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Epidemiology of coeliac disease in children and adolescents with type 1 diabetes: a 13-year population-based study using secondary data sources

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ABSTRACT

Aims: To study the epidemiology of Coeliac Disease (CD) in the general paediatric population and among children with Type 1 Diabetes (T1D) in a population of Central Italy, and to assess the temporal trends of these two chronic conditions.
Methods: A population-based longitudinal study on children aged < 15 was conducted using Healthcare Utilization Databases of the Marche Region, 2011–2023. Prevalent and incident cohorts of T1D and CD were identified using hospital discharges, drug prescriptions, and healthcare exemption databases. Prevalence ratios (PR), incidence rate ratios (IRR), temporal trends, and cumulative CD risk after T1D diagnosis were assessed with 95% confidence intervals (CI).
Results: Overall 13-year period prevalences of T1D and CD were 1.65‰ and 5.28‰, respectively. CD prevalence among children with T1D was 97.7‰, 18-fold higher than in the general population (PR 18.6; 95%CI 14.3–24.0). CD incidence was 65 per 100,000 person-years in the general population and 2,410 per 100,000 person-years among children with newly diagnosed T1D (IRR 37.0; 95%CI 24.7–55.4). The six-year cumulative probability of developing CD in the T1D cohort was 10.3% (95%CI: 6.2%-14.3%).
Conclusions: Children with T1D have a markedly increased risk of CD, particularly in the first years after diagnosis, supporting systematic CD screening in this high-risk population.

1. Introduction

Coeliac Disease (CD) and Type 1 Diabetes (T1D) are both chronic, autoimmune diseases that require long-term management and careful monitoring to ensure patient health and well-being.

T1D is determined by the destruction of pancreatic beta cells which are involved in the process of insulin production. T1D aetiology is still uncertain, nevertheless genetic and environmental factors play a role in the onset of the disease [1]. The target of disease management is to control blood glucose levels through regular insulin administrations [2,3] and a healthy lifestyle [4,5], to avoid T1D acute complications such as severe hypoglycaemia or diabetic ketoacidosis.

CD is an immune-mediated enteropathy triggered by gluten consumption in genetically susceptible individuals [6]. It primarily affects the small bowel, but it is a systemic disease with a variable clinical presentation, which can be responsible for delayed or missed diagnoses. A strict and permanent gluten free diet is the only effective treatment for the remission of disease symptoms; however, adherence to a gluten free diet can be incomplete and new strategies are under investigation [7].

The diagnostic criteria for CD, once based on the results of small-intestine biopsy, have undergone significant changes over the past 20–30 years and continue to evolve, mainly based on clinical

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recommendations developed by leading scientific societies [8–10].

T1D and CD occur usually in children or adolescents, and they are among the most common lifelong disorders worldwide in paediatric populations [11,12]. T1D frequently coexists with other autoimmune conditions likely due to a shared immune-mediated pathway and genetic susceptibility. The prevalence and incidence of CD have been shown to be notably higher in individuals with T1D compared to the general population [13–17], with CD more frequently diagnosed after the onset of T1D [18,19].

To our knowledge, in Italy, the incidence of CD in children with T1D remains understudied. The aim of this study is to estimate the prevalence and incidence of CD in children of the general population and in those with T1D in a Region of Central Italy, using secondary data sources.

2. Materials and methods

This is an observational longitudinal study conducted among children aged < 15 years residing in the Marche Region, Central Italy, which has approximately 1.5 million inhabitants and a paediatric population of 171,752 in 2024 [20]. The study was based on the regional Healthcare Utilization Databases (HUDs), in the period from 2011 to 2023. These databases are particularly useful for estimating epidemiological measures and for monitoring rare chronic diseases. [21,22].

Data were drawn from four HUDs, linked using a deterministic procedure based on the beneficiary's identification code: (1) Regional Beneficiaries Database (RBD), providing information on date of birth, date of death, sex, assistance start and end dates were taken; (2) Hospital Discharges (HD) database, including information of beneficiaries discharged from public or accredited private hospitals, with admission and discharge dates, one primary diagnosis, up to five secondary diagnoses, and up to six interventions coded according to the International Classification of Diseases, 9th Revision Clinical Modification (ICD-9-CM); (3) Drug Prescriptions (DP) database, containing information on all drug prescriptions dispensed and reimbursable by the regional health system to beneficiaries are recorded, including Anatomical Therapeutic Chemical (ATC) System code, commercial name, date of dispensation, and number of packages; (4) Exemption from healthcare Co-payment Database (ECD), recording beneficiaries exempt from paying certain healthcare charges; exemptions granted to citizens with specific conditions (chronic diseases, rare diseases, disabilities, invalidity) or those with an income below a certain threshold are listed by the Italian Ministry of Health.

