the overall incidence of T1DM.

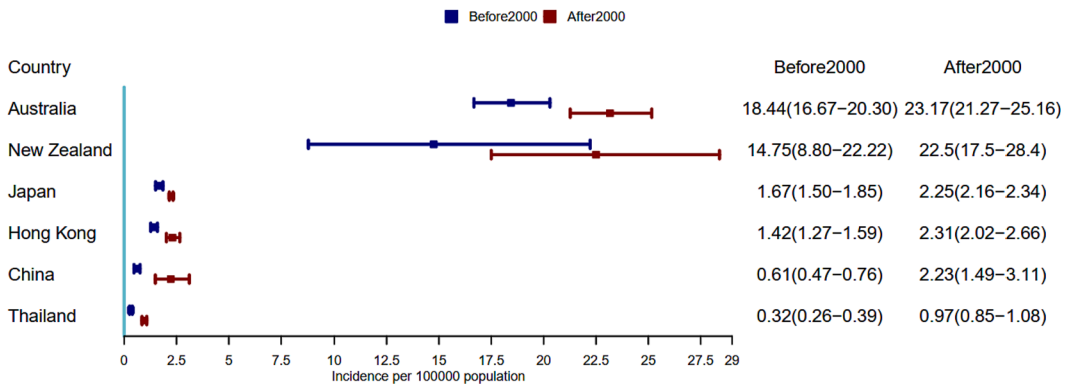

Fig. 3. Pooled meta estimate of Type 1 Diabetes incidence before and after 2000 across countries: Australia, New Zealand, East Asia (China, Japan, Hong Kong SAR) and Thailand.

[39] and PNG [40]. Additionally, China showed T1DM incidence increased with latitude among children aged under 15 years.

Sex differences in T1DM incidence were inconsistent across populations. Incidence was significantly higher in females compared with males aged 0—14 years in most East Asia countries, regions or territories: China (2010–2013) [13] (2.21 vs. 1.72, $p < 0.001$), Japan (2005–2012) [27] (2.5 vs. 1.9, $p < 0.01$), Korea (2012–2014) [34] (3.6 vs. 2.8, $p = 0.003$), Taiwan (2003–2008) [37] (6.0 vs. 4.7, $p < 0.001$), Singapore (1992–1994) [38] (girls vs. boys: 1.85-fold) and Thailand (1996–2005) [31] (girls vs. boys: 1.5- fold). The sex-difference (female vs. males) was not statistically significant in Hong Kong SAR (1997–2007) [29] (1.7 vs. 1.2), Shanghai (1997–2011) [41] (3.2 vs. 3.1), and Shenzhen (1999–2006) [44] (0.76 vs. 0.71). Additionally, a Shanghai study [41] reported a faster annual increase of incidence in boys than girls (16.1 % vs. 12.5 %) but was not statistically significant. Inconsistent findings were observed in Australia among the 0—14 year age group (female vs. male: 19.8 vs. 18.8, $p = 0.02$; [21] 22.1 vs. 23.1 [11], but the difference was not statistically significant in the latter. For older age groups, however, an inverse sex difference was observed. China [13] reported males had higher T1DM incidence rates than females aged over 15 years (males vs. females: 0.92 vs. 0.70, $p < 0.001$), with similar results in an Australian study [24] in 10–18 year old age groups (males vs. females: 24.2 vs. 19.6, $p < 0.001$); and in a Korean study [14] of T1DM patients with a mean (SD) age of 49.6 (21.7) years (male vs. female: 1.21–1.41-fold, $p < 0.001$). T1DM incidence was reported to be similar between sexes in a New Zealand study (1990–2009) [35,36]. Sex differences were not reported in Fiji and PNG studies. (Supplementary Table 3).

4. Discussion

In this systematic review, estimating the incidence of T1DM in the WPR in 45 population-based studies conducted from 1973 to 2017, the six main findings are as follows: first, of 45 studies from 11 countries, nearly half (21/45) were from China; secondly few studies evaluated adult-onset T1DM; and thirdly our pooled data found the increasing T1DM incidence trend was highest in China by 2.7-fold,followed by Thailand which increased 2-fold compared with studies conducted before 2000. China, a low T1DM incidence country, with a population of approximately 1.4 billion, constituting about 74 % of the Western Pacific Region's total population, also contributed the most incident cases per year of 5685, higher than the IDF 2019 estimate of 4800; fourth, geographical variation existed, such that the mean annual incidence of T1DM in children aged 0–14 years ranged from 0.92 (95 % CI,0.62–1.3) in Fiji to 23.17 (95 % CI, 21.27–25.16) per 100,000 person years in Australia after 2000; fifth, the average annual increase ranged from 2.8 % in an Australia study (1990–2002) to 14.2 % in a Shanghai China study (1997–2011) and a 5-year cyclical pattern was observed only in Australia. Finally, most studies, albeit in youth, document increasing T1DM incidence with increasing age, with significant sex differences. A key and clinically relevant finding is a lack of studies evaluating T1DM onset in young, middle-aged or older adults, as onset after childhood is common.

