Body Mass Index and Incident Type 1 and Type 2 Diabetes in Children and Young Adults: A Retrospective Cohort Study

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Context: Little is known about the association between obesity and temporal trends in the incidence of diabetes in children and young adults.

Objective: We examined the recent incidence of types 1 and 2 diabetes in relation to a high body mass index (BMI) in UK children and young adults.

Design: Cohort and nested case-control.

Setting: A total of 375 general practices that contribute to the UK Clinical Practice Research Datalink (CPRD).

Participants: A total of 369,362 participants aged 2 to 15 years at BMI measurement in CPRD from 1994 to 2013.

Intervention: None.

Main outcome measures: Incident type 1 diabetes (T1D) and type 2 diabetes (T2D) diagnoses up to age 25 years.

Results: A total of 654 incident cases of T2D and 1318 T1D cases were found. The incidence of T2D per 100,000 persons annually increased from 6.4 in 1994 to 1998 to 33.2 in 2009 to 2013; and that for T1D increased from 38.2 to 52.1 per 100,000 persons during the same period. The incidence of T2D increased in both overweight (85th to 95th percentile for age- and sex-specific BMI; $P = 0.01$) and obese ($\geq$95th percentile; $P < 0.01$) individuals from 1994 to 2013. Obese individuals, who constituted 47.1% of T2D cases, had a markedly greater risk of incident T2D [odds ratio, 3.75; 95% confidence interval (CI), 3.07 to 4.57], with an incidence rate ratio of 4.33 (95% CI, 3.68 to 5.08) compared with the normal BMI category. No positive linear association was found between obesity (greater BMI) and incident T1D cases.

Conclusions: Increasing obesity has contributed to the increasing incidence of T2D but not T1D among UK children and young adults, with a fourfold greater risk of developing T2D in obese individuals.

Obesity is a global health epidemic that is shifting toward children and young adults [1-3]. More than one-half of adults, aged ≥18 years, were obese or overweight in 2014 [4], and one of three children leaving primary school were considered obese or overweight in 2015 [5]. The rate of increase in obesity prevalence in children and young adults might have stabilized during the recent decade [6–8]; however, 37% of older children are now overweight or obese in the United Kingdom [6]. Observational and genetic evidence from traditional cohort studies has suggested that obesity is a well-documented risk factor for type 2 diabetes [9–11]. However, recent evidence exploring the association of childhood obesity [defined as the 95th percentile for body mass index (BMI)] with the presence of pediatric diabetes in a real world primary care setting has been less well studied [12–14]. A recent prospective study from Norway and Denmark showed a positive association between the weight increase during the first 12 months of life and the development of type 1 diabetes [15], suggesting that similar to type 2 diabetes, type 1 diabetes might have environmental origins.

Another study showed that the prevalence rates of both type 1 and type 2 diabetes increased among children and adolescents in the United States from 2001 to 2009 [16]. In England and Wales, 26,687 children and young adults aged ≤25 years receive diabetes care, with 95% classified as having type 1 diabetes and 2% having type 2 diabetes [17]. Previous studies of type 2 diabetes in children and young adults had included small number of participants or been conducted in selected cohorts [18, 19]. The present study evaluated the incidence and temporal trends of type 1 and type 2 diabetes and estimated the risk of developing diabetes in association with an elevated BMI in a cohort of children and young adults with BMI recorded from 1994 through 2013.

1. Methods

A. Study Design and Data Source

A cohort study was conducted using the electronic health records from the UK Clinical Practice Research Datalink (CPRD) [20]. The UK CPRD is one of the largest primary care databases of electronic health records worldwide [6] and collates anonymized data on the clinical diagnoses, prescriptions, laboratory test results, referrals to specialists, and hospital admissions [21]. Individuals were sampled from 375 English general practices that participate in the CPRD data linkage scheme, if they were aged 2 to15 years at BMI measurement and had BMI values recorded during the period 1994 to 2013. The Independent Scientific Advisory Committee approved the present protocol (Independent Scientific Advisory Committee no. 13-194).

B. Demographic Information, Measurements, and Outcomes

Demographic information, including sex, date of birth, and dates of the start and end of the record (Supplemental Fig. 1), was analyzed. We searched the database for the BMI, height, and weight records to calculate the BMI, as previously described [6, 22, 23]. Our main outcomes were the diagnosis of type 1 and type 2 diabetes, which were classified according to the medical diagnostic codes, prescriptions for antidiabetic drugs, or a hemoglobin A1c (HbA1c) value. The applicable prescriptions were insulin or an oral glucose-lowering agent, including sulfonylureas, metformin, dipeptidyl-peptidase-4 inhibitors, glitazones, acarbose, and glinides [24]. The first date in the record of a prescription of any of these was assigned as the diabetes start date. Patients attributed with a diabetes diagnosis before 12 months after the start of their CPRD record were excluded because these cases were considered to be prevalent diabetes (Supplemental Figs. 1 and 2) [24].

The patients were considered to have type 1 diabetes if they had a diagnosis of type 1 diabetes or had been prescribed insulin and had never been prescribed oral glucose-lowering medications in the CPRD. Type 2 diabetes was defined as a diagnosis of type 2 diabetes, the

prescription of oral glucose-lowering medications only, or a diagnosis of diabetes mellitus or HbA1c ≥6.5% (48 mmol/mol) but no insulin prescription. Those with diabetes that could not be classified were excluded. The excluded cases included diagnoses of both type 1 and type 2 diabetes, prescriptions for both oral glucose-lowering medications and insulin, diagnosis of type 1 diabetes without an insulin prescription, and diagnosis of type 2 diabetes with a prescription for insulin. We also excluded women with a diagnosis of polycystic ovary syndrome or gestational diabetes (Supplemental Fig. 2).

