# Prevalence of Celiac Disease in 52,721 Youth With Type 1 Diabetes: International Comparison Across Three Continents

*Diabetes Care 2017;40:1034–1040 | https://doi.org/10.2337/dc16-2508*

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## OBJECTIVE

**Celiac disease (CD) has a recognized association with type 1 diabetes. We examined international differences in CD prevalence and clinical characteristics of youth with coexisting type 1 diabetes and CD versus type 1 diabetes only.**

## RESEARCH DESIGN AND METHODS

**Data sources were as follows: the Prospective Diabetes Follow-up Registry (DPV) (Germany/Austria); the T1D Exchange Clinic Network (T1DX) (U.S.); the National Paediatric Diabetes Audit (NPDA) (U.K. [England/Wales]); and the Australasian Diabetes Data Network (ADDN) (Australia). The analysis included 52,721 youths <18 years of age with a clinic visit between April 2013 and March 2014. Multivariable linear and logistic regression models were constructed to analyze the relationship between outcomes ($HbA_{1c}$, height SD score [SDS], overweight/obesity) and type 1 diabetes/CD versus type 1 diabetes, adjusting for sex, age, and diabetes duration.**

## RESULTS

**Biopsy-confirmed CD was present in 1,835 youths (3.5%) and was diagnosed at a median age of 8.1 years (interquartile range 5.3–11.2 years). Diabetes duration at CD diagnosis was <1 year in 37% of youths, >1–2 years in 18% of youths, >3–5 years in 23% of youths, and >5 years in 17% of youths. CD prevalence ranged from 1.9% in the T1DX to 7.7% in the ADDN and was higher in girls than boys (4.3% vs. 2.7%, $P < 0.001$). Children with coexisting CD were younger at diabetes diagnosis compared with those with type 1 diabetes only (5.4 vs. 7.0 years of age, $P < 0.001$) and fewer were nonwhite (15 vs. 18%, $P < 0.001$). Height SDS was lower in those with CD (0.36 vs. 0.48, adjusted $P < 0.001$) and fewer were overweight/obese (34 vs. 37%, adjusted $P < 0.001$), whereas mean $HbA_{1c}$ values were comparable: 8.3 ± 1.5% (67 ± 17 mmol/mol) versus 8.4 ± 1.6% (68 ± 17 mmol/mol).**

## CONCLUSIONS

**CD is a common comorbidity in youth with type 1 diabetes. Differences in CD prevalence may reflect international variation in screening and diagnostic practices, and/or CD risk. Although glycemic control was not different, the lower height SDS supports close monitoring of growth and nutrition in this population.**



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The prevalence of celiac disease (CD) is higher in patients with type 1 diabetes compared with the general population (~5% vs. 1%) (1,2). However, case detection is likely to reflect screening practices within the type 1 diabetes population (3) and in at-risk cohorts (4), since the majority of case patients are asymptomatic at diagnosis. There is some evidence for a greater risk in association with type 1 diabetes diagnosed before the age of 5 years and European heritage (1). Conflicting data exist as to whether the risk of CD is higher in females or males with type 1 diabetes (1), which is in contrast to the general population where no sex bias is observed in children but there is a female sex bias in adults (5).

The burden of coexisting CD and type 1 diabetes may be expected to negatively impact glycemic control, although existing data are conflicting. Although several studies have shown no difference in glycemic control among people with type 1 diabetes, with or without CD (6–8), the $HbA_{1c}$ level was lower in adolescents with both conditions, except in those who did not adhere to the gluten-free diet (9).

There are no multinational studies that have systematically compared clinical characteristics and treatment between youths with coexisting CD and type 1 diabetes and youths with type 1 diabetes only. We therefore analyzed registry and audit data from the following four large databases across three continents: the Prospective Diabetes Follow-up Registry (DPV) in Germany and Austria; the National Pediatric Diabetes Audit (NPDA) in the U.K. (England and Wales); the T1D Exchange Clinic Network (T1DX) in the U.S.; and the Australasian Diabetes Data Network (ADDN). These registries record data on the screening and diagnosis of CD, along with clinical and demographic data and therapy. Our aim was to examine international differences in prevalence and management to improve our understanding of the impact of both conditions.

## RESEARCH DESIGN AND METHODS

### Participants

This analysis included 52,721 participants <18 years of age with a diagnosis of type 1 diabetes, who had made at least one clinic visit between 1 April 2013 and 31 March 2014. The characteristics and methods of each of the four participating registries are described below.