Reviewed studies (published between 1973 and 2017) span many decades, during which great advances have been made in case ascertainment and scale-up of T1DM registries. Despite this, findings of earlier studies deserve comment and comparison. Instead of comparing between five- or 10-year periods as earlier reports [45] we chose two longer time-periods - before 2000 and after 2000, for two reasons. Firstly, we found at least one high T1D incidence country (Australia) had 4–6 years cyclical variations in T1DM incidence [16] and if diabetes incidence rates were compared over only five or 10 years the upward/downward trends in a sinusoidal pattern may mask the the real longer-term trend. Secondly, some studies demonstrated an incidence trend only in longer studies (e.g. a 20-year [23] but not in 10-year studies [25,27]).

We report country-level *meta*-estimates for T1DM incidence in youth (aged 0–14 years) by two time-periods (pre- and post-2000). Our pooled data show a higher annual incidence rate in studies published after 2000 (11 of 17 from East Asia) compared with those published before 2000, with incidence increases ranging from 25 % in Australia to 266 % in China. This increase in T1DM incidence is in agreement with previous reports [16,45,46], and is potentially due to environmental factors such as childhood obesity43,46, nutrition43 and viral infections46. However, the cyclical pattern in Australia, is still unexplained and an area for further exploration. Few studies reported adult-onset T1DM. Data are reported for Australia and China with 55–65 % onset T1DM over 20 years old.

Additionally, in our pooled data, the remarkable country-level difference in the proportion of increase could be affected by the length of study periods (before 2000 and after 2000). For example, New Zealand reported a higher increase of 114 % in a 20-year period (2009 vs. 1990) than that (50 %) in our report (2009 vs. 10-yearly pooled incidence in 1990–2000). However, when similar lengths of study period were considered, the difference still existed, with a lower increase in Australia than in China. We postulate that the between-country differences are the result of an Australian 5-year cyclical pattern and inter-country genetic and environmental factors. The latter might be due to recent socioeconomic development with changes in economy, urbanisation and lifestyles, particularly in rural China, where the rural medical security system has undergone rapid reform and development, likely increasing the diagnosis and recording of incident T1DM43. Better case ascertainment and recording may also be contributory in many other WPR countries. When individual studies are considered, the significant increases in average annual T1DM incidence in most East Asia countries or territories (annual increase: 5.6 % in Korea34, 5.3 % in Taiwan37) are of

concern, and interestingly, was not identified in another Asian country – Japan. Overall, there is little research on T1DM incidence trends over the long-term, therefore findings should be interpreted with care.

Only six countries and regions supplied data in the two study time-periods, and contemporary studies conducted after 2000 include no data from Southeast Asia and countries with ethnically diverse populations such as Malaysia, and the Philippines, estimating T1DMincidence in Malays, Indians and South Chinese. The majority (11 of 17) contemporary studies were from East Asia. This recent surge in East Asian studies could be motivated by the excess burden of diabetes in Asia. Globally around 80 % of people with diabetes live in less advantaged regions 4, of which China contributes a large proportion. At present, high-quality registries are relatively limited and costly, and data collection from existing databases (i.e., medical record databases, outpatient-based pharmacies or medical insurance databases) like in China [13] and Hong Kong SAR[46], are needed, particularly in Southeast Asia and Western Pacific islands. This will enhance T1DM incidence studies in the long-term, which is important for care planning and for ongoing research, particularly with better predictors of T1DM onset [47,48] and the emergence of therapies that can delay T1DM onset or progression [49].