C. Statistical Analysis

The BMI values were converted to Z-scores, adjusting for exact age and sex using the British 1990 growth reference data population [23]. Normal weight was defined as a BMI Z-score <1.04 (<85th percentile on a growth chart). Overweight was defined as 1.04 to 1.64 (85th to 95th percentile) and obese as a Z-score of ≥1.64 (≥95th percentile) of the UK 1990 reference population [23]. We calculated the present age in each calendar year and calculated the person-years of observation from 1994 until the date of diabetes diagnosis for incident cases of diabetes or the end of the record for the remaining individuals. We estimated the incidence rates of diabetes (or age-standardized to the 2013 European Standard Population for reference) [25, 26], with person-years as the exposure variable. Incidence rates (per 100,000 persons per year) were presented for each 5-year period and according to the present age, sex, and BMI categories. We fitted unadjusted or jointly adjusted Poisson regression models to calculate the incidence rate ratios (IRRs) for all variables.

To replicate the Poisson regression models and estimate the relative risks, we also conducted a nested case-control study in which each case with diabetes was matched for sex, year of birth, and general practice with up to four randomly selected controls (without any relevant records for diabetes). We fitted conditional logistic regression models to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for incident diabetes in relation to an elevated BMI. We calculated the ORs per one standard deviation (SD) change in BMI, for overweight and obesity (normal weight as reference) or across BMI quintiles (first quintile as reference). We applied quintile values in controls to categorize the BMI. As a sensitivity analysis, we repeated this analysis using only data for BMI values recorded before the date of the diabetes diagnosis to reduce the likelihood of reverse causality. All data analyses were performed in Stata, version 14 (StataCorp, College Station, TX), and R, version 3.2.3 (R Foundation, Vienna, Austria). Owing to the large sample size of the present study, $P < 0.01$ was considered statistically significant.

2. Results

A. Population Characteristics

We analyzed the data from 369,362 eligible individuals with the BMI calculated using weight and height values (n = 321,597) or BMI as directly recorded in the CPRD (n = 47,765) from 1994 to 2013. The mean age at the last birthday before the BMI record was 8.8 ± 4.3 years (range, 2 to 15), and 49.5% were female. The median BMI Z-score was 0.36 [interquartile range (IQR), −0.5 to 1.2]. Of the participants, 45,228 were overweight (12.3%) overweight and 61,356 were obese (16.7%). The median BMI Z-score was greater in the obese category in 2009 to 2013 compared with 1994 to 1998 (2.3; IQR, 1.9 to 2.7; vs 2.2; IQR, 1.9 to 2.7; $P < 0.01$). For the overweight category, no statistically significant increase was observed ($P = 0.2$).

B. Incidence and Trends for Type 2 and Type 1 Diabetes

A total of 654 incident cases of type 2 diabetes and 1318 incident cases of type 1 diabetes were found. The incidence of both type 2 and type 1 diabetes increased from 1994 to 2013 (Fig. 1).
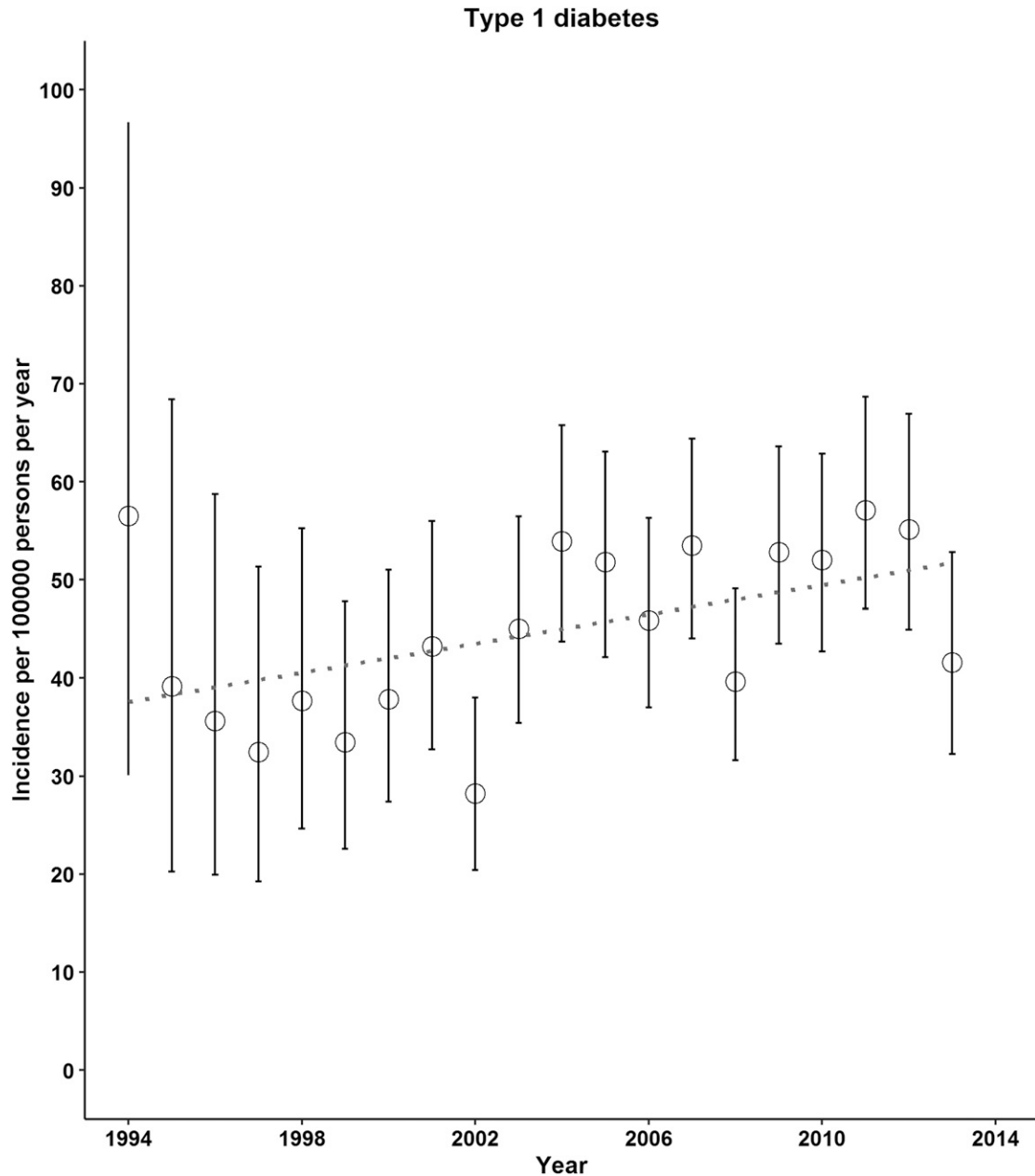
Figure 1. Incidence of type 2 and type 1 diabetes in UK children and young adults, 1994 to 2013. In 1997 and 2010, the diagnostic criteria for diabetes was changed (use of fasting plasma glucose ≥126 mg/dL or HbA1c ≥6.5%, respectively).