#### *DPV*

The DPV is a prospective longitudinal standardized computer-based documentation system for demographics, medical care, and outcome of patients with all diabetes types (www.d-p-v.eu) (10). Currently, >90% of German and >80% of Austrian children with diabetes, from 442 centers, are included in the registry. Since 1995, data have been documented locally by the participating centers in an electronic health record. Twice yearly, anonymized data are exported and transmitted for central analyses and external quality assurance. Missing and inconsistent data are reported back to the centers for correction. Data collection is approved by the ethics committee at Ulm University and by the institutional review boards (IRBs) at the participating centers (11).

#### *NPDA*

The NPDA collects data on outcomes and care processes for children and young people in whom diabetes has been diagnosed who attend pediatric diabetes units (PDUs) in the U.K. (in England and Wales) (http://www.rcpch.ac.uk/npda) (12). Each PDU submits data annually to the NPDA. A total of 177 PDUs from England and Wales submitted data during the study period. The Royal College of Pediatrics and Child Health, which delivers the NPDA, has ethical approval to collect and hold patient information for the NPDA without written consent. However, patients and their parents are informed of the submission of their data to the NPDA by the local PDUs. Data were pseudonomized for the purposes of this study.

#### *T1DX*

The T1DX includes 77 U.S.-based pediatric and adult endocrinology practices in 35 states. This registry of >30,000 individuals with type 1 diabetes commenced enrollment in September 2010 (13). Each clinic received approval from a local IRB. Informed consent was obtained according to IRB requirements. Data were collected for the central database of the registry from the participant's medical record and by having the participant or the participant's parent complete a comprehensive questionnaire, as previously described (14). This analysis included youth <18 years of age from the 52 registry sites caring for pediatric patients. All participating centers are listed at https://t1dexchange.org/pages/resources/clinic-network/#4/37.16/-96.33.

#### *ADDN*

The ADDN is a longitudinal centralized, standardized data collection system for patients with all diabetes types, which commenced enrollment in 2012 (15). Data are documented locally by the participating centers in an electronic database, and anonymized data are transferred twice yearly to the central database. Missing and inconsistent data are reported back to the centers for correction. Currently, the database contains longitudinal data on >5,000 children and adolescents with diabetes from five sites in Australia (16). Each participating center received approval from its local IRB, and informed consent was obtained according to IRB requirements.

### Study Measures

The main study measure was the rate of CD among participants with type 1 diabetes. Screening for CD was performed according to local practices, in keeping with the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines, which recommend screening at the time of diabetes diagnosis and every 1–2 years thereafter (17). CD was defined based on biopsy-proven results, in keeping with past and recent ISPAD guidelines (17,18). "Suspected CD" was defined as a positive CD screening result without small bowel biopsy.

Individual mean $HbA_{1c}$ values over the year of the registry assessment were used to represent $HbA_{1c}$ in this analysis. $HbA_{1c}$ values were standardized using values from the Diabetes Control and

*Received 1 December 2016 and accepted 23 April 2017.*

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*This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc16-2508/-/DC1.*

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**A listing of information for the ADDN, the T1DX, the NPDA, and the DPV initiative can be found in the Supplementary Data online.*

Complications Trial (DCCT) (19). Any use of a pump during the observation period was categorized as pump use; otherwise, patients were categorized as using injections. BMI was calculated from height and weight; *z* scores for height and BMI, adjusted for age and sex, were computed using the World Health Organization (WHO) reference tables (20,21). Overweight and obesity were defined according to the WHO as BMI *z* scores >1 SD and 2 SDs, respectively (21). Severe hypoglycemia was defined as an event in which the participant experienced a seizure or loss of consciousness.

Ethnic minority status for the DPV was defined as at least one parent born outside of Germany or Austria (positive migration history). Ethnicity data for England and Wales was reported to the NPDA by the participating center. This is a self-reported ethnicity by the patient and the patient's family using a list of contemporary ethnic categories (white, black, Asian, mixed, other, or not stated). Minority status was defined as nonwhite, with "not stated" being excluded as missing data. For the T1DX, ethnic minority status was defined as other than non-Hispanic white. For the ADDN, ethnicity was defined according to the Australian Standard Classification of Cultural and Ethnic Groups (22), and ethnic minority status was defined as other than white.