The majority of studies (not in Fiji, PNG and Korean adults) found an increasing trend in T1DM incidence with increasing age, albeit mainly in youth. This incidence peaked in the age groups of 10–14 years and the age effect did not differ between sexes, which in accordance with the DIAMOND study [15] in the 1990 s. However, an exception was found in a recent Hong Kong study [46] reporting female T1DM incidence peaking in 5–9-year-olds while it peaked in males aged 10–14 years. When stratified by sex, except for some Chinese studies [41,44,46] and a New Zealand study [35], most studies reported significant differences in incidence by sex, but findings were inconsistent. An Australian study (2001–2008) [24] (10–18 years), a China's study [13] (>15 years) and a Korean study [14] (>18 years) recruiting older age patients reported a higher incidence in males. Conversely, for a younger age group (0–14 years), females had a higher incidence than males in seven of 13 contemporary studies. This finding is also in agreement with the global DIAMOND project [15], that 88 % of low T1M incidence populations were predominantly female and those with high T1DM incidence were more likely to be predominantly male. Similarly, a recent study in Hong Kong SAR [46] of people aged < 20 years, the incidence rate ratio (IRR) was 1.38 for girls compared with boys, which was consistent with reports from Taiwan [37] (IRR 1.27).

4.1. Strengths & limitations

This systematic review and *meta*-analysis study included 45 studies from 11 countries in Asian and European-origin groups. We performed a series of subgroup analysis based on study periods, countries and subregions, providing more detail about T1DM incidence patterns. Improved methods used a broader search, including Chinese language databases and comparing studies stratified by longer study periods.

Our study has limitations. T1DM is not always rigorously phenotyped, such as by C-peptide levels, insulin autoantibodies and genetic markers, hence some misclassification of diabetes type may occur. People with T1DM may have been missed due to early death without diagnosis or not being captured in any of the databases. T1DM incidence is likely age dependent. However, most of the included studies did not report results using narrow age bands, which in turn limits ability to report age-specific estimates that could be used for targeted interventions. In particular the incidence of T1DM during the 3rd decade of life and beyond is infrequently studied. T1DM incidence within a country may differ by ethnicity, as was reported in some countries (e.g. Fiji and New Zealand), but ethnicity is not always recorded and may not always be accurate. Furthermore ethnic diversity in a country or region may change substantially in relatively short time-frames in our increasingly mobile world. Differences in enrolled populations, duration of follow-up, from a few years to a few decades, may limit the scope for generalisations and comparisons, although random-effects model and subgroup analysis were used in our analyses. However, the consistency of results across most studies, countries and regions, supports the main findings – T1DM incidence is increasings with time, with increasing age (in youth), and is more common in females. It is prudent to interpret differences between regions and studies in context.

4.2. Further research

On the basis of this review of contemporary studies, we recommend some areas for future research: to obtain precise age/sex specific incidence of T1DM across the full life-span, second, to phenotype T1DM well, including by ethnicity and early life residence; and also to obtain estimates of T1DM mortality, and more contemporary studies representative of Southeast Asia and Western Pacific island countries. More studies based on existing medical record and medical insurance databases capturing data on T1DM incidence with stratification by age and sex, are needed to consolidate the evidence-base. Our data are useful for understanding the T1DM incidence pattern across countries over time and for conceptualisation and development of major healthcare strategies and future research.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data for the systematic review and meta-analysis. Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2023.111055.

References

[1] Patterson CC, Karuranga S, Salpea P, et al. Worldwide estimates of incidence, prevalence and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas. Diabetes Res Clin Pract 2019;157:107842.
[2] Ogle GD, James S, Dabelea D, et al. Global estimates of incidence of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Atlas. Diabetes Res Clin Pract 2022;183:109083.
[3] James S, Maniam J, Cheung PT, et al. Epidemiology and phenotypes of diabetes in children and adolescents in non-European-origin populations in or from Western Pacific region. World J Clin Pediatr 2022;11(2):173–95.
[4] Gregory GA, Robinson TIG, Linklater SE, et al. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. Lancet Diabetes Endocrinol 2022;10(10):741–60.