The mean time lag between the BMI records as exposure and the date of diabetes diagnosis was 0.4 year (IQR, −1.5 to 4.5 years). From 1994 to 1998 through 2009 to 2013, the incidence of type 2 diabetes per 100,000 persons per year increased from 6.4 (95% CI, 3.5 to 10.7) to 33.2 (95% CI, 29.7 to 37.1; P for trend < 0.01; Table 1). We also observed increases in the incidence of type 1 diabetes across 5-year calendar periods: from 38.2 (95% CI, 30.4 to 47.2) in 1994 to 1998 to 52.1 (95% CI, 47.6 to 56.9) in 2009 to 2013 per 100,000 persons per year (P for trend < 0.01; Table 1). Increasing trends in type 2 diabetes incidence were observed for both sexes, for both children and young adults, and for those who were overweight or obese (Table 1). The incidence of type 1 diabetes continued to increase for those aged ≤15 years; however, this trend was evident for females and those with a normal BMI only (Table 1).
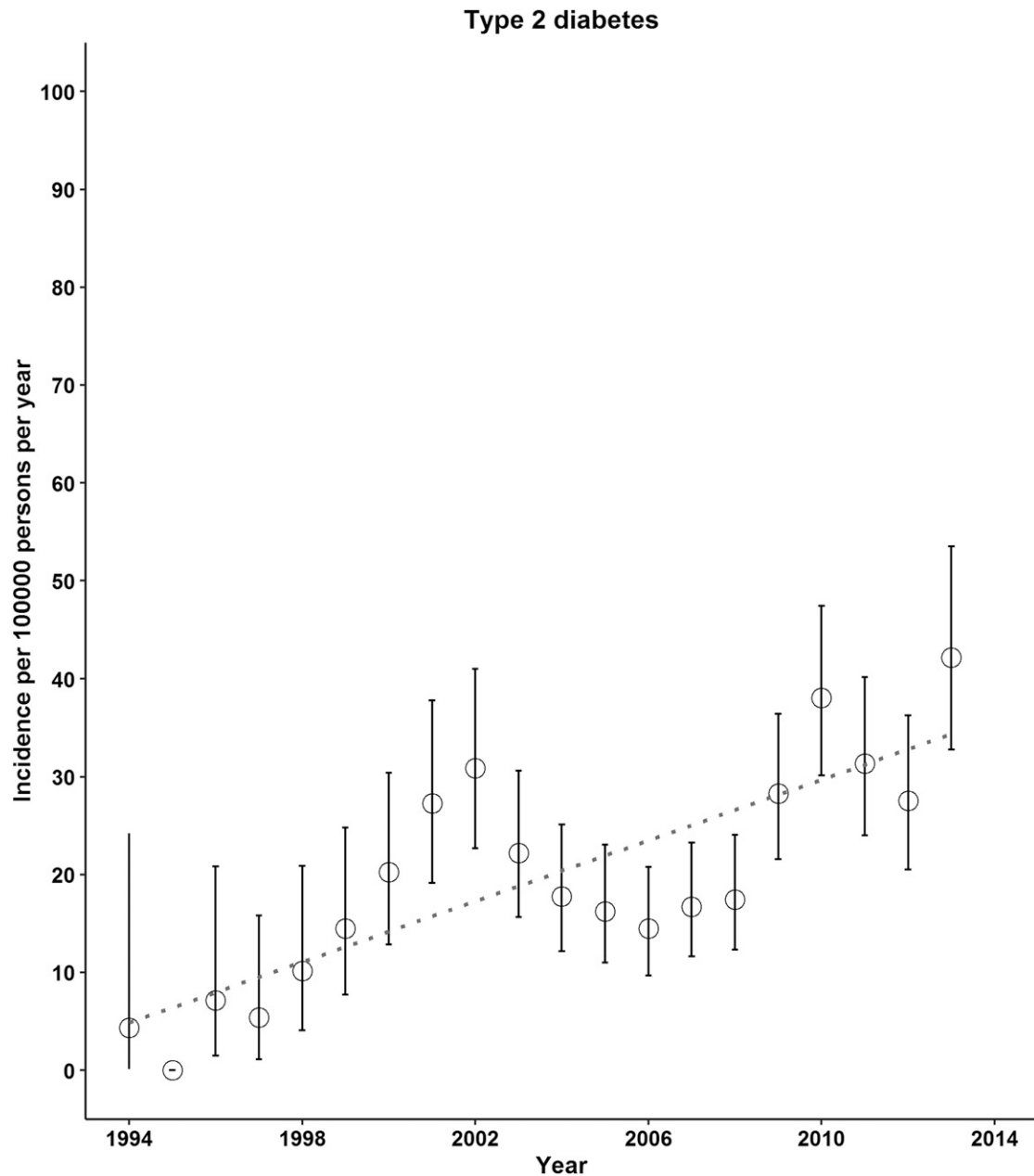
Type 2 diabetes