### Statistical Analysis

Summary statistics were calculated overall, within registries, and by the presence or absence of CD. For continuous variables results are reported as the median (interquartile range) or mean ± SD for $HbA_{1c}$ and for dichotomous variables as the percentage. A Kruskal-Wallis or $\chi^2$ test was performed to compare demographic and clinical characteristics between registries and by the presence or absence of CD.

Linear regression was performed to assess the relationship between the presence of CD and continuous variables ($HbA_{1c}$, height SD score [SDS], BMI SDS, insulin dose per kilogram of body weight), with models adjusted for sex, age, and duration of diabetes. For insulin dose as an outcome, models were also adjusted for insulin pump therapy. For $HbA_{1c}$ as an outcome, additional models were constructed adjusting for ethnicity (minority vs. nonminority) or the interaction between ethnicity and CD. Logistic regression was performed to assess the relationship between the presence of CD and categorical variables ($HbA_{1c}$ <7.5% or >9.0%; insulin pump therapy; severe hypoglycemia), with models adjusted for sex, age, and duration of diabetes. For pump therapy and severe hypoglycemia outcomes, additional models were constructed adjusting for ethnicity or ethnicity/CD interaction.

All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Inc., Cary, NC). A priori, in view of the large sample size and multiple comparisons, only *P* values <0.01 were considered to be statistically significant.

## RESULTS

Clinical characteristics including age at diabetes diagnosis and age at visit were similar across the four registries despite statistical significance due to the large sample size (Table 1). Median diabetes duration ranged from 3.8 years in the DPV to 6.0 years in the T1DX. Ethnic minority status ranged from 12.2% in the NPDA to 31.7% in the ADDN. Median height SDS was 0.47, and median BMI SDS was 0.67, indicating that participants overall were heavier and taller compared with reference standards. The proportion of overweight/obesity was highest in the T1DX (44%) and lowest in the DPV (33%). Mean $HbA_{1c}$ was lowest in the DPV (7.9% [63 mmol/mol]) and highest in the NPDA (8.9% [74 mmol/mol]). The DPV, T1DX, and ADDN had higher rates of pump use (43.0%, 60.5%, and 40.1%, respectively) compared with the NPDA (17.7%), Table 1.

Biopsy-proven CD was present in 1,835 participants (3.5%), with a higher prevalence in girls than in boys (4.3 vs. 2.7%, $P < 0.001$) and in those <5 versus ≥5 years of age at diabetes diagnosis (4.8%

**Table 1—Descriptive characteristics of patients overall and by registry**

| | Overall (*N* = 52,721) | DPV (*n* = 24,611) | T1DX (*n* = 7,536) | NPDA (*n* = 17,152) | ADDN (*n* = 3,422) | *P* value |
|---|---|---|---|---|---|---|
| Male | 52.3 | 52.5 | 52.1 | 52.1 | 51.7 | 0.692 |
| Age at visit (years) | 13.2 [10.0–15.7] | 12.8 [9.4–15.4] | 13.0 [10.0–15.0] | 14.1 [11.0–16.2] | 12.9 [9.6–15.3] | <0.001 |
| Age at diabetes diagnosis (years) | 7.0 [4.0–10.2] | 7.3 [4.2–10.6] | 6.0 [3.0–9.0] | 7.0 [3.8–10.1] | 6.9 [4.0–0.1] | <0.001 |
| Diabetes duration at visit (years) | 4.9 [2.6–7.9] | 3.8 [1.5–7.0] | 6.0 [3.0–8.0] | 5.7 [3.6–8.6] | 4.3 [1.9–7.5] | <0.001 |
| Ethnic minority | 18.2 | 20.4 | 20.9 | 12.2 | 31.7 | <0.001 |
| Height SDS WHO | 0.47 [−0.23 to 1.18] | 0.58 [−0.10 to 1.26] | 0.48 [−0.24 to 1.24] | 0.30 [−0.41 to 1.01] | 0.47 [−0.22 to 1.15] | <0.001 |
| BMI SDS WHO | 0.67 [−0.01 to 1.36] | 0.57 [−0.11–1.25] | 0.86 [0.24–1.53] | 0.71 [0.01–1.39] | 0.82 [0.13–1.49] | <0.001 |
| Overweight/obese | 37.0 | 33.1 | 44.2 | 38.6 | 42.5 | <0.001 |
| Mean $HbA_{1c}$ | | | | | | |
| % | 8.4 ± 1.6 | 7.9 ± 1.5 | 8.7 ± 1.5 | 8.9 ± 1.6 | 8.2 ± 1.4 | <0.001 |
| mmol/mol | 67.9 ± 17.5 | 62.8 ± 16.8 | 71.3 ± 16.5 | 73.8 ± 17.0 | 66.6 ± 15.3 | <0.001 |
| $HbA_{1c}$ | | | | | | |
| <7.5% (58 mmol/mol) | 30.5 | 45.8 | 18.0 | 14.3 | 29.1 | <0.001 |
| >9.0% (75 mmol/mol) | 26.4 | 17.0 | 30.5 | 39.0 | 22.1 | <0.001 |
| Insulin pump therapy | 37.0 | 43.0 | 60.5 | 17.7 | 40.1 | <0.001 |

