Diabetologia (2013) 56:1471–1488
DOI 10.1007/s00125-013-2915-z

SYSTEMATIC REVIEW

Global trends in the incidence and prevalence of type 2 diabetes in children and adolescents: a systematic review and evaluation of methodological approaches

S. Fazeli Farsani · M. P. van der Aa · M. M. J. van der Vorst · C. A. J. Knibbe · A. de Boer

Received: 16 January 2013 / Accepted: 4 April 2013 / Published online: 16 May 2013

Abstract
Aims/hypothesis This study aimed to systematically review what has been reported on the incidence and prevalence of type 2 diabetes in children and adolescents, to scrutinise the methodological issues observed in the included studies and to prepare recommendations for future research and surveillances.
Methods PubMed, the Cochrane Database of Systematic Reviews, Scopus, EMBASE and Web of Science were searched from inception to February 2013. Population-based studies on incidence and prevalence of type 2 diabetes in children and adolescents were summarised and methodologically evaluated. Owing to substantial methodological heterogeneity and considerable differences in study populations a quantitative meta-analysis was not performed.
Results Among 145 potentially relevant studies, 37 population-based studies met the inclusion criteria. Variations in the incidence and prevalence rates of type 2 diabetes in children and adolescents were mainly related to age of the study population, calendar time, geographical regions and ethnicity, resulting in a range of 0–330 per 100,000 person-years for incidence rates, and 0–5,300 per 100,000 population for prevalence rates. Furthermore, a substantial variation in the methodological characteristics was observed for response rates (60–96%), ascertainment rates (53–99%), diagnostic tests and criteria used to diagnose type 2 diabetes.
Conclusions/interpretation Worldwide incidence and prevalence of type 2 diabetes in children and adolescents vary substantially among countries, age categories and ethnic groups and this can be explained by variations in population characteristics and methodological dissimilarities between studies.

Keywords Adolescents · Children · Global trends · Incidence · Methodology · Prevalence · Systematic review · Type 2 diabetes

Abbreviations

AIHW	Australian Institute of Health And Welfare
BPSU	British Paediatric Surveillance Unit
CCDR	Chicago Childhood Diabetes Registry
CFPC-NaReS	College of Family Physicians of Canada National Research System
CPSP	Canadian Paediatric Surveillance Program
DIARY	Diabetes Registry
FPG	Fasting plasma glucose
IHS	Indian Health Service
NIH	National Institute of Health
NZHIS	New Zealand Health Information Service
NZPSU	New Zealand Paediatric Surveillance Unit
RLDR	Richmond/Lexington County Childhood and Adolescents Diabetes Registry

Electronic supplementary material The online version of this article (doi:10.1007/s00125-013-2915-z) contains peer-reviewed but unedited supplementary material, which is available to authorised users.

S. Fazeli Farsani · A. de Boer (✉)
Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University, P.O. Box 80082, 3508 TB, Utrecht, the Netherlands
e-mail: A.deBoer@uu.nl

M. P. van der Aa · M. M. J. van der Vorst
Department of Paediatrics, St Antonius Hospital, Nieuwegein, the Netherlands

C. A. J. Knibbe
Department of Clinical Pharmacy, St Antonius Hospital, Nieuwegein, the Netherlands

C. A. J. Knibbe
Division of Pharmacology, Leiden/Amsterdam Centre for Drug Research, Leiden University, Leiden, the Netherlands

US PHS	United States Public Health Service
WACDD	Western Australian Children's Diabetes Database

Introduction

Global prevalence of diabetes is increasing rapidly [1]. With an estimated 285 million patients (aged 20–79 years) in 2010, diabetes is becoming one of the main threats to human health in the 21st century in both developed and developing countries [1, 2]. Globally, type 2 diabetes accounts for more than 90% of the cases of diabetes [2]. Until recently, type 2 diabetes was barely diagnosed in children, since it was considered to be a disease of adulthood. Over the past two decades, an increase in prevalence of type 2 diabetes in children and adolescents has been reported in several countries [1, 3]. Early onset of type 2 diabetes is associated with increased risk of morbidity and mortality [4, 5]. Type 2 diabetes has a disrupting effect on young individuals during their most productive years and leads to increased healthcare costs. In addition, (severe) complications of type 2 diabetes, such as nephropathy, retinopathy, neuropathy, dyslipidaemia and cardiovascular disease are an ongoing threat [4–7].

An overview of global trends in the incidence and prevalence of type 2 diabetes in children and adolescents is important, since type 2 diabetes has significant effects on health and quality of life, use of medical services and reduced employability resulting in a huge economic burden [6–9]. To support appropriate healthcare policies, population-based epidemiological studies are required to show the actual burden of the disease and its secular trends [7]. We have performed a systematic search to detect systematic reviews or meta-analyses summarising the existing data on incidence and prevalence of type 2 diabetes in young age groups and the different methodologies used to estimate these population data. However, such studies have not been published. Therefore, the aims of our study are to review what is known about the incidence and prevalence of type 2 diabetes in children and adolescents, to scrutinise the methodological issues observed in the included studies and to prepare recommendations for future research and surveillances.

Methods

Data sources and searches This systematic review follows the guidelines of 'Meta-analysis of Observational Studies in Epidemiology (MOOSE)' [10]. After defining the research question and consulting a medical librarian in the library of Utrecht University, a search was performed in PubMed, the Cochrane Database of Systematic Reviews, Scopus, EMBASE and Web of Science. Our search covered all publications in the above databases, from the inception of each database up to the third week of February 2013. The search terms and search strategy are listed in Table 1. All search results were imported to a Refworks file (www.refworks.com).

Study selection After removing duplicates, the title and abstract of each article were screened by two of the authors (S. Fazeli Farsani and M. P. van der Aa) to exclude irrelevant studies. Articles were selected based on inclusion and exclusion criteria (Table 2). Reference lists of included articles were assessed to find additional articles. Full texts of all included articles were retrieved via the library of Utrecht University or through contact with the authors. Abstracts of conferences were not included in this review. Studies were excluded based on title and abstract if they were not population-based (e.g. studies were performed in specific populations like obese children and adolescents) or if they described prevalence or incidence of concurrent diseases in patients with type 2 diabetes.

Full text screening was performed when it was not clear whether the study population involved children and adolescents, or when the abstract was unclear about the type of diabetes. In case of disagreement the study was checked by a third author (A. de Boer or M. M. J. van der Vorst).

Data extraction and quality assessment Once consensus on the included articles was achieved, data was extracted from the full text articles. The following data—author, country of the study, calendar time, study design and denominator used, diagnostic criteria, characteristics of the study population (age, sex and ethnicity), excluded cases, incidence (per 100,000 person-years) and prevalence (per 100,000 population)—were separately extracted, entered into a table by two of the authors (S. Fazeli Farsani and M. P. van der Aa) and then compared for similarity (see Table 3 and electronic supplementary material [ESM] Table 1).

Data synthesis and analysis Two authors (S. Fazeli Farsani and M. P. van der Aa) checked the extracted data. For the methodological evaluation the following aspects were assessed: response rates of population-based screening studies (the percentage of the invited population that consented to participate), ascertainment rate of studies in which children diagnosed by doctors were captured (the percentage of children with type 2 diabetes identified and registered by healthcare providers of all diagnosed children with type 2 diabetes), the performed diagnostic tests (e.g. measurement of glucose concentration in urine or in plasma), diagnostic guidelines, classification and differentiation between type 1 and 2 diabetes, quality of denominators used to calculate incidence and prevalence rates, sample size of the

Table 1 Search terms and search strategy

Search terms and search strategy	
Search terms	
Population	('Infant' OR 'Infants' OR 'Toddler' OR 'Toddlers' OR 'Child' OR 'Children' OR 'Adolescent' OR 'Adolescents' OR 'Teens' OR 'Teen' OR 'Teenagers' OR 'Teenager' OR 'Youth' OR 'Youths' OR 'Adolescence')
AND	
Outcome	('Incidence' OR 'Incidences' OR 'Prevalence' OR 'Prevalences') AND ('Diabetes Mellitus, Non Insulin Dependent' OR 'Diabetes Mellitus, Non-Insulin-Dependent' OR 'Non-Insulin-Dependent Diabetes Mellitus' OR 'Type 2 Diabetes Mellitus' OR 'Diabetes Mellitus, Slow-Onset' OR 'Diabetes Mellitus, Slow Onset' OR 'Slow-Onset Diabetes Mellitus' OR 'Diabetes Mellitus, Stable' OR 'Stable Diabetes Mellitus' OR 'Diabetes Mellitus, Type II' OR 'NIDDM' OR 'Diabetes Mellitus, Adult-Onset' OR 'Adult-Onset Diabetes Mellitus' OR 'Diabetes Mellitus, Adult Onset' OR 'Diabetes Mellitus, Noninsulin Dependent' OR 'T2DM' OR 'T2D')
AND	
Limitations (if possible)	Language English, Dutch, German

NIDDM, non-insulin-dependent diabetes mellitus

population on which the rate estimates were based and representativeness of the evaluated population for the whole population in the defined geographic area.