Figure 1. (Continued)

C. Incidence Rate and Risk Ratios

The increase in diabetes risk with time was evaluated using IRRs from Poisson regression models. The adjusted IRRs for type 2 diabetes for 2004 to 2008 or 2009 to 2013 were 1.7 to 3.3 times as high as the rate in 1994 to 1998. For type 1 diabetes, the rates were significantly greater in 2004 to 2008 or 2009 to 2013 compared with the rate in 1994 to 1998 (adjusted IRRs, 1.5 or 2.0; Table 2). The incidence rate of type 2 diabetes was greater in females, but type 1 diabetes was greater in males. The incidence of type 2 diabetes was more evident in those aged 11 to 15 years and in those aged >15 years compared with children aged <5 years. In contrast, the type 1 diabetes incidence decreased with age (adjusted IRR, 0.83 for those aged 11 to 15 years and 0.2 for those aged >15 years compared with those aged <5 years; Table 2). The incidence of type 2 diabetes showed an increase in overweight or obese during 1994 to 2013,

Table 1.   Incidence (Rates per 100,000 Persons per Year) of Type 2 and Type 1 Diabetes in UK Children and Young Adults, 1994 to 2013

Variable	1994–1998		1999–2003		2004–2008		2009–2013		P Value for Trend
	Cases	IR (95% CI)	Cases	IR (95% CI)	Cases	IR (95% CI)	Cases	IR (95% CI)	
Type 2 diabetes									
Total	14	6.4 (3.5–10.7)	156	23.9 (20.3–27.9)	164	16.5 (14.1–19.3)	320	33.2 (29.7–37.1)	< 0.01
Sex									
Female	7	6.3 (2.5–13)	89	27.1 (21.8–33.4)	90	18.3 (14.8–22.5)	206	43.9 (38.1–50.3)	< 0.01
Male	7	6.4 (2.6–13.2)	67	20.6 (15.9–26.1)	74	14.7 (11.6–18.5)	114	23.1 (19–27.7)	< 0.01
Age group, y									
≤15	11	5.4 (2.7–9.6)	89	16 (12.8–19.7)	86	11.6 (9.3–14.3)	149	25.6 (21.7–30.1)	< 0.01
16–25	3	19.9 (4.1–58.2)	67	69.2 (53.6–87.9)	78	31 (24.5–38.6)	171	44.8 (38.4–52.1)	0.43
BMI category[a]									
Normal	12	7.6 (3.9–13.2)	99	21.3 (17.3–25.9)	55	7.9 (5.9–10.2)	119	17.6 (14.6–21)	0.48
Overweight	0	0 (0–14)	12	15.3 (7.9–26.7)	22	18.2 (11.4–27.5)	27	22.8 (15–33.2)	0.01
Obese	2	5.7 (0.7–20.5)	45	40.9 (29.9–54.8)	87	50.7 (40.6–62.6)	174	103.3 (88.5–119.9)	< 0.01
Type 1 diabetes									
Total	84	38.2 (30.4–47.2)	248	37.9 (33.3–42.9)	484	48.8 (44.5–53.3)	502	52.1 (47.6–56.9)	< 0.01
Sex									
Female	36	32.5 (22.8–45)	110	33.5 (27.6–40.4)	208	42.4 (36.8–48.6)	238	50.7 (44.5–57.6)	< 0.01
Male	48	43.8 (32.3–58.1)	138	42.4 (35.6–50)	276	55 (48.7–61.9)	264	53.5 (47.2–60.3)	0.03
Age group, y									
≤15	81	39.5 (31.4–49.1)	237	42.5 (37.3–48.3)	451	60.9 (55.4–66.8)	434	74.6 (67.7–81.9)	< 0.01
16–25	3	19.9 (4.1–58.2)	11	11.4 (5.7–20.3)	33	13.1 (9–18.4)	68	17.8 (13.8–22.6)	0.15
BMI category[a]									
Normal	57	36 (27.2–46.6)	170	36.5 (31.2–42.4)	346	49.4 (44.4–54.9)	365	53.9 (48.5–59.8)	< 0.01
Overweight	18	68.4 (40.6–108.2)	41	52.2 (37.4–70.7)	80	66.1 (52.4–82.3)	62	52.4 (40.2–67.2)	0.58
Obese	9	25.5 (11.7–48.4)	37	33.7 (23.7–46.4)	58	33.8 (25.7–43.7)	75	44.5 (35–55.8)	0.046

Abbreviation: IR, incidence rate.