2.1. T1D prevalent and incident cohorts

The T1D prevalent cohort included subjects that in the period from 2011 to 2023 had at least one insulin prescription (ATC: A10A), or at least one hospitalization with a diagnosis of diabetes (ICD-9CM: 250.*, in any diagnosis fields) followed by at least one insulin prescription, or an active exemption for diabetes (code 013), released upon diagnosis, followed by at least one insulin prescription. The first event between insulin prescription, hospitalization and exemption was considered as the index date. Subjects aged ≥ 15 years at index date or with at least one prescription of oral glucose-lowering medications (ATC: A10B) over the entire study period or not resident in the Marche Region at index date were excluded.

The T1D incident cohort included individuals newly diagnosed between 2014 and 2023 who met at least one of the following criteria: a) at least two insulin prescriptions; b) at least one hospitalization with a diagnosis of diabetes; c) an active exemption for diabetes. The last two criteria had to be followed by at least two consecutive insulin prescriptions. The first insulin prescription, hospitalization or exemption was considered as the diagnosis date.

Excluded from this cohort were individuals aged 15 or older at the diagnosis date, those who had been resident in Marche Region for less than two years prior to the diagnosis, those who had received at least one prescription of oral glucose-lowering medications from 2011 to 2023, those who, in the two years before the diagnosis date, had been hospitalized or exempted for diabetes or had an insulin prescription.

2.2. CD prevalent and incident cohorts

Prevalent CD cases were subjects who, during the period from 2011 to 2023, had at least one hospitalization with a primary or secondary diagnosis of CD (ICD-9CM: 579.0*) or an exemption for CD (Coeliac sprue: RI0060; Coeliac disease-059.579.0; Coeliac Disease for Dermatitis Herpetiformis – 059.694.0) that is released after clinical confirmation of the diagnosis; the earliest event occurred was considered as the index date. Individuals aged ≥ 15 years or not resident in the Marche Region at index date were excluded.

The CD incident cohort included individuals who had at least one hospital admission or exemption for CD in the period from 2014 to 2023. The first event among these healthcare contacts was considered as the diagnosis date. Individuals aged 15 years or older at the diagnosis date, or those who, in the three years preceding the diagnosis date, had least one hospitalization or an exemption for CD and who were not resident of the Marche Region were excluded from this cohort.

2.3. Statistical analysis

The cohorts were described by summarizing continuous variables as mean and standard deviation, or median and interquartile range (IQR), according to the shape of data distribution, and qualitative as absolute and percentage frequencies.

The prevalence with 95% confidence interval (95% CI) of T1D and CD in the general paediatric population, as well as the prevalence of CD among children with prevalent T1D, was estimated annually from 2011 to 2023. For each calendar year, the denominator included all children who were resident in the Marche Region for at least one day between 1 January and 31 December of the index year and who were aged < 15 years on 31 December (age computed as 31 December minus date of birth). Individuals who died or moved in or out of the region during the index year were retained in the denominator provided they met the above criteria. For each year, the numerator included individuals in the denominator who met the case definition on or before 31 December of the index year. Additionally, a 13-year period prevalence (2011–2023) was estimated using as denominator all unique individuals aged < 15 years who were resident in the Marche Region at any time during the study period (n = 401,842), and as numerator all individuals meeting the case definition during 2011–2023. The Prevalence Ratio (PR) was estimated to compare the prevalence of CD in the T1D cohort to the one in the general population in the entire period.