Due to substantial methodological heterogeneity and considerable variations in study populations a quantitative meta-analysis of the data was not performed.

Results

The search of the five electronic databases yielded 5,920 articles, of which 145 were potentially relevant after screening title and abstract. Out of these papers, 37 articles met the inclusion criteria. Manual reference screening did not result in additional articles (Fig. 1). All included articles were written in English. Of the total of 37 included articles, 12 described prevalence studies, 16 described incidence studies and 9 contained both incidence and prevalence data. As shown in Table 3, the included studies originated from four continents (13 different countries). Most of the studies were conducted in the USA and North European countries, while there were no studies from African or South American countries or from a major part of Asia. Three Japanese [11–13], two Austrian [14, 15] and two American studies [16, 17] were based on the same data source, albeit the data were analysed differently and comprised other study periods. There was a substantial variation in population characteristics and methodological aspects in the identified studies (Table 3), as described below.

Study population and ethnicities The number of children in the populations in which type 2 diabetes was detected ranged from 1,647 [18] to several millions [11–13, 19–25] and covered different age categories. The 37 included studies described data about many different ethnicities—Japanese, Taiwanese, multi-ethnic, New Zealand-Maori, New Zealand-European, Turkish, South Asian, Black, Aboriginal, African-American, American Indian, Pima Indian, Ojibwa-Cree, non-Hispanic whites, Hispanic, etc. (ESM Table 1).

Table 2 Inclusion/exclusion criteria for screening studies

Inclusion/exclusion criterion	Study attributes/characteristics of groups studied
Inclusion criteria	
Study design	Population-based observational studies
Age	Children (0–9 years[a]) and/or adolescents (10–19 years[a])
Population	General population
Outcome	Incidence/prevalence of type 2 diabetes
Exclusion criteria	
Language	Language other than English, German and Dutch
Age	Study population of adults only
Restricted groups	Study population restricted to a group of people (e.g. obese children)

[a]Based on WHO definition

Table 3 Studies investigating the incidence and prevalence of type 2 diabetes in children and adolescents

First author, year (by region)	Country	Calendar time	Study design and denominator used	Diagnosis of type 2 diabetes	Limitations
Asia					
Kitagawa, 1994 [31]	Japan	1975–1990	• Screening of school children • Denominator: not clearly stated	• Measurement of diabetes: urine glucose screening (using glucose oxidase tapes) and performing OGTT in cases with two positive urine tests • Differentiation between type 1 and 2: based on insulin secretion ability, auto-antibodies, beta cell function. Type of diabetes was reported by healthcare provider • Guidelines: WHO/US PHS • Excluded cases: not specified	Case ascertainment: not applicable Response rate: approximately 60% Test of diabetes: optimal Misclassification of type 2 diabetes: yes (not excluding other types [e.g. MODY]) Representativeness: of Tokyo school children Denominator: not clearly stated
Urakami, 2005, 2006, 2007 [11–13]	Japan, Tokyo metropolitan area	1974–2004	• Population-based screening of school children • Denominator: total number of children examined in each period	• Measurement of diabetes: urine glucose screening (using glucose oxidase tapes) and performing OGTT in cases with two positive urine tests • Differentiation between type 1 and 2: based on insulin secretion ability, checking for obesity, auto-antibodies, beta cell function. Type of diabetes was reported by healthcare provider • Guidelines: WHO/US PHS • Excluded cases: not specified	Case ascertainment: not applicable Response rate: not specified Test of diabetes: optimal Misclassification of type 2 diabetes: yes (not excluding other types [e.g. MODY]) Representativeness: of Tokyo school children Denominator: not optimal
Wei, 2003 [32]	Taiwan	1992–1999	• Nationwide screening of school children • Denominator: not specified	• Measurement of diabetes: urine glucose screening (using Hemscomistix IV urine strip) and using FPG test in cases with 2 positive urine test, physical examination confirmed by a follow-up telephone survey • Differentiation between type 1 and 2: based on retrospective questionnaire interview with parents and reports from family physicians, history of using oral glucose-lowering agents (type 2) or insulin (type 1), not having diabetic acidosis, checking for obesity. Type of diabetes was reported by parents or family physician • Guidelines: ADA • Excluded cases: cases in which type of DM could not be confirmed	Case ascertainment: not applicable Response rate: not complete Test of diabetes: not optimal Misclassification of type 2 diabetes: yes (not excluding other types [e.g. MODY]) Representativeness: Taiwanese school children Denominator: not specified
Australia and New Zealand					
Craig, 2007 [46]	Australia, NSW	2001–2006	• Prospective population-based incidence study (primary ascertainment was from Australian Paediatric Endocrine Group New South Wales Diabetes Register[a], with secondary ascertainment from the national diabetes registry[b] [AIHW])	• Measurement of diabetes: physical examination and blood tests (fasting insulin and C-peptide) • Differentiation between type 1 and 2: based on the presence of acanthosis nigricans, elevated fasting insulin and C-peptide auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: ADA	Case ascertainment: overall more than 99% Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases, older

Table 3 (continued)

First author, year (by region)	Country	Calendar time	Study design and denominator used	Diagnosis of type 2 diabetes	Limitations
			• Denominator: from Australian Bureau of Statistics	• Excluded cases: cases with secondary diabetes (e.g. cystic fibrosis or hyperinsulinism), genetic beta cell defects (MODY), not NSW residents	adolescents or children from remote areas) Representativeness: of NSW children and adolescents Denominator: no limitation
McMahon, 2004 [42]	Australia, WA	1990–2002	• Review of prospectively recorded diabetes on the WACDD database[c] • Denominator: from Australian Bureau of Statistics[d]	• Measurement of diabetes: demographic and anthropometric data, blood tests (OGTT, fasting insulin, C-peptide, HbA_{1c}) • Differentiation between type 1 and 2: based on physical examination, anthropometry (weight, BMI), presence of acanthosis nigricans, family history, C-peptide and auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: not specified • Excluded cases: not specified	Case ascertainment: not specified Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases, not excluding other types [e.g. MODY]) Representativeness: not clear Denominator: not specified
Campbell-Stokes, 2005 [34]	New Zealand	1999–2000	• Monthly reporting of type 2 diabetes cases by paediatricians to the NZPSU and using hospital discharge data from NZHIS • Denominator: from 1996 census data (includes <15-year-old residents of New Zealand)	• Measurement of diabetes: at least one of the following tests (random blood glucose, FPG, OGTT) • Differentiation between type 1 and 2: based on demographics, ethnicity, family history, presence of acanthosis nigricans, auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: not specified • Excluded cases: cases secondary to drugs or stress (e.g. sepsis); cases >15 years old; not New Zealand residents	Case ascertainment: 95.2% Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of New Zealand children (<15 years) Denominator: no limitation
Jefferies, 2012 [40]	New Zealand, Auckland region	1995–2007	• Retrospective analysis of prospectively recorded data of the referred cases by Starship Paediatric diabetes service (regional care) • Denominator: National census data from New Zealand statistics	• Measurement of diabetes: Anthropometry criteria, laboratory tests (HbA_{1c}), history of treatments • Differentiation between type 1 and 2: based on obesity, family history, ethnicity, insulin resistance, presence of acanthosis nigricans, polycystic ovarian syndrome, auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: not specified • Excluded cases: not specified	Case ascertainment: over 95% Response rate: not applicable Test of diabetes: not optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases, levels of C-peptide and insulin were not measured) Representativeness: of Auckland children (<15 years) Denominator: no limitation
Caribbean					
Perez-Perdomo, 2005 [35]	Puerto Rico	1995–2003	• Cases were reported by 11 paediatric endocrinologists	• Measurement of diabetes: demographic, clinical and biochemical data, BMI, blood tests (C-peptide, fasting blood sugar)	Case ascertainment: 84.6% (of paediatric endocrinologists) and 85.3% (of defined cases)

Table 3 (continued)