Data are reported as percentages, median [interquartile range], or mean ± SD.

vs. 2.8%, $P < 0.001$). The ADDN had the highest prevalence of CD (7.7%) followed by the NPDA (3.8%), DPV (3.2%), and T1DX (1.9%). An additional 2% of patients (from the DPV and T1DX only) had a positive CD screen result without small bowel biopsy. The median age at diabetes diagnosis was younger in those participants with coexisting CD compared with those with type 1 diabetes alone (5.4 vs. 7.0 years of age, $P < 0.001$) (Table 2). Among participants with CD, the proportion from an ethnic minority group was lower overall compared with type 1 diabetes alone (15% vs. 18%, $P = 0.001$) in the T1DX ($P = 0.002$) and ADDN ($P = 0.002$) but not in the NPDA ($P = 0.04$) or DPV ($P = 0.53$). Youth with coexisting CD had a slightly lower height SDS (0.36 vs. 0.48, adjusted $P < 0.001$), after adjusting for age, sex, and diabetes duration (Table 2); the adjusted difference in height SDS was also significantly lower in the DPV ($P < 0.001$) and NPDA ($P = 0.003$) but not in the T1DX ($P = 0.06$) or ADDN ($P = 0.47$). When stratified by ethnic minority status, height SDS was lowest in nonwhite youth with CD compared with white youth without CD (0.17 vs. 0.50). The difference in BMI SDS overall (0.61 vs. 0.67, adjusted $P = 0.006$) was not clinically important, and the differences were not statistically significant across the individual registries after adjustment for age, sex, and diabetes duration. When stratified by ethnic minority status, BMI SDS was lowest in white youth with CD versus ethnic minority youth without CD (0.51 vs. 0.68, adjusted $P < 0.001$). The proportion of overweight/obesity was slightly lower overall for those with coexisting CD compared with type 1 diabetes alone (34% vs. 37%, adjusted $P < 0.001$) and in the DPV (27% vs. 33%, adjusted $P < 0.001$) but not in the other registries.

The characteristics of participants with CD by registry are shown in Table 3. Overall, CD was diagnosed in 5.4% of patients before the diagnosis of type 1 diabetes, in 37% of patients with diabetes duration of <1 year, in 18% of patients during year 2 of diabetes, in 23% of patients during years 3–5 of diabetes, and in 17% of patients after >5 years of diabetes. Despite differences in the rates of CD across registries, the median age at the diagnosis of CD was very similar (~8 years). $HbA_{1c}$ and the proportion of patients with $HbA_{1c}$ levels <7.5% or >9.0% did not differ clinically overall between those with coexisting type 1 diabetes and CD and those with type 1 diabetes alone (Table 2) or within individual registries when adjusted for age, sex, and duration of diabetes, with the exception of the DPV where the difference was statistically significant but not clinically important (7.8% vs. 7.9%, $P = 0.007$). In the multivariable linear regression model, $HbA_{1c}$ level was slightly higher in ethnic minority youth with type 1 diabetes alone (8.5% vs. 8.3%, adjusted $P < 0.001$) but did not differ between ethnicities among youth with type 1 diabetes and comorbid CD (8.3% vs. 8.3%, adjusted $P = 0.42$).