[5] Karvonen M, Viik-Kajander M, Moltchanova E, Libman I, LaPorte R, Tuomilehto J. Incidence of childhood type 1 diabetes worldwide. Diabetes Mondiale (DiaMond) Project Group. Diabetes Care 2000;23(10):1516–26.
[6] Karvonen M, Pitkaniemi M, Pitkaniemi J, Kohtamaki K, Tajima N, Tuomilehto J. Sex difference in the incidence of insulin-dependent diabetes mellitus: an analysis of the recent epidemiological data. World Health Organization DIAMOND Project Group. Diabetes Metab Rev 1997;13(4):275–91.
[7] Federation ID. IDF Diabetes Atlas, 10th ed. Brussels, Belgium; 2021.
[8] International Diabetes Federation. IDF Diabetes Atlas, 7th ed.; 2015. Available at: https://www.diabetesatlas.org.
[9] International Diabetes Federation. IDF Diabetes Atlas, 6th ed.; 2013. Available at: https://www.diabetesatlas.org.
[10] International Diabetes Federation. IDF Diabetes Atlas, 4th ed.; 2010.
[11] Catanzariti L, Faulks K, Moon L, Waters AM, Flack J, Craig ME. Australia's national trends in the incidence of Type 1 diabetes in 0–14-year-olds, 2000–2006. Diabet Med 2009;26(6):596–601.
[12] Haynes A, Bulsara MK, Bergman P, et al. Incidence of type 1 diabetes in 0 to 14 year olds in Australia from 2002 to 2017. Pediatr Diabetes 2020;21(5):707–12.
[13] Weng J, Zhou Z, Guo L, et al. Incidence of type 1 diabetes in China, 2010–13: population based study. BMJ 2018;360:j5295.
[14] Lee YB, Han K, Kim B, et al. High Proportion of Adult Cases and Prevalence of Metabolic Syndrome in Type 1 Diabetes Mellitus Population in Korea: A Nationwide Study. Diabetes Metab J 2019;43(1):76–89.
[15] Group DP. Incidence and trends of childhood Type 1 diabetes worldwide 1990–1999. Diabet Med 2006;23(8):857–66.
[16] Patterson CC, Harjutsalo V, Rosenbauer J, et al. Trends and cyclical variation in the incidence of childhood type 1 diabetes in 26 European centres in the 25 year period 1989–2013: a multicentre prospective registration study. Diabetologia 2019;62(3):408–17.
[17] Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.
[18] Zaza S, Wright-De Aguero LK, Briss PA, et al. Data collection instrument and procedure for systematic reviews in the Guide to Community Preventive Services. Task Force on Community Preventive Services. Am J Prev Med 2000;18(1 Suppl):44–74.
[19] Haynes A, Bulsara MK, Jones TW, Davis EA. Incidence of childhood onset type 1 diabetes in Western Australia from 1985 to 2016: Evidence for a plateau. Pediatr Diabetes 2018;19(4):690–2.
[20] Kou QH, Qian C, Bai XH, et al. Incidence and trends of Childhood type 1 diabetes in Shenyang, China. Chin J Health Stat 2009;26(2).
[21] Taplin CE, Craig ME, Lloyd M, et al. The rising incidence of childhood type 1 diabetes in New South Wales, 1990–2002. Med J Aust 2005;183(5):243–6.
[22] Chong JW, Craig ME, Cameron FJ, et al. Marked increase in type 1 diabetes mellitus incidence in children aged 0–14 yr in Victoria, Australia, from 1999 to 2002. Pediatr Diabetes 2007;8(2):67–73.
[23] Matsuura N, Fukuda K, Okuno A, et al. Descriptive epidemiology of IDDM in Hokkaido, Japan: the Childhood IDDM Hokkaido Registry. Diabetes Care 1998;21(10):1632–6.
[24] Tran F, Stone M, Huang CY, et al. Population-based incidence of diabetes in Australian youth aged 10–18 yr: increase in type 1 diabetes but not type 2 diabetes. Pediatr Diabetes 2014;15(8):585–90.
[25] Kida K, Mimura G, Ito T, Murakami K, Ashkenazi I, Laron Z. Incidence of Type 1 diabetes mellitus in children aged 0–14 in Japan, 1986–1990, including an analysis for seasonality of onset and month of birth: JDS study. The Data Committee for Childhood Diabetes of the Japan Diabetes Society (JDS). Diabet Med 2000;17(1):59–63.
[26] Kitagawa T, Owada M, Urakami T, Tajima N. Epidemiology of type 1 (insulin-dependent) and type 2 (non-insulin-dependent) diabetes mellitus in Japanese children. Diabetes Res Clin Pract 1994;24(Suppl):S7–.