First author, year (by region)	Country	Calendar time	Study design and denominator used	Diagnosis of type 2 diabetes	Limitations
			• Denominator: age-specific population data obtained from municipalities	• Differentiation between type 1 and 2: based on obesity, family history, presence of acanthosis nigricans and insulin resistance. Type of diabetes was reported by healthcare provider • Guidelines: cases were classified according to national standards • Excluded cases: not specified	Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases and cases of type 2 diabetes who were visited by primary healthcare physicians) Representativeness: of Puerto Rico children and adolescents Denominator: no limitation
Europe					
Rami, 2003; Schober, 2009 [14, 15]	Austria	1999–2007	• Prospective population-based epidemiological study and nationwide registration[e] • Denominator: from the National Population Registry (Statistics Austria)	• Measurement of diabetes: clinical and laboratory findings (C-peptide, insulin levels) • Differentiation between type 1 and 2: based on obesity, family history, insulin resistance, presence of acanthosis nigricans, elevated levels of C-peptide, lack of ketonuria and insulin dependence, auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: ADA • Excluded cases: cases >15 years old	Case ascertainment: >93% Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of Austrian children ≤15 years old Denominator: no limitation
Neu, 2009 [36]	Germany, Baden-Württemberg	2004–2005	• Using diabetes registry (DIARY)[f] • Denominator: from the national census of 1987 and the subsequent annual updates	• Measurement of diabetes: clinical examination, blood tests (C-peptide, HbA_{1c}), information regarding therapy modalities • Differentiation between type 1 and 2: based on BMI, HbA_{1c}, family history, C-peptide levels, presence of acanthosis nigricans, auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: ADA • Excluded cases: duplicate entries	Case ascertainment: 97.2% Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of Baden-Württemberg area in Germany Denominator: no limitation
Ubink-Veltmaat, 2003 [37]	the Netherlands	1998–2000	• Prospective population-based study[g] • Denominator: from the Central Bureau for Statistics	• Measurement of diabetes: blood tests (glucose measurement, HbA_{1c}), using glucose-lowering medications • Differentiation between type 1 and 2: based on age. Type of diabetes was reported by healthcare provider • Guidelines: national guidelines of the Dutch college of general practitioners 1989 and 1999 (based on 1985 WHO and 1997 ADA criteria) • Excluded cases: not specified	Case ascertainment: not specified Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases, revising guidelines during the study period may have led to some under- or overestimation, lack of appropriate tests for classification, not excluding other types [e.g. MODY])

Table 3 (continued)

First author, year (by region)	Country	Calendar time	Study design and denominator used	Diagnosis of type 2 diabetes	Limitations
Thunander, 2008 [43]	Sweden, Kronoberg	1998–2001	• Data obtained retrospectively from paediatric departments • Denominator: from regional and national authorities	• Measurement of diabetes: blood tests (FPG, C-peptide) • Differentiation between type 1 and 2: based on levels of C-peptide, auto-antibodies (not all children were checked). Type of diabetes was reported by healthcare provider • Guidelines: WHO/ADA • Excluded cases: cases with unconfirmed diagnosis of diabetes after extra testing	Representativeness: not clear Denominator: no limitation Case ascertainment: not specified Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases, lack of appropriate tests for classification of all cases)
Uckun-Kitapci, 2004 [18]	Turkey, Ankara	Not specified	• Cross-sectional population-based study in six randomly selected schools • Denominator: not specified	• Measurement of diabetes: Standardised physical examination, blood tests (FPG, OGTT, and HbA_{1c}) • Differentiation between type 1 and 2: not specified. Type of diabetes was reported by healthcare provider • Guidelines: ADA • Excluded cases: three cases as they were over 19 years of age, other ethnicities than white	Representativeness: not clear Denominator: no limitation Case ascertainment: not applicable Response rate: 86.9% Misclassification of type 2 diabetes: yes (not excluding other types [e.g. MODY]) Test of diabetes: optimal Representativeness: of Ankara school children (12–18 years old) Denominator: not specified
Ehtisham, 2004 [27]	UK	2000	• Cross-sectional postal questionnaire survey of paediatric diabetes centres in the UK[h] • Denominator: from the Office of National Statistics for mid-year 2000	• Measurement of diabetes: physical examination, blood tests (insulin, C-peptide, lipid profile) • Differentiation between type 1 and 2: based on BMI, family history, presence of acanthosis nigricans, raised insulin and C-peptide, abnormal lipid profile, auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: WHO • Excluded cases: Not specified	Case ascertainment: 75% Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of UK children Denominator: no limitation
Ehtisham, 2001 [28]	UK, Birmingham	2000	• Hospital-based study by the Paediatric Diabetes Subgroup of the Pan-Birmingham Diabetes Advisory Group • Denominator: not specified	• Measurement of diabetes: blood tests (C-peptide, insulin) • Differentiation between type 1 and 2: not clearly specified but they checked for the presence of acanthosis nigricans and elevated levels of insulin and C-peptide. Type of diabetes was reported by healthcare provider • Guidelines: not specified • Excluded cases: not specified	Case ascertainment: not specified Response rate: not applicable Test of diabetes: not clearly specified Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: not clear Denominator: not specified
Feltbower, 2003 [29]	UK, Leeds	2000	• Hospital-based cross-sectional study[i]	• Measurement of diabetes: demographic detail and clinical information	Case ascertainment: not specified Response rate: not applicable

Table 3 (continued)

First author, year (by region)	Country	Calendar time	Study design and denominator used	Diagnosis of type 2 diabetes	Limitations
			• Denominator: mid-year (2000) population estimates for the district of Leeds were used for each group (which is co-terminus with Leeds Health Authority); for South Asians and non-South Asians data derived from the 1991 Census	• Differentiation between type 1 and 2: based on clinical expert opinion, auto-antibodies (a few children). Type of diabetes was reported by healthcare provider • Guidelines: WHO/ADA • Excluded cases: patients with other forms of diabetes (other than type 1 diabetes, type 2 diabetes and MODY), uncertain type 1 diabetes or type 2 diabetes, secondary diabetes (e.g. secondary to pancreatectomy, haematoma or lipodystrophy), insulin-treated 'J' type (West Indian), and unclassified diabetes	Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of children in Leeds Denominator: no limitation
Haines, 2007 [30]	UK and Republic of Ireland	2004–2005	• Prospective monthly surveillance through the BPSU framework[j] • Denominator: from the Office of National Statistics	• Measurement of diabetes: anthropometric data, physical examination and blood tests (fasting insulin, C-peptide) • Differentiation between type 1 and 2: based on insulin resistance, presence of acanthosis nigricans, increased fasting insulin or C-peptide, family history, auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: ADA • Excluded cases: duplicate cases, cases >17 years and cases who were diagnosed outside the study period or whose diagnosis was not non-type 1 diabetes	Case ascertainment: 93% for BPSU; 91% for nurses and 94% of clinical questionnaires were received Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of the UK and Republic of Ireland children Denominator: no limitation
Hsia, 2009 [41]	UK	January 1998 to December 2005	• Retrospective cohort study using UK IMS disease analyser database[k] • Denominator: total number of children registered in the database in the same year	• Measurement of diabetes: using prescriptions for glucose-lowering therapy as a proxy for detecting cases with diabetes • Differentiation between type 1 and 2: using prescription of insulin and oral glucose-lowering drugs as a proxy to classify the type of diabetes • Guidelines: not specified • Excluded cases: not specified	Case ascertainment: not specified Response rate: not applicable Test of diabetes: not optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases and cases treated with diet only, not excluding other types [e.g. MODY] and classification was based on prescription data) Representativeness: not clear Denominator: not optimal
North America					
Dean, 1992 [38]	Canada, North-Eastern Manitoba	1984–1990	• Referred cases to the diabetes clinics[l] • Denominator: 5- to 14-year-old children in mid-1987 in Manitoba (Manitoba Health Service Commission)	• Measurement of diabetes: BMI, blood tests (HbA_{1c}, serum insulin level), family history of type 2 diabetes • Differentiation between type 1 and 2: based on symptoms of polyuria and nocturia with ketonuria and severe hyperglycaemia may	Case ascertainment: not specified Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases)

Table 3 (continued)