For the period from 2014 to 2023, annual incidence rates and 95%CI of T1D and CD per 100,000 person-year (PY) were estimated in the general paediatric population, as well as annual incidence rates of CD among the T1D incident cohort, using the Poisson distribution. The incidence rate was calculated as the number of new cases occurring in each calendar year divided by the total person-time at risk accrued during that year. Person-time was calculated as the sum of individual days of observation contributed within each calendar year and converted into person-years. Individuals contributed time from the beginning of each calendar year or from cohort entry until diagnosis, death, end of healthcare assistance, reaching 15 years of age, or 31 December of the same year, whichever occurred first. Additionally, an overall incidence rate for 2014–2023 was estimated by dividing the total number of incident cases by the total person-time accumulated during the study period. The incidence rate ratio was calculated to compare the incidence of CD in the T1D incident cohort to the one in the general population.

The temporal trends in the prevalence and incidence of CD and T1D were estimated by applying Poisson regression models with log-link, including calendar year as a continuous variable and adjusting for age

group and sex. The log of the yearly population at risk (for prevalence) or person-time at risk (for incidence) was included as an offset. The regression coefficient for calendar year was transformed as $(e^{\hat{\beta}} - 1) \bullet 100$ to obtain the mean annual percentage change and corresponding 95% CI.

Additionally, the probability of developing CD from T1D diagnosis was estimated using the Kaplan-Meier method and its relative 95% CI. The analysis included all children newly diagnosed with T1D between 2014 and 2022 and followed from the date of T1D diagnosis. Participants were censored at the earliest of CD diagnosis, death, end of healthcare assistance (including migration out of the region), reaching 15 years of age, or 31 December 2023 (end of study period).

The case identification procedures and analysis were carried out using the statistical software R (v. 4.4.0). Significance level was set at 0.05 in all analyses.

3. Results

3.1. Cohorts' selection

Fig. 1 shows in detail the identification process of type 1 diabetes and coeliac disease cases in prevalent and incident cohorts, based on HUDs.

A total of 663 prevalent cases of T1D were identified from 2011 to 2023, of whom 75% were traced from all three databases and 315 new T1D diagnosis were found in the period from 2014 to 2023 in Marche Region.