[a]Normal weight defined as BMI Z-score <1.04 (<85th percentile of growth chart); overweight, BMI Z-score of 1.04–1.64 (85th–95th percentile); obese, BMI Z-score >1.64 (>95th percentile) of 1990 reference population.

and the type 1 diabetes incidence increased gradually in those with normal BMI (Fig. 2). For type 2 diabetes, obese individuals had significantly greater incidence rates than those with a normal BMI (adjusted IRR, 4.3; 95% CI, 3.7 to 5.1; Table 2). We refitted models with two-way interaction terms for BMI categories to assess effect modification by sex, age, and period. Higher rates of type 2 diabetes with obesity were noted in those aged 11 to 15 years and in the last two periods ($P < 0.01$ for interaction; Supplemental Fig. 3). We observed no similar associations between the BMI categories and type 1 diabetes (Table 2).

The ORs, which approximate the relative risks in the nested case-control analysis, are listed in Table 3 [27]. We observed that obese individuals constituted 47.1% (n = 308 of 654) of type 2 diabetes cases and had approximately four times the risk of incident type 2 diabetes as those with a normal BMI (OR, 3.7; 95% CI, 3.1 to 4.6; Table 3). Overweight and obesity were not similarly associated with type 1 diabetes (Table 2). We observed no association between obesity and incident type 1 diabetes in analyses limited to diabetes cases assigned after BMI records as exposure (Supplemental Table 1). The age-adjusted OR was 4.0 (95% CI, 2.9 to 5.3) for type 2 diabetes when comparing the top quintile and the bottom quintile of the BMI Z-score (Supplemental Table 2). With BMI as a continuous variable, we observed an OR of 1.6 (95% CI, 1.5 to 1.7) per 1-SD increase in BMI Z-score. BMI was positively associated with type 1 diabetes at the middle range of BMI, and the association was nonsignificant for the top quintile vs the bottom quintile (Supplemental Table 2). The corresponding OR per 1-SD increase in BMI was not statistically significant (age-adjusted OR, 1.01; 95% CI, 0.96 to 1.05).

3. Discussion

The present large cohort study was based on primary care electronic health records. Our results showed that the incidence of both type 1 and type 2 diabetes has been increasing among UK children and young adults from 1994 to 2013. A greater incidence (fourfold) of type

Table 2. Incidence Rate Ratio for Type 2 and Type 1 Diabetes According to Sex, Age, BMI, and Period Categories in UK Children and Young Adults, 1994 to 2013

Variable	Unadjusted IRR (95% CI)	*P* Value	Adjusted IRR[a] (95% CI)	*P* Value
Type 2 diabetes				
Sex				
Male	Reference		Reference	
Female	1.5 (1.3–1.8)	< 0.01	1.5 (1.3–1.8)	< 0.01
Age group, y				
≤5	Reference		Reference	
6–10	1.2 (0.8–1.7)	0.36	1.1 (0.8–1.6)	0.65
11–15	2.8 (2.0–3.9)	< 0.01	2.3 (1.6–3.2)	< 0.01
16–25	4.8 (3.4–6.6)	< 0.01	4.7 (3.3–6.6)	< 0.01
BMI category[b]				
Normal	Reference		Reference	
Overweight	1.2 (0.9–1.6)	0.13	1.2 (0.9–1.6)	0.17
Obese	4.5 (3.8–5.2)	< 0.01	4.3 (3.7–5.1)	< 0.01
Period				
1994–1998	Reference	-	Reference	-
1999–2003	3.8 (2.2–6.5)	< 0.01	3.0 (1.7–5.1)	< 0.01
2004–2008	2.6 (1.5–4.5)	< 0.01	1.7 (1.0–3.0)	0.06
2009–2013	5.2 (3.1–8.9)	< 0.01	3.3 (1.9–5.8)	< 0.01
Type 1 diabetes				
Sex				
Male	Reference	-	Reference	-
Female	0.8 (0.8–0.9)	< 0.01	0.8 (0.8–0.9)	< 0.01
Age group, y				
≤5	Reference		Reference	
6–10	1.1 (0.9–1.2)	0.46	1.0 (0.8–1.1)	0.70
11–15	0.9 (0.8–1.1)	0.39	0.8 (0.7–1.0)	0.02
16–25	0.3 (0.2–0.3)	< 0.01	0.2 (0.2–0.3)	< 0.01
BMI category[b]				
Normal	Reference	-	Reference	-
Overweight	1.3 (1.1–1.5)	< 0.01	1.3 (1.1–1.5)	< 0.01
Obese	0.8 (0.7–0.9)	< 0.01	0.8 (0.7–0.9)	< 0.01
Period				
1994–1998	Reference		Reference	
1999–2003	1.0 (0.8–1.3)	0.96	1.0 (0.8–1.3)	0.79
2004–2008	1.3 (1.0–1.6)	0.03	1.5 (1.2–1.9)	< 0.01
2009–2013	1.4 (1.1–1.7)	< 0.01	2.0 (1.6–2.5)	< 0.01

[a]Model was adjusted for present age, sex, BMI and period.
[b]Normal weight was defined as BMI Z-score <1.04 (<85th percentile of growth chart); overweight, BMI Z-score 1.04–1.64 (85th–95th percentile); and obese, BMI Z-score >1.64 (>95th percentile) of 1990 reference population.

2 diabetes was observed in obese (constituting about one-half of cases). Given that no linear association was found between the BMI and the incidence of type 1 diabetes and that a higher BMI was not associated with type 1 diabetes when analyzing only those individuals with a BMI value before the date of diabetes diagnosis, further work is needed to replicate our observational evidence from children and young adults.