First author, year (by region)	Country	Calendar time	Study design and denominator used	Diagnosis of type 2 diabetes	Limitations
				mimic type 1. Type of diabetes was reported by healthcare provider • Guidelines: National Diabetes Data Group (1979) guidelines • Excluded cases: cases with the history of diabetic ketoacidosis	Representativeness: of native Indian children in Manitoba Denominator: no limitation
Dean, 1998 [33]	Canada, St Theresa point First Nation	1996–1997	• Cross-sectional survey of school children • Denominator: not specified	• Measurement of diabetes: blood tests (fasting serum glucose and insulin), anthropometric data • Differentiation between type 1 and 2: not specified. Type of diabetes was reported by healthcare provider • Guidelines: ADA • Excluded cases: not specified	Case ascertainment: not applicable Response rate: 82% Test of diabetes: optimal Misclassification of type 2 diabetes: yes (not excluding other types [e.g. MODY]) Representativeness: of remote northern Ojibwa-Cree community of St Theresa Denominator: not specified
Amed, 2010 [26]	Canada	2006–2008	• Prospective national surveillance (with collaboration of CPSP and CFPC-NaReS)[m] • Denominator: from 2006 Canadian Census estimates; for specific ethnic groups population estimated from 2001 Canadian Census[n]	• Measurement of diabetes: clinical presentation and laboratory investigations • Differentiation between type 1 and 2: based on obesity, insulin resistance, family history, auto-antibodies (varied across Canada). Type of diabetes was reported by healthcare provider • Guidelines: Canadian Diabetes Association 2003 clinical practice guidelines • Excluded cases: duplicate cases	Case ascertainment: 83% Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of Canadian children Denominator: no limitation
Pavkov, 2007 [17]	USA, Gila River Indian Community, AZ	1965–2003	• Systematic population screening[o] • Denominator: not specified	• Measurement of diabetes: OGTT, BMI, self-reported treatment with glucose-lowering medicines (insulin or oral medicines) • Differentiation between type 1 and 2: not specified. Type of diabetes was reported by healthcare provider • Guidelines: not specified • Excluded cases: not specified	Case ascertainment: not applicable Response rate: not specified Test of diabetes: optimal Misclassification of type 2 diabetes: yes (revising guidelines during the study period may lead to some under or overestimation) Representativeness: of Gila River Indians Denominator: not specified
Dabelea, 1998 [16]	USA, Gila River Indian Community, AZ	1967–1996	• Systematic population screening[o] • Denominator: not specified	• Measurement of diabetes: OGTT, BMI, medical history, family history • Differentiation between type 1 and 2: not Specified. Type of diabetes was reported by healthcare provider • Guidelines: WHO • Excluded cases: not specified	Case ascertainment: not applicable Response rate: 53.2% to 96.3% Test of diabetes: optimal Misclassification of type 2 diabetes: yes (revising guidelines during the study period may have led to some under or overestimation)

Table 3 (continued)

First author, year (by region)	Country	Calendar time	Study design and denominator used	Diagnosis of type 2 diabetes	Limitations
					Representativeness: of Gila River Indians Denominator: not specified
Fagot-Campagna, 1999 [7]	USA, Gila River Community, AZ	1988–1997	• Systematic population screening of the Gila River community by NIH and also reported cases by the IHS from clinics in south-western USA[p] • Denominator: for NIH was the exact number of adolescents examined at the NIH clinics; and for IHS was from the US census	NIH study: • Measurement of diabetes: OGTT • Differentiation between type 1 and 2: not specified. Type of diabetes was reported by healthcare provider • Guidelines: not specified • Excluded cases: not specified	NIH study: Case ascertainment: not applicable Response rate: not specified Test of diabetes: optimal Misclassification of type 2 diabetes: yes (not excluding other types) Representativeness: of Gila River Indians Denominator: not optimal
				IHS study: •Measurement of diabetes: Medical records • Differentiation between type 1 and 2: not specified. Type of diabetes was reported by healthcare provider • Guidelines: not specified • Excluded cases: not specified	IHS study: Case ascertainment: not specified Response rate: not applicable Test of diabetes: not specified Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases, and Indians who did not use IHS services, and not excluding other types) Representativeness: not clear Denominator: no limitation
Oeltmann, 2003 [39]	USA, SC	1999	• Population-based surveillance RLDR[q] • Denominator: From the USA 2000 census data for the two-county region	• Measurement of diabetes: using billing data to identify all potential patients who were billed with a diabetes related code • Differentiation between type 1 and 2: based on the latest clinical impression of the paediatric endocrinologist, auto-antibodies (not available for patients who were diagnosed years ago). Type of diabetes was reported by healthcare provider, parents or children • Guidelines: ADA • Excluded cases: 71 records were excluded because the status of diabetes could not be validated to type 1 diabetes or type 2 diabetes	Case ascertainment: ~98% Response rate: not applicable Test of diabetes: not specified Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of African-American and non-Hispanic whites in SC Denominator: no limitation
Moore, 2003 [44]	USA, MT and WY	1999–2001	• Annually reviewing the medical records of all diabetic patients at six IHS facilities • Denominator: in this study the most currently available IHS user	• Measurement of diabetes: Demographic, clinical information, documentation of diagnostic blood tests (C-peptide, insulin), history of using glucose-lowering treatments, and other laboratory information	Case ascertainment: not specified Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases)

Table 3 (continued)

First author, year (by region)	Country	Calendar time	Study design and denominator used	Diagnosis of type 2 diabetes	Limitations
			populations for youths ≤19 years were used[r] – Prevalence: sum of the population estimates for 1995–1997, divided by 3 – Incidence: 1997 population estimate minus the prevalent cases in 2001	• Differentiation between type 1 and 2: based on BMI, presence of acanthosis nigricans, age, insulin resistance, elevated C-peptide and insulin, family history, auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: ADA • Excluded cases: American Indian youths who received services solely from non-IHS providers	Representativeness: of American Indians in MT and WY who used IHS services Denominator: no limitation
Smith, 2007 [45]	USA, Chicago	1 January 1994 to 31 December 2003	• Population-based incidence study (CCDR)[s] • Denominator: from census data	• Measurement of diabetes: from medical records and interviews • Differentiation between type 1 and 2: physician diagnosis based on clinical judgement, and history of using glucose-lowering medications, BMI, signs of polycystic ovary syndrome or acanthosis nigricans. Type of diabetes was reported by healthcare provider • Guidelines: not specified • Excluded cases: secondary cases of diabetes (e.g. due to cystic fibrosis, Prader-Willi syndrome or steroid use)	Case ascertainment: 85% Response rate: not applicable Test of diabetes: not optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of Chicago children and adolescents Denominator: not optimal (inaccurate because of undercount of minorities in the used US census)
SEARCH study (Bell 2009, Dabelea 2009, Lawrence 2009, Liu 2009, Mayer-Davis 2009, Liese 2006, Dabelea 2007) [19–25]	USA	2001 (prevalence), 2002–2005 (incidence)	• Observational multicentre population-based study[t] • Denominator: – 2001: four geographically based sites[u] which used non-military non-institutionalised 2000 census. – 2002 and beyond: geographically based centres were using projections of population changes based on 2000 census to estimate denominator of incidence	• Measurement of diabetes: diagnosed by physicians, or self-report of parents or children about the physician diagnosis of diabetes, questionnaire on medical history, a brief physical examination, blood tests (C-peptide, insulin, etc.) • Differentiation between type 1 and 2: based on anthropometry criteria, presence of acanthosis nigricans, C-peptide, auto-antibodies. Type of diabetes was reported by healthcare provider • Guidelines: based on recommendation of ADA expert committee • Excluded cases: cases of gestational diabetes, participants older than 20 years in the index year, non-residents of the study area, active duty military or institutionalised members, cases with maturity-onset of the young, hybrid, other types, or missing type were excluded	Case ascertainment: 93% (for incidence study), 92% (for prevalence study) Response rate: not applicable Test of diabetes: optimal Misclassification of type 2 diabetes: yes (underestimation of asymptomatic cases) Representativeness: of US children and adolescents Denominator: no limitation

[a] Cases of type 2 diabetes were reported by paediatricians, physicians, paediatric endocrinologists, endocrinologist, diabetes educators and nurses

[b] Cases of insulin-treated diabetes obtained from the National Diabetes Supply Scheme

[c] Cases of type 2 diabetes were reported from Princess Margaret Hospital Diabetes Unit (the only tertiary referral hospital for diabetic children in WA)

[d] Estimates of the indigenous population were made by the Epidemiology Branch of the WA Department of Health based on 2001 census

[e] Newly diagnosed type 2 diabetes cases were registered by the Austrian Diabetes Incidence Study Group based on clinical definition by a network covering all paediatric hospitals, wards and dialectologists

[f] Cases of type 2 diabetes were reported and classified by healthcare providers in institutions belonging to the DIARY network including children hospitals (n=31) and one diabetes centre in Baden-Württemberg (BW). In addition, diabetologists in private practice (n=122), internal medicine units (n=164) and a few other institutions (n=6) in BW participated. Questionnaires were used and missing data were obtained by telephone calls

[g] Cases of type 2 diabetes were reported by 61 general practitioners participating in the Zwolle Outpatient Diabetes project Integrating Available Care (ZODIAC) study

[h] Cases of type 2 diabetes were reported by healthcare givers by a cross-sectional postal questionnaire survey. All paediatric diabetes centres and all consultants involved in the care of children with diabetes (281 paediatricians) participated in the survey, which was undertaken by the British Society for Paediatric Endocrinology and Diabetes Clinical Trials/Audit Group

[i] Cases of type 2 diabetes were identified from diabetes clinic lists of the following hospitals: the General Infirmary at Leeds, Wharfedale General Hospital, St James's University Hospital and Seacroft Hospital

[j] Active monthly reporting of type 2 diabetes cases by 2,665 consultant paediatricians in the UK and the Republic of Ireland through the BPSU of the Royal College of Paediatrics and Child Health, with additional (every 2 months) reports from 157 specialist diabetes nurses to identify adolescents directly referred to adult services. A questionnaire was sent to the clinicians who reported new cases to complete the information about cases