The proportion of patients treated with insulin pumps was significantly higher in those with CD in the T1DX (75% vs. 60%, adjusted $P = 0.003$) but did not differ overall (adjusted $P = 0.41$) or within the other registries. Among youth with CD, the proportion treated with continuous subcutaneous insulin infusion was lower for those of ethnicity minority status compared with white ethnicity (33% vs. 43%, adjusted $P < 0.001$); a lower rate of pump therapy was also observed in those with type 1 diabetes alone (nonwhite vs. white ethnicity 33% vs. 39%, adjusted $P < 0.001$). The insulin dose per kilogram of body weight was not clinically different in those with versus those without CD (0.80 vs. 0.82 units/kg/day, adjusted $P = 0.025$) (Table 2), and differences approached statistical significance for the DPV (0.78 vs. 0.80 units/kg/day, $P = 0.018$) and T1DX (0.78 vs. 0.85, $P = 0.05$).

## CONCLUSIONS

This analysis from four international registries spanning three continents demonstrates that CD is common in children

**Table 2—Characteristics of patients with type 1 diabetes with or without CD**

| | CD and type 1 diabetes ($n$ = 1,835) | Type 1 diabetes ($n$ = 50,886) | $P$ value |
|---|---|---|---|
| Male | 41.0 | 52.7 | <0.001 |
| Age at visit (years) | 12.8 [9.9–15.2] | 13.2 [10.0–15.7] | <0.001 |
| Age of diabetes diagnosis (years) | 5.4 [2.9–8.7] | 7.0 [4.0–10.2] | <0.001 |
| Age <5 years at diabetes onset | 45.6 | 32.8 | <0.001 |
| Diabetes duration at visit (years) | 5.7 [3.1–9.0] | 4.8 [2.5–7.8] | <0.001 |
| Ethnic minority | 15.0 | 18.3 | <0.001 |
| Height SDS | 0.36 [−0.40 to 1.05] | 0.48 [−0.23 to 1.18] | <0.001* |
| BMI SDS | 0.61 [−0.07 to 1.25] | 0.67 [−0.01 to 1.36] | 0.006* |
| Overweight/obese | 34.0 | 37.1 | <0.001* |
| Mean $HbA_{1c}$ | | | |
| % | 8.3 ± 1.5 | 8.4 ± 1.6 | 0.052* |
| mmol/mol | 67.4 ± 16.6 | 67.9 ± 17.5 | 0.052* |
| $HbA_{1c}$ | | | |
| <7.5% (58 mmol/mol) | 30.9 | 30.5 | 0.054* |
| >9.0% (75 mmol/mol) | 24.7 | 26.5 | 0.047* |
| Insulin pump therapy | 40.9 | 36.8 | 0.405* |
| Insulin dose (units/kg/day) | 0.80 [0.64–1.01] | 0.82 [0.65–1.02] | 0.025** |
| Number of SMBG/day | 5.5 [4.3–7.0] | 5.0 [4.0–7.0] | 0.016* |
| Severe hypoglycemia | 2.5 | 1.8 | 0.094* |

Data are reported as percentages, median [interquartile range], or mean ± SD. SMBG, self-monitoring of blood glucose. *$P$ values adjusted for age, sex, and diabetes duration. **$P$ value adjusted for age, sex, diabetes duration, and insulin pump use.

**Table 3—Characteristics of patients with CD by registry**

| | DPV (*n* = 785) | T1DX (*n* = 143) | NPDA (*n* = 645) | ADDN (*n* = 262) | *P* value |
|---|---|---|---|---|---|
| CD prevalence | 3.2 | 1.9 | 3.8 | 7.7 | <0.001 |
| CD diagnosed before diabetes | 6.3 | 3.5 | | 2.1 | 0.05 |
| CD diagnosed within 2 years of diabetes diagnosis | 55.9 | 31.6 | | 69.1 | <0.001 |
| Age at CD diagnosis (years) | 8.1 [5.3–11.2] | 8.0 [6.0–11.0] | | 8.0 [4.8–11.6] | 0.94 |
| Age <5 years at CD diagnosis | 21.9 | 17.5 | | 26.3 | 0.28 |
| Diabetes duration (years) | 5.2 [2.3–8.6] | 6.0 [4.0–9.0] | 6.4 [4.0–9.5] | 5.3 [2.8–8.8] | <0.001 |
| Male | 40.9 | 44.8 | 41.5 | 38.2 | 0.62 |
| Ethnic minority | 19.5 | 10.5 | 9.6 | 22.0 | <0.001 |
| Insulin pump therapy | 50.7 | 75.0 | 20.9 | 43.0 | <0.001 |
| Severe hypoglycemia | 1.7 | 2.1 | | 6.9 | <0.001 |