Diabetes increasingly imposes a large burden on health and society worldwide, as indicated by estimates that 1 in 11 adults have type 2 diabetes (415 million people) and >0.5 million children (aged ≤14 years) had type 1 diabetes in 2015 [28–30]. Understanding the temporal trends and incidence of diabetes and the modifiable factors is paramount to providing timely prevention or delaying the occurrence of diabetes during the life course [31]. Previous work has mainly reported the burden and incidence of type 1 diabetes in children [32, 33]. Little evidence is available concerning type 2 diabetes and little is known about the potential association of obesity with either type 1 or type 2 diabetes in children and young adults [30, 34]. The SEARCH study for the 2002 to 2003 period has reported that type 2 diabetes in youth is predominantly occurring in higher risk ethnic groups, accounting for 14.9% of all diabetes
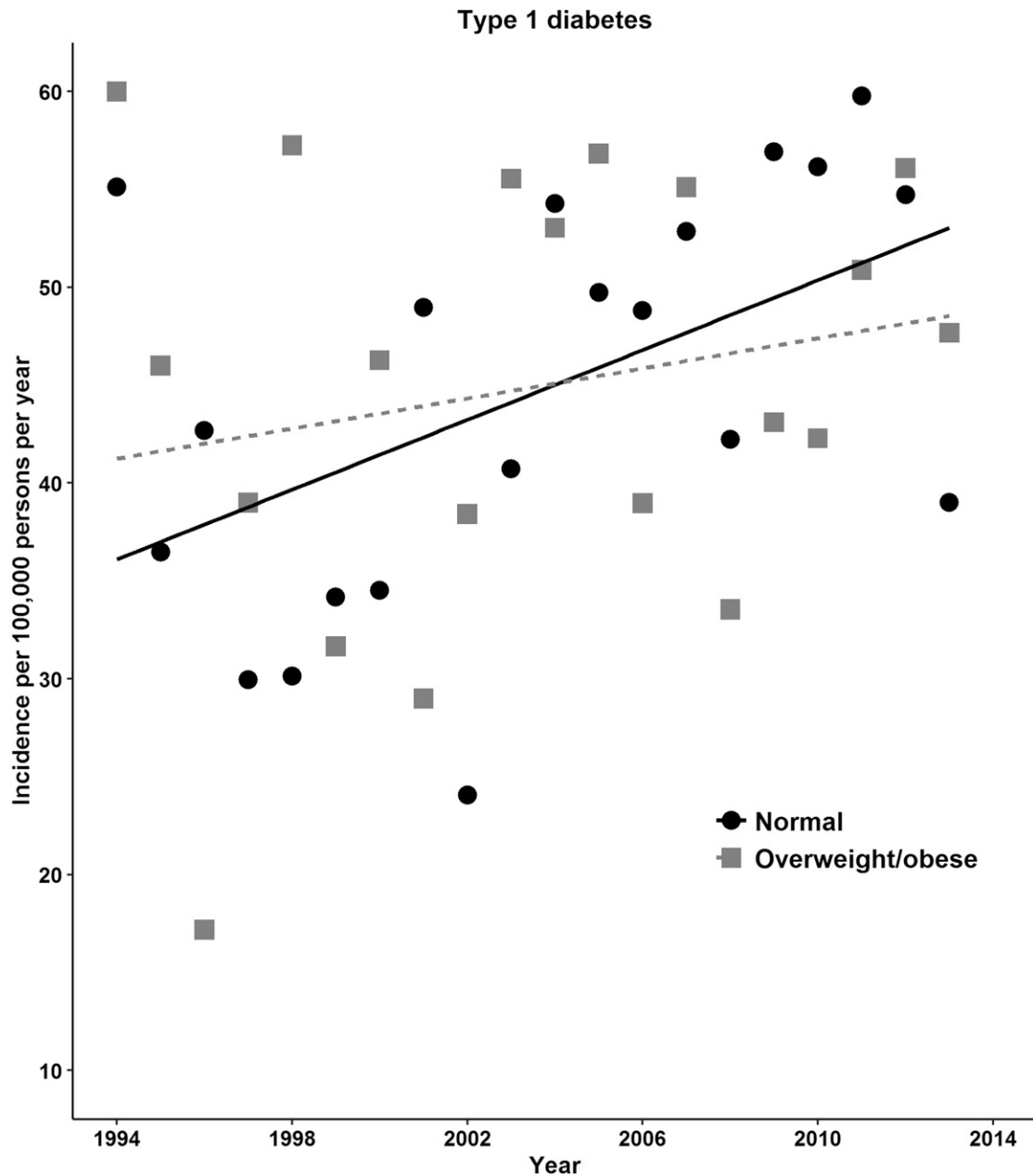
Figure 2. Incidence of type 2 and type 1 diabetes in UK children and young adults according to BMI category, 1994 to 2013.