[k] General practitioners contribute data to the IMS DA database

[l] Cases of type 2 diabetes were obtained from referred patients to the diabetes clinic at the Children's Hospital of Winnipeg and also family practitioners who provide on-site care or consultation to all northern Manitoba Indian reserves and chronic disease registry of the Medical Services Branch, Manitoba Region Department of National Health and Welfare was searched

[m] A network of paediatricians (n=2,567), paediatric endocrinologists, family physicians (n=98) and adult endocrinologists (n=49) was established for a surveillance study. New cases of physician-diagnosed type 2 diabetes were reported monthly and followed by a detailed questionnaire on clinical presentation and other information. Physician classifications were reviewed by clinician investigators

[n] Population estimates for children belonging to Hispanic, Middle Eastern or mixed ethnicity were not available and therefore were not included

[o] Every 2 years, OGTT and anthropometric measurements were carried out in Pima Indians (≥5 years) regardless of their health situation and new cases of type 2 diabetes were obtained

[p] Study population of NIH was limited to Pima Indians and their close relatives while in the IHS study all other south-western tribes were included

[q] Physician diagnosed cases of type 2 diabetes residing in a two-county region were ascertained from hospitals, the sole office of paediatric endocrinologists, two large-area paediatric outpatient clinics, adult endocrinology clinics and several smaller sources

[r] IHS user populations were somewhat larger than the census estimates of American Indian youth living in counties or near these reservations

[s] Cases of type 2 diabetes for CCDR were ascertained primarily from medical records of 29 hospitals and general paediatric services located in Chicago and its suburbs. The Illinois Department of Public Aid payment database provided a third source of cases through 2001

[t] Physician-diagnosed cases of type 2 diabetes were obtained in this study

[u] Four geographically based sites were Cincinnati, Colorado, Seattle and South Carolina

AIHW, Australian Institute of Health and Welfare; BPSU, British Paediatric Surveillance Unit; CCDR, Chicago Childhood Diabetes Registry; CFPC-NaReS, College of Family Physicians of Canada National Research System; CPSP, Canadian Paediatric Surveillance Program; DIARY, Diabetes Registry; FPG, fasting plasma glucose; IHS, Indian Health Service; NIH, National Institute of Health; NZHIS, New Zealand Health Information Service; NZPSU, New Zealand Paediatric Surveillance Unit; RLDR, Richmond/Lexington County Childhood and Adolescents Diabetes Registry; US PHS, United States Public Health Service; WACDD, Western Australian Children's Diabetes Database

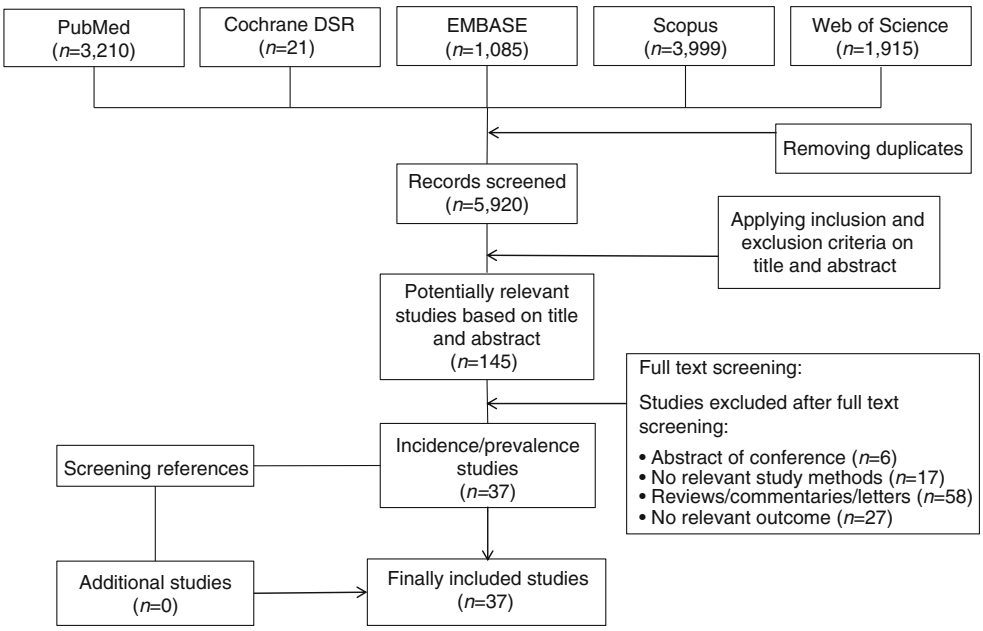

Fig. 1 Flowchart of search results. DSR, Database of Systematic Reviews

Calendar time and duration of the study Calendar time of the 37 studies varied widely. The first population-based study that reported on the epidemiology of type 2 diabetes in children and adolescents was started in 1965 in Pima Indians in the USA [17], while the most recent study was a Canadian study performed between 2006 and 2008 [26]. Pavkov et al reported the longest follow-up of 39 years [17], followed by a Japanese study with a follow-up of 30 years [11–13]. The shortest follow-up was 1 year [27–30].

Study design and case ascertainment methods Different methods were used in the studies for investigating incidence and prevalence of type 2 diabetes. In nine studies, cases of type 2 diabetes were found through population screening [11–13, 16–18, 31–33]. The population that was invited for screening also varied between studies. The complete Pima Indian population was screened regardless of their health situation [16, 17], in Japan and Taiwan school children from all schools were screened [11–13, 31, 32] and in Ankara (Turkey) only children in six randomly selected schools participated in the screening programme [18]. In a Canadian study, all school children (aged 4–19 years) in the remote northern Ojibwa-Cree community of St Theresa Point First Nation were screened [33].

The second method, which was the one most commonly applied (in 20 studies), was to capture all cases of type 2 diabetes in children and adolescents that had been diagnosed by the healthcare provider. In these 20 studies, healthcare providers with different backgrounds (e.g. general practitioners, paediatric endocrinologists, adult endocrinologists, diabetes nurses, etc.) participated in a surveillance system [14, 15, 19–28, 30, 34–40]. The numbers of diagnosed cases were related to denominators of numbers of children in the relevant geographical areas (Table 3).

A third method, applied in six studies, involved the use of administrative databases (e.g. using prescriptions for glucose-lowering treatment listed in a database as a proxy for finding cases of diabetes [41]) or medical chart reviews in hospitals or medical centres [29, 42–45].

Two of the included studies (Fagot-Campagna et al and Craig et al) used a combination of methods for identifying cases of type 2 diabetes [7, 46]. Fagot-Campagna et al used both population screening and medical chart reviews while Craig et al used administrative databases and a surveillance system to find cases of type 2 diabetes.

In the population-based screening studies, when reported, response rates varied from 60% to 96%. In the studies that used healthcare provider diagnosis or administrative databases, case ascertainment ranged from 53% to 99% (Table 3).

Diagnosis of type 2 diabetes and classification Another source of variation in the methodology of the included studies was the use of different diagnostic guidelines for type 2 diabetes. In most studies, the ADA or WHO guidelines were used to identify cases. In a few studies, national guidelines were used to diagnose type 2 diabetes [26, 37, 38].

Different diagnostic tests were used to identify type 2 diabetes cases (e.g. in two screening programmes, urine strips were used to diagnose glycosuria and children with two positive results were checked with additional diagnostic tests) [11–13, 31, 32]. In most studies diabetes was diagnosed based on clinical presentation in combination with

diagnostic tests (e.g. OGTT, fasting plasma glucose (FPG), fasting plasma insulin and/or C-peptide level, etc.). Classification of the type of diabetes was another major issue. Differentiation between type 2 and type 1 diabetes was difficult, especially in the earliest and retrospective studies and in studies in which questionnaires (or telephone surveys) were used. In the 37 included studies, different criteria were used to differentiate between type 1 and type 2 diabetes (Table 3) (e.g. 26 of the included studies reported that they used tests for detecting auto-antibodies or beta cell function [11–15, 19–27, 29–31, 34, 36, 39, 40, 42–46]).

In almost all studies, the healthcare providers or investigators confirmed the type of diabetes, except in two studies in which the type of diabetes was reported by parents or children themselves via questionnaire or telephone survey [32, 39].

Incidence and prevalence estimates Data on incidence and prevalence from all studies are summarised in Figs 2 and 3. Incidence and prevalence rates were found to vary widely depending on age, sex and ethnicity of the study population and geographical region, resulting in a range of 0–330 per 100,000 person-years for incidence and 0–5,300 per 100,000 children and adolescents for prevalence [7, 17, 18, 37]. Detailed information from all studies is presented in ESM Table 1.

The lowest incidence rates were observed in European countries. The Netherlands, with no new cases of type 2 diabetes during the 1998–2000 period, and Austria, with an incidence rate of 0.29 per 100,000 person-years for the 1999–2007 period, had the lowest reported incidences [14, 15, 37].