Data are reported as percentages or median [interquartile range].

with type 1 diabetes, with an overall prevalence of 3.5%. Rates varied across the registries, from 1.9% (T1DX) to 7.7% (ADDN). The prevalence of CD was higher in girls than in boys (4.3% vs. 2.9%), and the mean age at diabetes diagnosis was lower in those with coexisting CD (5.4 vs. 7.0 years). Fewer children with coexisting CD were from minority ethnic groups compared with type 1 diabetes only (15% vs. 18%); however, this was not a consistent finding across all registries. Reassuringly, mean $HbA_{1c}$ over the previous 12 months was not different in those with CD after adjusting for age, sex, and diabetes duration. However, it is of concern that only 31% of young people with type 1 diabetes overall achieved the international target $HbA_{1c}$ level of <7.5% (23), irrespective of the diagnosis of CD.

The prevalence estimate for CD is slightly lower than the rate of 5.1% reported in a recent systematic review (1), although it falls within the 95% CI (3.1–7.4%). Notably, the systematic review included only longitudinal cohort studies with at least 5 years of follow-up, whereas the data in this report are cross-sectional over a 12-month period, with a median diabetes duration of 4.9 years; therefore, prevalence estimates would be expected to be lower. Furthermore, since most patients with type 1 diabetes who have coexisting CD are asymptomatic and the diagnosis of CD depends on screening practices, prevalence rates may be underestimated in some of the registries. The frequency of screening was not documented in all registries, but the positive relationship between the prevalence of CD and the proportion of children who received a diagnosis within 2 years after the diagnosis of diabetes implies variable screening frequency.

The differences in the rates of CD may reflect our strict definition of biopsy-proven CD, which aligns with the ISPAD and American Diabetes Association guidelines (17,18,24). However, diagnostic practices vary internationally, including whether a small bowel biopsy is required for the diagnosis of CD (25,26). Two of the registries (the DPV and T1DX) additionally reported "suspected CD"; it is likely that a proportion of the 2% of patients in this category have CD. The variation in prevalence across the registries is also likely to reflect differences in CD risk, particularly given the diversity in ethnicity across the registries.

Overall, 5.4% of children received a diagnosis of CD before a diagnosis of type 1 diabetes, which is similar to the 7% of children reported in a recent systematic review (1). In cohort studies of children who are at increased risk for both conditions where serial screening is performed from birth, CD is commonly detected. For example, CD developed in 11% of children homozygous for DR3-DQ2 by age 5 years in the TEDDY study (4). Long-term follow-up of such cohorts will further our understanding of the temporal relationship between the development of type 1 diabetes and the development of CD.

In the general population, the prevalence of CD is higher in females (27). In contrast, a female sex bias was observed in only two of nine cohort studies that reported data on 587 cases of CD in patients with type 1 diabetes (1), and several small European studies reported a male sex bias. The current study represents a much larger sample size (*n* = 1,835) and greater ethnic diversity, with a female sex bias observed in all four registries. The registry data also confirm the greater risk of CD in children who have received a diagnosis of type 1 diabetes at a young age, particularly at <5 years of age. Since more than half of CD case patients received a diagnosis within 2 years of the diagnosis of diabetes, the findings highlight the importance of recommendations to screen for CD at diagnosis and at least once within the subsequent 2 years (1,17).

CD was traditionally considered a disease predominantly affecting people of white European heritage; however, the disease is increasingly recognized in people from nonwhite ethnic groups (27–29). Although the proportion of CD case patients from nonwhite ethnic groups was slightly lower overall in this study (15% vs. 18%), subgroup analysis by registry demonstrated significant differences by ethnicity in the T1DX and ADDN. Genetic susceptibility to CD is well established, and the genetic susceptibility to both type 1 diabetes and CD shares common alleles (30,31). Our findings highlight the interplay between genetic and environmental factors in the development of CD, including the rising incidence of CD in "low risk" populations, which parallels the increase in wheat consumption globally.