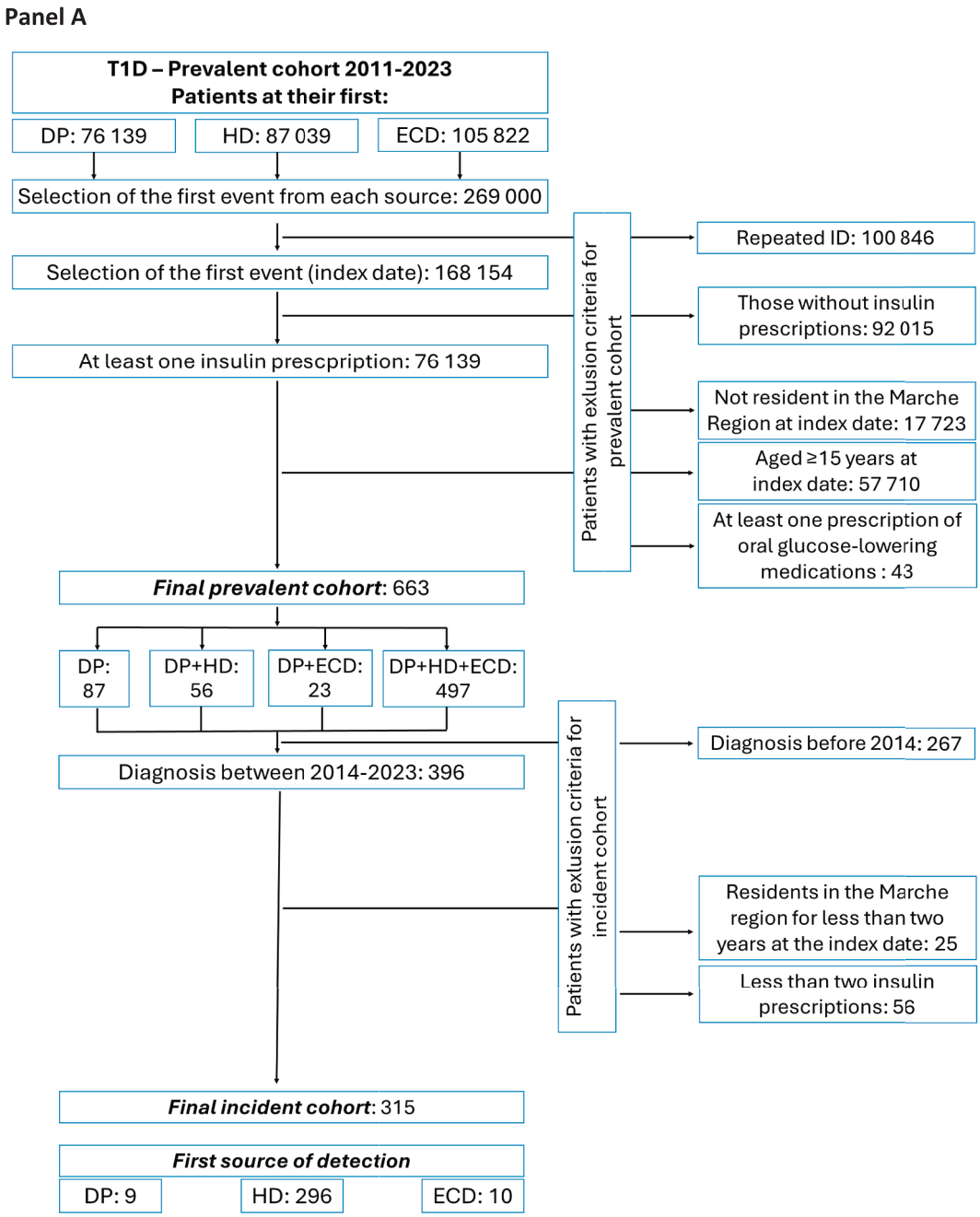

Fig. 1. Flowchart of the identification process of type 1 diabetes (A) and coeliac diseases (B) in prevalent and incident cohorts. *CD: Celiac Disease; HD: Hospital Discharge; DP: Drug Prescription; ECD: Exemption from healthcare Co-payment Database. Exclusion criteria were applied sequentially; the number of individuals reported at each step refers to the remaining eligible population after the previous exclusions.*