The highest incidence of type 2 diabetes in youth was observed in 4- to 15-year-old Pima Indians in the USA (330 per 100,000 person-years) [17]. This was followed by the Navajo population (USA), American Indians (USA) and African-Americans (USA) (27.7, 23.3 and 19, respectively, per 100,000 person-years) [20, 23, 44]. The Aboriginal population in Canada also had a high incidence rate (23.3 per 100,000 person-years) [26] (Fig. 2).

Among European countries, a study from the UK showed incidence rates of type 2 diabetes stratified by ethnicity: black individuals had 3.9 cases per 100,000 person-years, while South Asian and white individuals had rates of 1.25 and 0.35 per 100,000 person-years, respectively [30].

In Europe, the UK had the highest number of prevalence studies [27–29, 41]. Of four prevalence studies in the UK, two covered the whole country but produced different results. In one study, the prevalence for the population 0–16 years of age in 2000 was reported to be 0.21 per 100,000 children/adolescents, while in another study in the same year the reported prevalence rate was 1.9 per 100,000 for the 0- to 18-year-old study population [27, 41]. Among the European countries, the highest prevalence rate of type 2 diabetes was reported in 15- to 19-year-old adolescents in

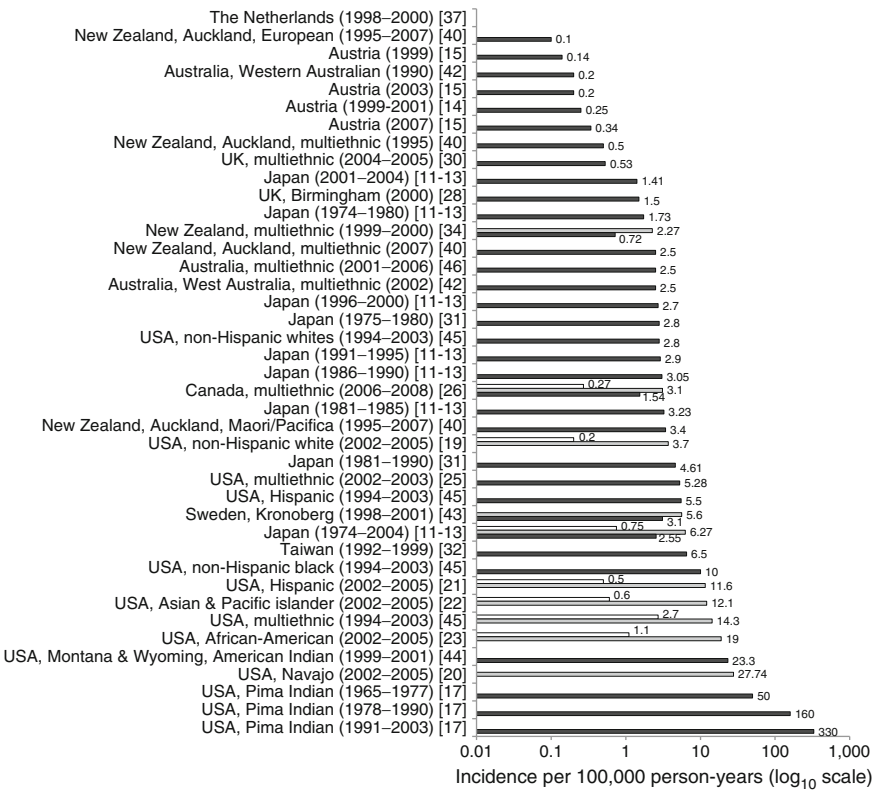

Fig. 2 Overview of the reported incidences of type 2 diabetes per 100,000 person-years (because of considerable variations in the observed rates, incidence data are graphed on a base 10 logarithmic scale). The incidence rates were calculated for male/female populations. White bars represent children (0–9 years), grey bars represent adolescents (10–19 years) and black bars represent children and adolescents (0–19 years)

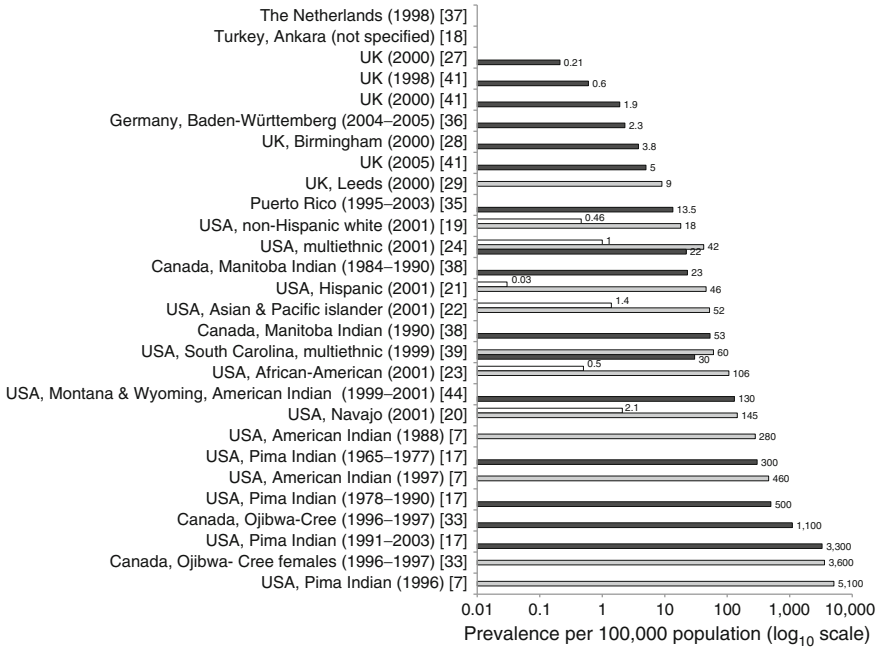

Fig. 3 Overview of the reported prevalences of type 2 diabetes per 100,000 children and/or adolescents (because of considerable variations in the observed rates, prevalence data are graphed on a base 10 logarithmic scale). The prevalence rates were calculated for male/female populations, except for the prevalence rate of 3,600 per 100,000 which was for Ojibwa-Cree females. White bars represent children (0–9 years), grey bars represent adolescents (10–19 years) and black bars represent children and adolescents (0–19 years)

Leeds (UK) with a prevalence of 9 per 100,000 adolescents in 2000 [29].

The highest prevalence of type 2 diabetes in youth was observed in female Pima Indians (USA) aged 15–19 years (5,300 per 100,000 in 1987–1996), while for male Pima Indians the rate was lower (3,800 per 100,000) [16, 17]. For 10- to 14-year-old Pima Indians in the same time period, the respective prevalence for female and male subjects was 2,900 and 1,400 per 100,000 [7]. The Ojibwa-Cree population in Canada had the second highest prevalence rate with 3,600 per 100,000 for 10- to 19-year old females and 1,100 per 100,000 for 4- to 19-year-old male and female children and adolescents in 1996–1997 [33] (Fig. 3). High prevalence rates were also reported in American Indians, Navajo population and African-American children and adolescents [20, 23–25]. Among the different ethnicities in the USA, non-Hispanic white individuals had the lowest prevalence of type 2 diabetes [24, 25] (ESM Table 1).

Discussion

According to the findings of this systematic review, the epidemiological studies of type 2 diabetes in children and adolescents differed widely in population characteristics and study methods, which resulted in a substantial variation in incidence and prevalence estimates. While these differences in the rates of type 2 diabetes could in part be explained by differences in age, ethnicity, country and calendar time, methodological dissimilarities contributed as well. Referring to two studies performed in the UK in 2000, Hsia et al reported a prevalence rate for type 2 diabetes which was almost ten times higher than that reported by Ehtisham et al [27, 41]. Although there was only a slight difference in age between the two study populations, the different methods used (Ehtisham et al used a survey to find cases of type 2 diabetes while Hsia et al used an administrative database) and the lower case ascertainment in the study by Ehtisham et al probably led to an underestimation of the type 2 diabetes cases. Another example of the impact of methodological differences on the rate estimates is the study of Fagot-Campagna et al, which compared the prevalence of type 2 diabetes in adolescents aged 15–19 years, obtained from two different sources using different methods of data collection and analysis. The prevalence estimate of 5.1% vs 0.46% shows the remarkable effect of methodological differences on rate estimation [7].

In most of the studies included in this review, cases of type 2 diabetes were reported by healthcare providers who participated in a surveillance system. There are several drawbacks of using this method to estimate the occurrence of type 2 diabetes. First, children and adolescents with type 2 diabetes may remain asymptomatic and undiagnosed for a long period of time [47, 48] leading to underestimation of the number of type 2 diabetes cases [14, 15, 19–27, 29, 30, 34, 37, 39, 43, 44, 46]. Although the Princeton study recently showed that undiagnosed type 2 diabetes is very uncommon in adolescents and that this has not changed over the last decades [49], the findings from the Princeton study probably cannot be extrapolated to countries in which patients have only limited access to healthcare and/or the healthcare system has a suboptimal quality. Second, the quality of detection and classification of type 2 diabetes might differ between healthcare providers [29, 32, 35, 36].