The significantly lower height SDS in participants with coexisting CD is of concern and contrasts with several reports (32,33) that have found no difference in

height SDS or growth in youth with coexisting CD compared with type 1 diabetes only. However, catch-up growth and improved height SDS were reported after 1 year of adherence to the gluten-free diet in a small Italian study (34). Since dietary adherence was not documented in the four registries, it is possible that the lower height SDS may reflect a subgroup of patients who do not adhere to the gluten-free diet. Alternatively, there may be a subgroup of patients who have not achieved catch-up growth after the diagnosis of CD. Poor glycemic control can impact growth and final height in patients with type 1 diabetes (35); however, $HbA_{1c}$ level was not worse in those with CD in the current study, suggesting that other factors influence growth in patients with CD. For example, the higher glycemic index of the gluten-free diet may contribute to greater glycemic variability. In addition, an altered dietary micronutrient composition associated with the gluten-free diet may influence growth in young people with CD.

Across the four registries, the glycemic control of young people with coexisting type 1 diabetes and CD did not differ from that of their counterparts with type 1 diabetes alone. It is reassuring that their glycemic control was not worse, given that the risk of vascular complications including retinopathy and nephropathy may be higher in patients with CD (7,36), particularly in association with nonadherence to the gluten-free diet (9).

The analysis of international registry data provides an important opportunity to compare and contrast clinical outcomes and to explore similarities and differences in clinical characteristics and therapy. Although this is a strength of the current study, which is the largest analysis of case patients with type 1 diabetes and CD to date, the cross-sectional design limits the conclusions that can be drawn from the analyses. Nevertheless, the role of benchmarking is established as a tool to improve patient care and outcomes. In particular, these data suggest variability in the screening, diagnosis, and treatment practices for CD in youth with type 1 diabetes. More data are needed to inform best practice.

The multicenter data on >50,000 youths with type 1 diabetes spanning three continents demonstrate the variable prevalence of CD but that confirm it is a common comorbidity. The findings support universal screening for CD in patients with type 1 diabetes, particularly within the first 2 years after the diagnosis of diabetes, irrespective of ethnicity (17). Although the lower height SDS in those with CD warrants further investigation using longitudinal data and documentation of adherence to the gluten-free diet, the observation emphasizes the importance of monitoring growth and nutrition in this population.

**Acknowledgments.** The authors thank the thousands of patients and families who contributed to these registries/audits and the numerous investigators.

**Funding.** The DPV is supported through the German Federal Ministry for Education and Research within the Competence Network for Diabetes Mellitus (grant FKZ 01GI1106), which was integrated into the German Center for Diabetes Research (DZD) as of January 2015. A listing of sites contributing data for the DPV is available at http://www.d-p-v.eu. The T1DX is supported through The Leona M. and Harry B. Helmsley Charitable Trust. A listing of the T1DX sites is available at https://t1dexchange.org/pages/resources/clinic-network/#4/37.16/-96.33. The NPDA is funded by the Healthcare Quality Improvement Partnership and delivered by the Royal College of Paediatrics and Child Health. A listing of the NPDA sites in England and Wales sites contributing data is available at http://www.rcpch.ac.uk/nationalpaediatric-diabetes-audit-npda. The ADDN is supported by The Australian Type 1 Diabetes Clinical Research Network, led by JDRF Australia (grant 17-2011-665), the recipient of Australian Government funding from the Australian Research Council (through a Special Research Initiative) and the Department of Health and Ageing. A listing of the ADDN sites contributing data and ADDN Study Group Investigators is available at http://addn.org.au/. M.E.C. is a recipient of a National Health and Medical Research Council Practitioner fellowship (APP1045777).

**Duality of Interest.** R.W.H. holds an equity fund that may contain stock from pharmaceutical companies. No other potential conflicts of interest relevant to this article were reported.

**Author Contributions.** M.E.C. researched data, performed statistical analyses, and wrote and edited the manuscript. N.P. and R.W.H. performed statistical analyses and reviewed and edited the manuscript. C.T.B., F.M.C., T.W.J., S.E.H., J.H.S., N.H., E.T., E.F.-R., S.D., H.T., D.M.M., and J.T.W. researched the data and reviewed and edited the manuscript. B.K. reviewed and edited the manuscript. The registries are represented by the following authors: M.E.C., T.W.J., E.T., and B.K. (ADDN); N.P., S.E.H., E.F.-R., and R.W.H. (DPV); C.T.B., J.H.S., S.D., and D.M.M. (T1DX); and F.M.C., N.H., H.T., and J.T.W. (NPDA). M.E.C. and R.W.H. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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