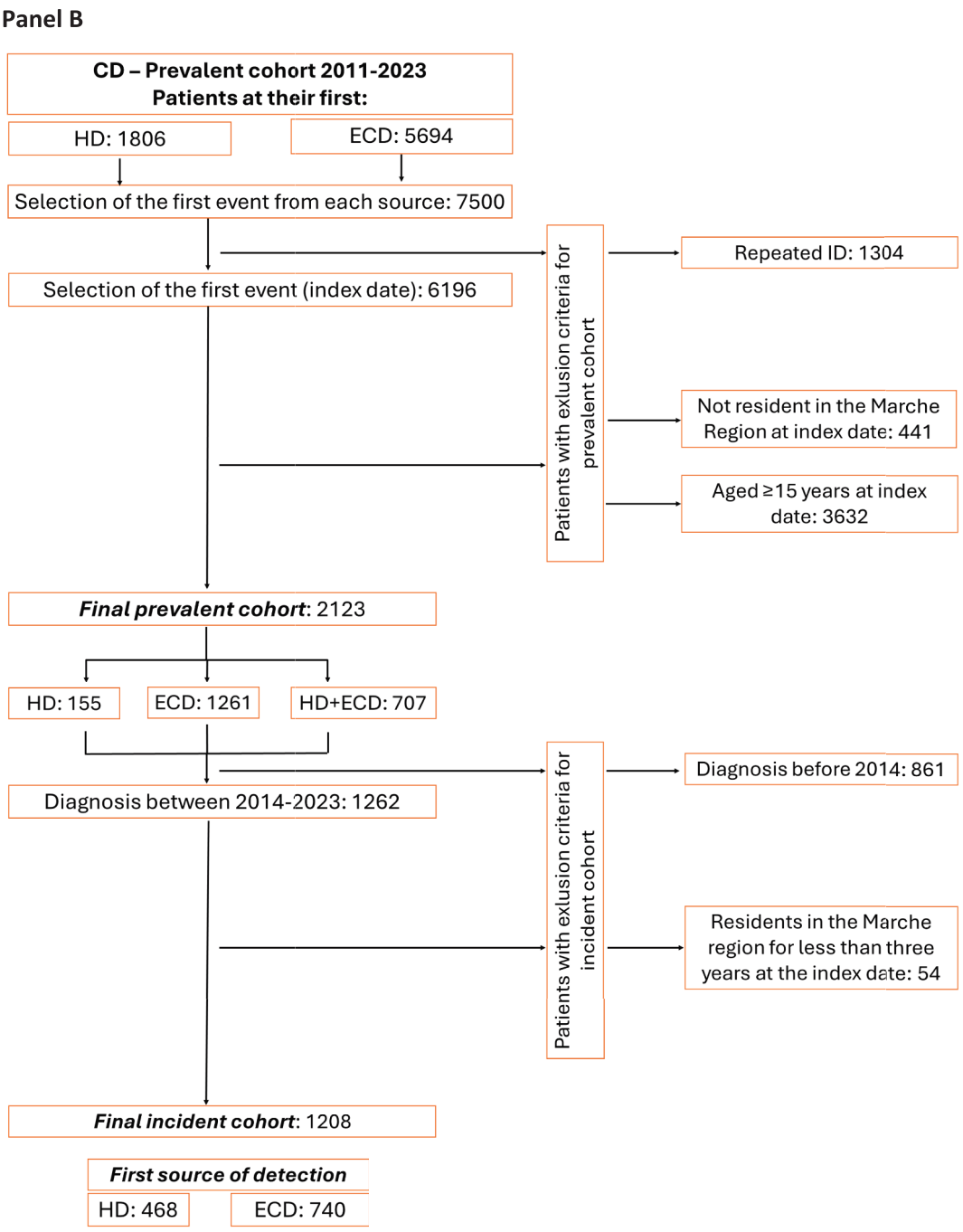

Fig. 1. (*continued*).

Prevalent cases of CD were 2,123 (Fig. 1), and there were 1208 new diagnosis of CD between 2014 and 2023.

3.2. Prevalence analysis

Prevalent T1D cases had a median age of 9 years (IQR: 6–12 years), 48.3% was female, with a modal age class of 10–14 years (44.2%); prevalent CD cases had a median age of 7 years (IQR: 4–10 years), 61.5% was female, with a modal age class of 5–9 years (41.0%, Table 1).

The 13-year period prevalence (2011–2023) of T1D and of CD was 1.65‰ (95% CI: 1.53–1.78) and 5.28‰ (95% CI: 5.06–5.51), respectively, in the paediatric population of Marche Region (Supplementary Material Tables S1 and S2).

Fig. 2 shows the annual cumulative prevalence estimates and 95% CI of T1D and CD over the study period and the estimated temporal trend with 95% confidence bands.

The annual cumulative prevalence of T1D rose from 0.98‰ (95% CI: 0.84–1.12) in 2011 to 1.28‰ (95% CI: 1.12–1.46) in 2023, with a significant mean annual percentage increase of 1.9% (95%CI 0.9%-2.9%, $p < 0.001$).

The observed annual cumulative CD prevalence was 3.13‰ (95% CI: 2.88–3.38) in 2011 and 5.43‰ (95% CI: 5.10–5.78) in 2023, showing a significant mean annual percentage increase of 4.4% (95% CI 3.9%-5.0%, $p < 0.001$).

The 13-year period prevalence of CD in the T1D prevalent cohort was 97.74‰ (95%CI: 76.25–122.89), 18 times higher (PR: 18.55, 95%CI: 14.33–24.02) than prevalence of CD in the general population.

Table 1
Demographic characteristics of the prevalent and incident cohorts.

	Prevalent cohorts 2011–2023		Incident cohorts 2014–2023	
	T1D (n = 663)	CD (n = 2123)	T1D (n = 315)	CD (n = 1208)
Sex, n (%)				
Male	343 (51.7)	814 (38.3)	162 (51.4)	477 (39.5)
Female	320 (48.3)	1309 (61.5)	153 (48.6)	731 (60.5)
Age (years), median (IQR)	9 (6–12)	7 (4–10)	9 (5–11)	7 (4–10)
Age class, n (%)				
0–4	123 (18.5)	612 (28.8)	61 (19.4)	383 (31.7)
5–9	247 (37.3)	870 (41.0)	116 (36.8)	504 (41.7)
10–14	293 (44.2)	641 (30.2)	138 (43.8)	321 (26.6)

T1D: Type 1 Diabetes; CD: Celiac Disease; IQR: Interquartile Range.