cases among non-Hispanic white adolescents aged ≥10 years (incidence rates ranged from 5.6 among whites to 49.4 per 100,000 persons per year among Native Americans) [35]. Other studies, which were mainly conducted 10 years earlier in Europe, reported type 2 diabetes as an uncommon condition in white young populations or showed no trend [34, 36]. A prospective surveillance UK study in 2004 to 2005 reported 67 cases of type 2 diabetes of all 363 diabetes diagnoses based on notification by pediatricians in children aged ≤17 years [37]. Using CPRD data, another study analyzing the data from 0.5 million children aged 0 to 18 years showed an eightfold increase in the prevalence of oral antidiabetic drugs, from 0.6 per 100,000 children in 1998 to 5 per 100,000 children in 2005 [38]. A relative risk for incident type 2 diabetes has been estimated as approximately twice as large per 1-SD difference in BMI in European adults. Recently, a longitudinal study showed an association between adolescent BMI and incident
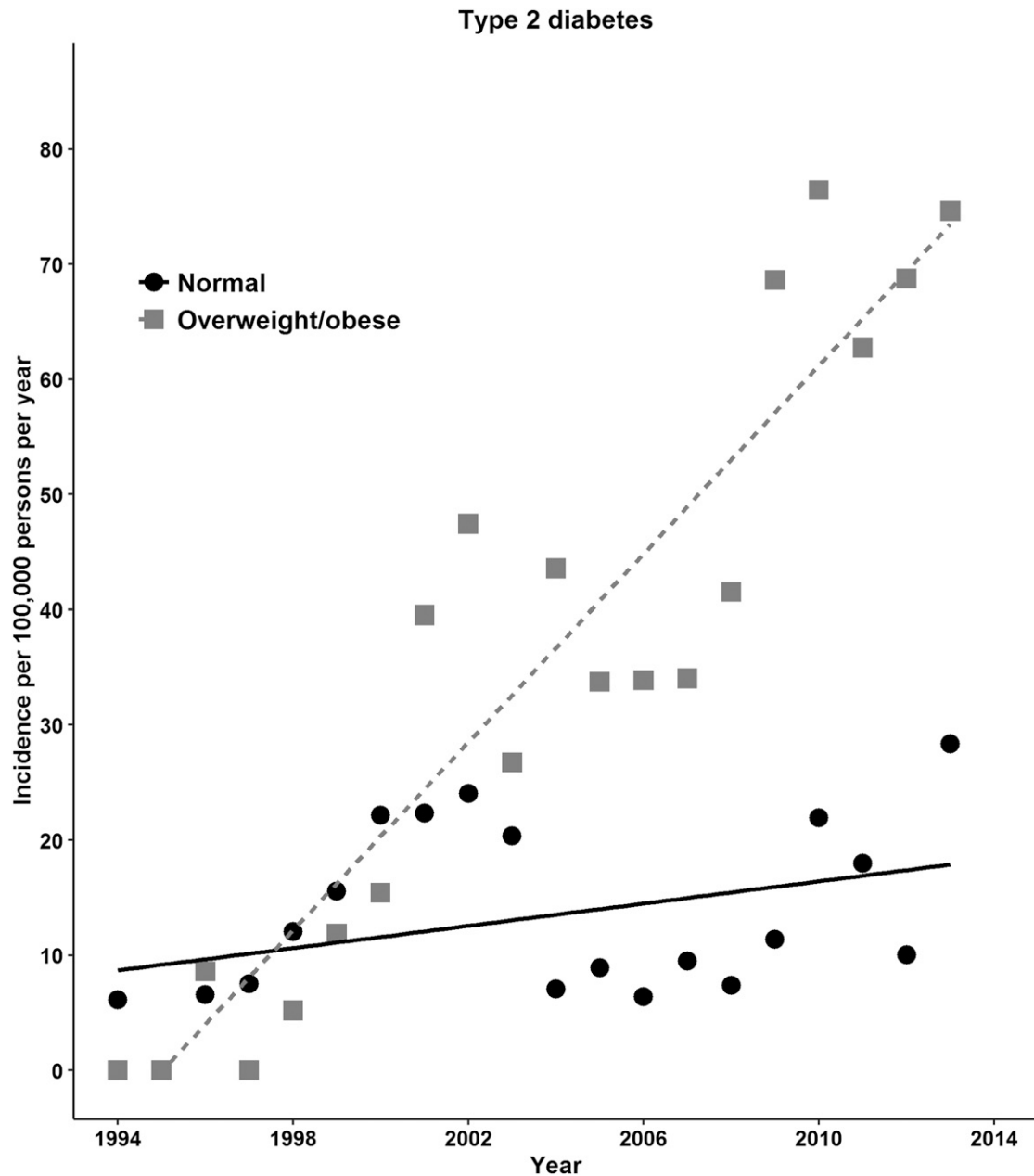
Type 2 diabetes

Figure 2. (Continued)

diabetes in adults, which was not independent of the adult BMI [30]. Another study in Finland showed a link between a change in childhood BMI and type 2 diabetes in adults [39].

We add to previous observational evidence that childhood or adolescent obesity is associated with an increase in the incidence of type 2 diabetes (but not type 1) in children and young adults. Moreover, increases in type 2 diabetes incidence by obese category were greater among those aged 11 to 15 years and in the last two calendar periods. This pattern is consistent with increased BMI values during the period in the obese category. Although our estimates were greater than those previously reported in white populations, similar data are lacking, in terms of time period and observational setting, to judge recent estimates of type 2 diabetes incidence. We observed that most children and young adults with type 2 diabetes were overweight or obese, in line with the results of the surveillance UK study [37]. Moreover,

Table 3. Odds Ratios for Type 2 and Type 1 Diabetes According to BMI Categories in UK Children and Young Adults, 1994 to 2013

Variable	Cases	Controls	Unadjusted Model OR (95% CI)	P Value	Adjusted Model[a] OR (95% CI)	P Value
Type 2 diabetes	654	8589				
Normal BMI	285	5996	Reference		Reference	
Overweight	61	1028	1.3 (0.9–1.7)	0.13	1.3 (0.9–1.8)	0.12
Obese	308	1565	3.9 (3.2–4.8)	< 0.01	3.8 (3.1–4.6)	< 0.01
Type 1 diabetes	1318	8589				
Normal BMI	938	5996	Reference		Reference	
Overweight	201	1028	1.3 (1.1–1.5)	< 0.01	1.3 (1.0–1.5)	0.02
Obese	179	1565	0.8 (0.6–0.9)	< 0.01	0.7 (0.6–0.8)	< 0.01

[a]Model adjusted for age at BMI and weight or height records in the UK CRPD.

we estimated that obese children and young adults have approximately four times the risk of incident type 2 diabetes as those with a normal BMI.