This may be related to the different backgrounds of the healthcare providers (e.g. general practitioners, paediatricians and endocrinologists have different test strategies) and also to the lack of an internationally agreed diagnostic method and classification system for identifying cases of type 2 diabetes in children and adolescents. Third, case ascertainment rates in surveillance systems showed substantial differences, again leading to different rates and underestimation of incidence and prevalence rates [27, 41].

Administrative databases (e.g. prescription databases) are sometimes used for incidence and prevalence estimation, with the advantage that this approach for some aspects is less susceptible to ascertainment and selection biases. For instance when a prescription record database of pharmacies is used, the registration of prescriptions is often similar and complete [50]. However, the problem of missing undiagnosed cases of type 2 diabetes and differences in testing and treatments of diabetes between healthcare providers remain important limitations [41].

Retrospectively reviewing the medical charts and patient files in medical centres to find cases of diabetes, and to classify them based on the retrieved data, is often suboptimal because of missing information and differences by which healthcare providers test for diabetes and record medical information [44].

For all three methods mentioned above (capturing of cases by participation of healthcare providers in surveillance systems, administrative databases and reviewing of medical charts) an important difficulty is that of retrieving a valid denominator. Often the denominator originates from organisations registering vital statistics. A valid demarcation of the area from which the cases derive is a challenge.

Although population-based screening was not often applied among our 37 studies, it has a number of important advantages when compared with the other methods discussed. The starting point is that all people, regardless of their health situation, are screened and the same valid screening method and diagnostic criteria can be used. Thereby, the chance of finding all (and even asymptomatic undiagnosed) type 2 diabetes cases will increase. Furthermore, the denominator is directly available, being the total number of screened children and adolescents. However, in these population-based screening programmes some important issues should also be taken into account. For instance, non-participation of invited children (suboptimal response rate) can lead to biased estimations. Also, just as in the other methods, the sensitivity and specificity of the diagnostic tests, with the potential risks of under- or over-diagnosis, respectively, can be a problem. Wei et al reported that the sensitivity of the glycosuria test used in the screening for diabetes ranged from 20% to more than 80% [32]. Finally, the performance of a population-based screening is probably more costly than the other methods. As far as we know the different methods have not been compared with respect to cost-effectiveness. Recently Wu et al conducted a cost-effectiveness analysis of screening strategies for identifying type 2 diabetes and dysglycaemia (prediabetes) in children and adolescents (aged 10–17 years) [51]. Although they found that the cost of screening per case was high for diabetes, they mentioned that screening for diabetes in youth could be more cost-effective if dysglycaemia was explicitly considered as a screening outcome. However, Wu et al did not address the benefits and harms of early detection of type 2 diabetes and prediabetes in children and adolescents.

Even if case ascertainment, classification and definition of type 2 diabetes and response rates are satisfactory, the researchers involved in all methods face the challenge of choosing the right sample(s) of the population to be really representative for the intended population [7]. Regional differences may be expected in vital statistics, reflecting geographical, ethnic, genetic, environmental and socioeconomic factors. For this reason, the demographic characteristics of the population sample should be well described and the analysis should take into account such differences.

After considering all methodological differences, we can state in general that ethnic minorities have higher rates of type 2 diabetes than white individuals in almost all countries. There is also a great difference among type 2 diabetes rates in ethnic minorities in the USA and Canada compared with ethnic groups in other locations (e.g. in Europe and Australia) [19–27, 30, 34, 46]. Although genetics plays an important role in the development of diabetes, environmental and lifestyle factors, such as dietary habits and having a sedentary lifestyle, are also relevant. For instance, Pima Indians in Arizona have the highest reported prevalence of type 2 diabetes in the world [7] while Pima Indians in Mexico with the same ethnicity have a much lower prevalence [7]. Pima Indians in Mexico have a healthier and more active lifestyle than Arizona Pima Indians, which indicates the importance of environmental factors in the development of type 2 diabetes [7].

Both incidence and prevalence data were considerably higher in female vs male subjects and, in addition, there was a great difference between adolescents (aged 10–19 years) and children (aged 0–9 years) [24, 25].

Concerning changes in the occurrence of type 2 diabetes over time, existing data are limited for most countries. Only a few studies (e.g. Urakami et al in Japan and Pavkov et al in the USA) evaluated trends in incidence/prevalence of type 2 diabetes over a prolonged period of time [11–13, 17]. Pavkov's study demonstrated a significant increase in type 2 diabetes rates while the Japanese study showed a decrease in incidence of type 2 diabetes in Japanese school children [11–13, 17].

The lack of studies performed in some parts of the world, mostly developing countries, and the absence of data on the socioeconomic status of the study populations are

limitations of our review. In addition, the heterogeneity of study designs and population characteristics did not allow for a more rigorous quantitative analysis (such as a meta-analysis).

In conclusion, the incidence and prevalence of type 2 diabetes in children and adolescents show important variations among countries and ethnic groups worldwide, caused by both population characteristics and methodological differences. Based on our findings it is important to continue to follow global trends in the incidence and prevalence of type 2 diabetes in the young population and to use a valid study design, appropriate diagnostic tools and the same diagnostic criteria. Population-based screening programmes appear to fulfil most of these requirements although the cost-effectiveness of such programmes is not clear yet.

Acknowledgements The authors would like to thank N. Zuiverloon (librarian at the library of Utrecht University) for her helpful suggestions for searching databases.

Funding No funding source had any role in the design and conduct of the study, the collection, management, analysis and interpretation of the data or the preparation, review or approval of the manuscript.

The Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, has received unrestricted funding from the Netherlands Organisation for Health Research and Development (ZonMW), the Dutch Health Care Insurance Board (CVZ), the Royal Dutch Pharmacists Association (KNMP), the private-public funded Top Institute Pharma (www.tipharma.nl, includes co-funding from universities, government, and industry), the EU Innovative Medicines Initiative (IMI), the EU 7th Framework Program (FP7) and the Dutch Ministry of Health and industry (including GlaxoSmithKline, Pfizer, and others).

Duality of interest The authors declare that there is no duality of interest associated with this manuscript, no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

Contribution statement SFF and MPA searched the literature and extracted data. In case of disagreement AB and MMJV checked the study. All authors discussed the data and interpreted the results. SFF and MPA wrote the manuscript. MMJV, CAJK and AB reviewed and edited the manuscript. All authors approved the final version and take full responsibility for the contents of the manuscript.