3.3. Incidence analysis

The distribution by age and sex of T1D and CD incident cases were highly comparable with that of the prevalent cohorts (Table 1).

In the ten-year period, a CD and T1D incidence rates of 65 cases (95% CI 62–69) and of 17 (95%CI 15–19) per 100,000 PY were respectively estimated (Supplementary Material Tables S3 and S4).

Fig. 3 shows the annual incidence rates and 95% CI of T1D and CD over the study period and the estimated temporal trend with 95% confidence bands. No significant trend was found in T1D and CD incidence over time.

Overall, 24 new cases of CD among the 315 newly T1D diagnoses were observed over the study period, with a rate of 2410 per 100,000 PY (95%CI: 1544–3585); this CD incidence was 37 times higher (IRR: 36.96, 95%CI: 24.67–55.35) than the one observed in the general population of Marche Region.

Fig. 4 shows the cumulative CD-free survival in the T1D incident cohort. A median time from T1D diagnosis to CD diagnosis of 357 days [IQR: 84–548] was observed, and 95% of new CD cases occurred within three years after T1D diagnosis.

The probability of developing CD in the T1D cohort at one, two and six years were 4.4% (95%CI: 1.9%-6.8%), 7.8% (95%CI: 4.4%-11.0%), and 10.3% (95%CI: 6.2%-14.3%), respectively.

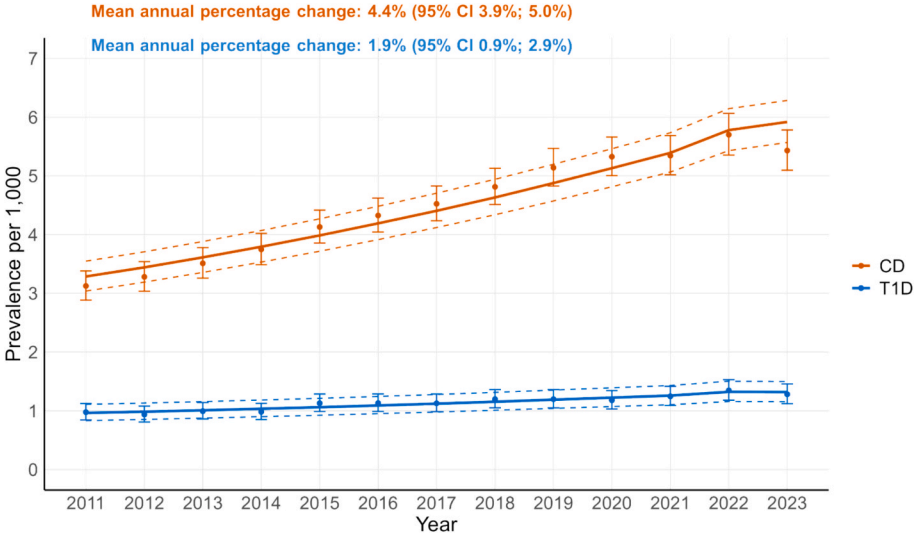

Fig. 2. Annual cumulative prevalence of coeliac disease (CD) and type 1 diabetes (T1D) in children aged < 15 years over time, adjusted by sex and age class, from 2011 to 2023.