Our finding of the increasing incidence of type 1 diabetes in those aged ≤15 years is consistent with previous studies from population-based or primary care data. Although estimates have varied across populations and time, temporal trends have shown an increasing diabetes incidence in children and young adults from the 1990s through the 2000s and beyond [16, 32–37, 40–42]. We, and others, have shown that the incidence of childhood type 1 diabetes has increased during recent decades [32, 38, 40, 42]. Similar to these studies, we observed that the type 1 diabetes incidence continued to increase in female individuals and those aged ≤15 years from 1994 to 2013. However, our study, and other studies in Europe, has shown that the incidence of type 1 diabetes is somewhat greater in male than in female individuals [32]. Although both genetic and environmental factors have been proposed in the etiology of type 1 diabetes, the reason for the increase in type 1 diabetes incidence is unknown. Obviously, the improved survival in children with type 1 diabetes and the potential for successful reproduction are contributors to this increase [32]. No linear association was found between BMI and the incidence of type 1 diabetes in our study. However, we observed a greater incidence among overweight children but a lower incidence among obese children. The results of a few cohort or case-control studies have suggested that weight in the first year of life is positively associated with type 1 diabetes. However, observational evidence for an association between BMI and type 1 diabetes has varied [15]. Given that the autoimmune response encoded by the HLA class genes strongly contributes to the etiology of type 1 diabetes, questions exist regarding whether early life obesity might have a biologically beneficial effect on type 1 diabetes risk later in life [43]. Apart from this, it is plausible that disease-related weight loss or a selection bias might account for an apparently paradoxical association between obesity and type 1 diabetes in our observational study [44].

Taken together, we have updated observational evidence that the rate of type 2 diabetes incidence, although less common than type 1, is increasing among UK children and young adults in parallel with the increasing childhood obesity during the past decades [1, 30, 31, 45]. Our observational findings support the use of a real world practice database to broadly estimate the risks and rates of major global health issues, such as incident diabetes in children. Such evidence can also extend our understanding of disease burden and temporal trends beyond surveillance from the secondary-care pediatric setting and traditional cohorts, which have usually included a limited size and select population [46]. Our results will add value to the research that informs policy makers to identify emerging health care needs and how to prioritize future clinical studies for targeted management of childhood obesity and diabetes. Children with type 2 diabetes potentially have related disorders such as dyslipidemia and hypertension [37, 47]. Given the age of onset, it seems that childhood diabetes is more severe than diabetes in adults. Also, the effects of diabetes-related outcomes on health and society will be greater throughout the life course [2, 48].

The present study had certain limitations. First, data on BMI, height, and weight were not available for all individuals in the CPRD. It is possible that children had their weight and height recorded not as a part of routine practice and that a general practitioner in primary care had decided to measure BMI because of the child's high weight or health status [21]. In the CPRD, the method of height and weight measurements (*e.g.,* shoes on or off) and the quality of data collected might be varied in each practice; however, such variance can be random, and power can be maintained by the large numbers. Therefore, a potential for selection bias exists that one cannot completely rule out in clinical or observational research, and randomness remains an assumption [21]. Previous studies using the CPRD suggested the consistency of results obtained from primary care data with those from cohort observations and that up-to-date BMI values and obesity prevalence in CPRD were as close as population-based survey data [21, 22]. Furthermore, the magnitude and direction of associations of demographic information and BMI with diabetes types, which were observed in our study, are consistent with those reported in published studies. We also observed similar results when only data on the BMI records before the date of a diabetes diagnosis were used as a sensitivity analysis. As previously reported, most (~77%) children contributed one BMI observation to the CPRD [6]. It also seems plausible that the incidence of diabetes could have been artificially increased, because we used a single measure of BMI to constitute exposure. However, completeness of the BMI data in the CPRD did not fundamentally vary over time among children and young adults from 1994 through 2011 [22], reducing the probability that our results occurred by chance. Although important questions remain regarding how the BMI trajectory measured early in childhood might contribute to the development of type 2 diabetes [31], we did not have enough information about the BMI trend between the time point the BMI was measured and the onset date of diabetes in our study. Second, we used data from clinical cases, prescriptions for diabetes drugs, and HbA1c tests. Nevertheless, we could have missed false-negative cases in the remainder of the CPRD, because diabetes, in particular, type 2 diabetes, can remain undiagnosed for several months to years [29]. Given the large size of the CPRD cohort, combined with the low incidence of type 2 diabetes among children and young adults, we would not expect this to have largely affected our findings [16, 20, 22, 29, 35, 36]. Although we applied some strict criteria for the definition of diabetes types and some misclassification of outcomes or the onset date of diabetes is inevitable, the effect on our estimates was likely small [21]. Other limitations included that the present study could not provide information on autoantibodies for type 1 diabetes, physical activity, puberty effect on changes in the BMI, and the extent of glycemia control. Finally, generalization of these findings is limited, because the data in the UK CPRD are predominantly from those of European ancestry.

In conclusion, the incidence of type 1 and type 2 diabetes among UK children and young adults continued to increase from 1994 to 2013 in both sexes and in those aged ≤15 years. An increasing trend in the incidence of type 2 diabetes was more evident among the overweight and obese. The incidence of type 2 diabetes was four times as high among obese individuals (constituting about one-half of cases) as among those with a normal BMI. No linear association was found between the childhood BMI and the incidence of type 1 diabetes. Further work is needed to explore potential targets for the prevention of childhood obesity and early-onset type 2 diabetes.

Acknowledgments

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