References

1. Chen L, Magliano DJ, Zimmet PZ (2011) The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. Nat Rev Endocrinol 8:228–236
2. Zimmet P, Alberti KG, Shaw J (2001) Global and societal implications of the diabetes epidemic. Nature 414:782–787
3. Botero D, Wolfsdorf JI (2005) Diabetes mellitus in children and adolescents. Arch Med Res 36:281–290
4. D'Adamo E, Caprio S (2011) Type 2 diabetes in youth: epidemiology and pathophysiology. Diabetes Care 34(suppl 2):S161–S165
5. Pinhas-Hamiel O, Zeitler P (2007) Acute and chronic complications of type 2 diabetes mellitus in children and adolescents. Lancet 369:1823–1831
6. Lipton RB (2007) Incidence of diabetes in children and youth—tracking a moving target. JAMA 297:2760–2762
7. Fagot-Campagna A, Burrows NR, Williamson DF (1999) The public health epidemiology of type 2 diabetes in children and adolescents: a case study of American Indian adolescents in the Southwestern United States. Clin Chim Acta 286:81–95
8. Cali AM, Caprio S (2008) Prediabetes and type 2 diabetes in youth: an emerging epidemic disease? Curr Opin Endocrinol Diabetes Obes 15:123–127
9. American Diabetes Association (2008) Economic costs of diabetes in the U.S. In 2007. Diabetes Care 31:596–615
10. Stroup DF, Berlin JA, Morton SC et al (2000) Meta-analysis of observational studies in epidemiology. JAMA 283:2008–2012
11. Urakami T, Kubota S, Nitadori Y, Harada K, Owada M, Kitagawa T (2005) Annual incidence and clinical characteristics of type 2 diabetes in children as detected by urine glucose screening in the Tokyo metropolitan area. Diabetes Care 28:1876–1881
12. Urakami T, Morimoto S, Nitadori Y, Harada K, Owada M, Kitagawa T (2007) Recent change in the annual incidence of childhood type 2 diabetes in the Tokyo metropolitan area. Clin Pediatr Endocrinol 16:53–58
13. Urakami T, Owada M, Kitagawa T (2006) Recent trend toward decrease in the incidence of childhood type 2 diabetes in Tokyo. Diabetes Care 29:2176–2177
14. Rami B, Schober E, Nachbauer E, Waldhor T, Austrian Diabetes Incidence Study Group (2003) Type 2 diabetes mellitus is rare but not absent in children under 15 years of age in Austria. Eur J Pediatr 162:850–852
15. Schober E, Waldhoer T, Rami B, Hofer S, Austrian Diabetes Incidence Study Group (2009) Incidence and time trend of type 1 and type 2 diabetes in Austrian children 1999-2007. J Pediatr 155:190–193
16. Dabelea D, Hanson RL, Bennett PH, Roumain J, Knowler WC, Pettitt DJ (1998) Increasing prevalence of type II diabetes in American Indian children. Diabetologia 41:904–910
17. Pavkov ME, Hanson RL, Knowler WC, Bennett PH, Krakoff J, Nelson RG (2007) Changing patterns of type 2 diabetes incidence among Pima Indians. Diabetes Care 30:1758–1763
18. Uckun-Kitapci A, Tezic T, Firat S et al (2004) Obesity and type 2 diabetes mellitus: a population-based study of adolescents. J Pediatr Endocrinol Metab 17:1633–1640
19. Bell RA, Mayer-Davis EJ, Beyer JW et al (2009) Diabetes in non-Hispanic white youth: prevalence, incidence, and clinical characteristics: the SEARCH for Diabetes in Youth Study. Diabetes Care 32(suppl 2):S102–S111
20. Dabelea D, DeGroat J, Sorrelman C et al (2009) Diabetes in Navajo youth: prevalence, incidence, and clinical characteristics: the SEARCH for Diabetes in Youth Study. Diabetes Care 32(suppl 2):S141–S147
21. Lawrence JM, Mayer-Davis EJ, Reynolds K et al (2009) Diabetes in Hispanic American youth: prevalence, incidence, demographics, and clinical characteristics: the SEARCH for Diabetes in Youth Study. Diabetes Care 32(suppl 2):S123–S132
22. Liu LL, Yi JP, Beyer J et al (2009) Type 1 and type 2 diabetes in Asian and Pacific Islander U.S. youth: the SEARCH for Diabetes in Youth Study. Diabetes Care 32(suppl 2):S133–S140
23. Mayer-Davis EJ, Beyer J, Bell RA et al (2009) Diabetes in African American youth: prevalence, incidence, and clinical characteristics: the SEARCH for Diabetes in Youth Study. Diabetes Care 32(suppl 2):S112–S122
24. Group SEARCH for Diabetes in Youth Study, Liese AD, D'Agostino RB Jr et al (2006) The burden of diabetes mellitus

among US youth: prevalence estimates from the SEARCH for Diabetes in Youth Study. Pediatrics 118:1510–1518
25. Writing Group for the SEARCH for Diabetes in Youth Study Group, Dabelea D, Bell RA et al (2007) Incidence of diabetes in youth in the United States. JAMA 297:2716–2724
26. Amed S, Dean HJ, Panagiotopoulos C et al (2010) Type 2 diabetes, medication-induced diabetes, and monogenic diabetes in Canadian children: a prospective national surveillance study. Diabetes Care 33:786–791
27. Ehtisham S, Hattersley AT, Dunger DB, Barrett TG, British Society for Paediatric Endocrinology and Diabetes Clinical Trials Group (2004) First UK survey of paediatric type 2 diabetes and MODY. Arch Dis Child 89:526–529
28. Ehtisham S, Kirk J, McEvilly A et al (2001) Prevalence of type 2 diabetes in children in Birmingham. BMJ 322:1428
29. Feltbower RG, McKinney PA, Campbell FM, Stephenson CR, Bodansky HJ (2003) Type 2 and other forms of diabetes in 0-30 year olds: a hospital based study in Leeds, UK. Arch Dis Child 88:676–679
30. Haines L, Wan KC, Lynn R, Barrett TG, Shield JP (2007) Rising incidence of type 2 diabetes in children in the U.K. Diabetes Care 30:1097–1101
31. Kitagawa T, Owada M, Urakami T, Tajima N (1994) Epidemiology of type 1 (insulin-dependent) and type 2 (non-insulin-dependent) diabetes mellitus in Japanese children. Diabetes Res Clin Pract 24 (Suppl):S7–S13
32. Wei JN, Sung FC, Lin CC, Lin RS, Chiang CC, Chuang LM (2003) National surveillance for type 2 diabetes mellitus in Taiwanese children. JAMA 290:1345–1350
33. Dean HJ, Young TK, Flett B, Wood-Steiman P (1998) Screening for type-2 diabetes in aboriginal children in northern Canada. Lancet 352:1523–1524
34. Campbell-Stokes PL, Taylor BJ, New Zealand Children's Diabetes Working Group (2005) Prospective incidence study of diabetes mellitus in New Zealand children aged 0 to 14 years. Diabetologia 48:643–648
35. Perez-Perdomo R, Perez-Cardona CM, Allende-Vigo M, Rivera-Rodriguez MI, Rodriguez-Lugo LA (2005) Type 2 diabetes mellitus among youth in Puerto Rico, 2003. P R Health Sci J 24:111–117
36. Neu A, Feldhahn L, Ehehalt S, Hub R, Ranke MB, DIARY group Baden-Wurttemberg (2009) Type 2 diabetes mellitus in children and adolescents is still a rare disease in Germany: a population-based assessment of the prevalence of type 2 diabetes and MODY in patients aged 0-20 years. Pediatr Diabetes 10:468–473
37. Ubink-Veltmaat LJ, Bilo HJ, Groenier KH, Houweling ST, Rischen RO, Meyboom-de Jong B (2003) Prevalence, incidence and mortality of type 2 diabetes mellitus revisited: a prospective population-based study in The Netherlands (ZODIAC-1). Eur J Epidemiol 18:793–800
38. Dean HJ, Mundy RL, Moffatt M (1992) Non-insulin-dependent diabetes mellitus in Indian children in Manitoba. CMAJ 147:52–57
39. Oeltmann JE, Liese AD, Heinze HJ, Addy CL, Mayer-Davis EJ (2003) Prevalence of diagnosed diabetes among African-American and non-Hispanic white youth, 1999. Diabetes Care 26:2531–2535
40. Jefferies C, Carter P, Reed PW et al (2012) The incidence, clinical features, and treatment of type 2 diabetes in children <15 yr in a population-based cohort from Auckland, New Zealand, 1995-2007. Pediatr Diabetes 13:294–300
41. Hsia Y, Neubert AC, Rani F, Viner RM, Hindmarsh PC, Wong IC (2009) An increase in the prevalence of type 1 and 2 diabetes in children and adolescents: results from prescription data from a UK general practice database. Br J Clin Pharmacol 67:242–249
42. McMahon SK, Haynes A, Ratnam N et al (2004) Increase in type 2 diabetes in children and adolescents in Western Australia. Med J Aust 180:459–461
43. Thunander M, Petersson C, Jonzon K et al (2008) Incidence of type 1 and type 2 diabetes in adults and children in Kronoberg, Sweden. Diabetes Res Clin Pract 82:247–255
44. Moore KR, Harwell TS, McDowall JM, Helgerson SD, Gohdes D (2003) Three-year prevalence and incidence of diabetes among American Indian youth in Montana and Wyoming, 1999 to 2001. J Pediatr 143:368–371
45. Smith TLS, Drum ML, Lipton RB (2007) Incidence of childhood type 1 and non-type 1 diabetes mellitus in a diverse population: The Chicago Childhood Diabetes Registry, 1994 to 2003. J Pediatr Endocrinol Metab 20:1093–1107
46. Craig ME, Femia G, Broyda V, Lloyd M, Howard NJ (2007) Type 2 diabetes in indigenous and non-indigenous children and adolescents in New South Wales. Med J Aust 186:497–499
47. Shaw J (2007) Epidemiology of childhood type 2 diabetes and obesity. Pediatr Diabetes 8(suppl 9):7–15
48. Ludwig DS, Ebbeling CB (2001) Type 2 diabetes mellitus in children: primary care and public health considerations. JAMA 286:1427–1430
49. Dolan LM, Bean J, D'Alessio D et al (2005) Frequency of abnormal carbohydrate metabolism and diabetes in a population-based screening of adolescents. J Pediatr 146:751–758
50. Herings RM, de Boer A, Stricker BH, Bakker A, Sturmans F (1995) A rapid method to estimate the incidence rate and prevalence of insulin-dependent diabetes mellitus in children 0-19 years of age. Pharm World Sci 17:17–19
51. Wu EL, Kazzi NG, Lee JM (2013) Cost-effectiveness of screening strategies for identifying pediatric diabetes mellitus and dysglycemia. JAMA Pediatr 167:32–39