[27] Onda Y, Sugihara S, Ogata T, et al. Incidence and prevalence of childhood-onset Type 1 diabetes in Japan: the T1D study. Diabet Med 2017;34(7):909–15.
[28] Huen KF, Low LC, Wong GW, et al. Epidemiology of diabetes mellitus in children in Hong Kong: the Hong Kong childhood diabetes register. J Pediatr Endocrinol Metab 2000;13(3):297–302.
[29] Huen KF, Low LCK, Cheung PT, et al. An Update on the Epidemiology of Childhood Diabetes in Hong Kong. HK J Paediatr (new series) 2009;14:252–9.
[30] Wong GW. Insulin-dependent diabetes mellitus in southern Chinese children: an overview. J Paediatr Child Health 1994;30(6):490–1.
[31] Panamonta O, Thamjaroen J, Panamonta M, Panamonta N, Suesirisawat C. The rising incidence of type 1 diabetes in the northeastern part of Thailand. J Med Assoc Thai 2011;94(12):1447–50.
[32] Tuchinda C, Likitmaskul S, Unachak K, Panamonta O, Patarakijavanich N, Chetthakul T. The epidemiology of type 1 diabetes in Thai children. J Med Assoc Thai 2002;85(6):648–52.
[33] Unachak K, Tuchinda C. Incidence of type 1 diabetes in children under 15 years in northern Thailand, from 1991 to 1997. J Med Assoc Thai 2001;84(7):923–8.
[34] Kim JH, Lee CG, Lee YA, Yang SW, Shin CH. Increasing incidence of type 1 diabetes among Korean children and adolescents: analysis of data from a nationwide registry in Korea. Pediatr Diabetes 2016;17(7):519–24.
[35] Campbell-Stokes PL, Taylor BJ. New Zealand Children's Diabetes Working G. Prospective incidence study of diabetes mellitus in New Zealand children aged 0 to 14 years. Diabetologia 2005;48(4):643–8.
[36] Derraik JG, Reed PW, Jefferies C, Cutfield SW, Hofman PL, Cutfield WS. Increasing incidence and age at diagnosis among children with type 1 diabetes mellitus over a 20-year period in Auckland (New Zealand). PLoS One 2012;7(2):e32640.
[37] Lu CL, Shen HN, Chen HF, Li CY. Epidemiology of childhood Type 1 diabetes in Taiwan, 2003 to 2008. Diabet Med 2014;31(6):666–73.
[38] Lee WR. The changing demography of diabetes mellitus in Singapore. Diabetes Res Clin Pract 2000;50(Suppl 2):S35–9.
[39] Ogle GD, Morrison MK, Silink M, Taito RS. Incidence and prevalence of diabetes in children aged <15 yr in Fiji, 2001–2012. Pediatr Diabetes 2016;17(3):222–6.
[40] Ogle GD, Lesley J, Sine P, McMaster P. Type 1 diabetes mellitus in children in Papua New Guinea. P N G Med J 2001;44(3–4):96–100.
[41] Zhao Z, Sun C, Wang C, et al. Rapidly rising incidence of childhood type 1 diabetes in Chinese population: epidemiology in Shanghai during 1997–2011. Acta Diabetol 2014;51(6):947–53.
[42] Zhang H, Xia W, Yu Q, et al. Increasing incidence of type 1 diabetes in children aged 0–14 years in Harbin, China (1990–2000). Prim Care Diabetes 2008;2(3):121–6.
[43] Wu HB, Zhong JM, Hu RY, et al. Rapidly rising incidence of Type 1 diabetes in children and adolescents aged 0–19 years in Zhejiang, China, 2007 to 2013. Diabet Med 2016;33(10):1339–46.
[44] Yuan SX, Lin JM, Dong GQ, Lin Y, Zhao GL, Pan RY. Investigation on incidence of childhood type1 diabetes mellitus in Shenzhen. China Maternal Health 2009;24.
[45] Adeloye D, Chan KY, Thorley N, et al. Global and regional estimates of the morbidity due to type I diabetes among children aged 0–4 years: a systematic review and analysis. J Glob Health 2018;8(2):021101.
[46] Tung JY, Kwan EY, But BW, et al. Increasing incidence of type 1 diabetes among Hong Kong children and adolescents: The Hong Kong Childhood Diabetes Registry 2008 to 2017. Pediatr Diabetes 2020;21(5):713–9.
[47] Ferrat LA, Vehik K, Sharp SA, et al. A combined risk score enhances prediction of type 1 diabetes among susceptible children. Nat Med 2020;26(8):1247–55.
[48] Rewers M, Hyoty H, Lernmark A, et al. The Environmental Determinants of Diabetes in the Young (TEDDY) Study: 2018 Update. Curr Diab Rep 2018;18(12):136.
[49] Greenbaum C, VanBuecken D, Lord S. Disease-Modifying Therapies in Type 1 Diabetes: A Look into the Future of Diabetes Practice. Drugs 2019;79(1):43–61.