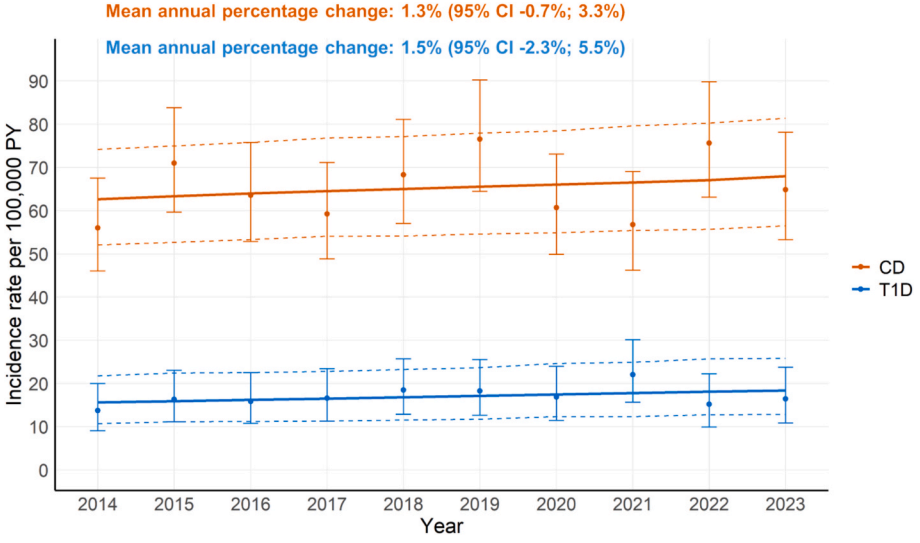

Fig. 3. Incidence of coeliac disease (CD) and type 1 diabetes (T1D) in children aged < 15 years over time, adjusted by sex and age class, from 2014 to 2023.

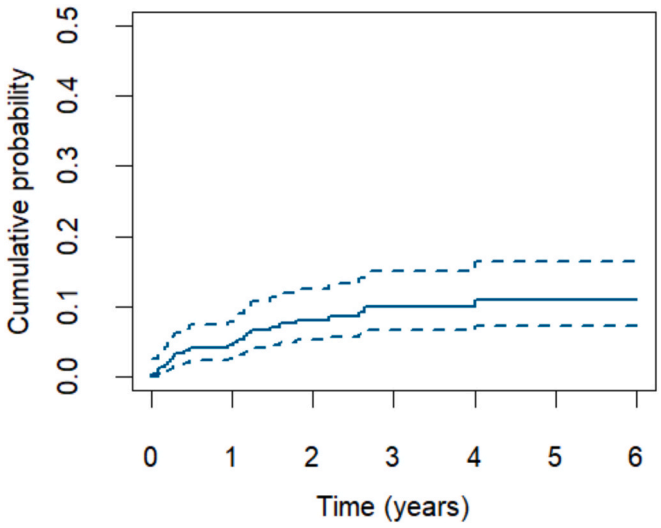

Fig. 4. Probability of developing coeliac disease after type 1 diabetes diagnosis in children aged < 15 years, among incident T1D cases diagnosed between 2014 and 2022 and followed until 31 December 2023.

4. Discussion

This population-based study provides updated evidence on the prevalence and incidence of two chronic conditions with a substantial impact on quality of life – type 1 diabetes and coeliac disease – and their co-occurrence in a real-world setting in Italy.

From 2011 to 2023, in the Marche region, nearly 2 per 1,000 children were living with T1D and approximately 5 per 1,000 with CD.

The incidence rates of new diagnosis of T1D and of CD were found to be 17 and 65 children per 100,000 person-years, respectively. Moreover, the burden of the two diseases was increasing, while the occurrence of new cases remained essentially stable over time.

The epidemiology of T1D varies considerably across countries. In 2021, approximately 8.4 million individuals worldwide were living with T1D, of whom 1.5 million were younger than 20 years [23]. In Italy, The National Institute of Health reported a prevalence of 2.2‰ for T1D [24] in the country, consistent with our findings. Similarly, national estimates of T1D incidence derived from HUDs [25] or from population registry data [26] are in line with rates observed in our study.

Although a global increase in T1D incidence has been reported over the past three decades, with annual growth rates of 3% to 4% [27], a recent Italian registry-based study indicates that incidence rose between 1986 and 2003 by 3.6% and then stabilized through 2019 [26], a pattern consistent with our results.

The pooled global prevalence of CD in the biopsy-confirmed general population was 0.7%, ranging from 0.4% in South America to 0.8% in Europe and Oceania [28]. Increased awareness of CD clinical manifestations and the wide-spread use of serological screening in clinical practice, have led a marked rise in detected cases of CD over the past four decades. In Europe, United States, Canada, and New Zealand, CD incidence increased from fewer than 2 cases per 100,000 person-years in the 1980 s and 1990 s, to more than 20 cases per 100,000 person-years by 2010 [14]. Our findings corroborate the increasing trend in prevalence, while incidence rates remained relatively stable over time.

Italian estimates of CD remain heterogeneous, with CD prevalence of 1.5% among children aged 6–11 years [29] and 1.1% among those aged 0–16 years [30], and an incidence of 27 cases per 100,000 person-years [31]. Differences with our results may reflect variation in data sources and case-ascertainment. Clinical studies are typically based on patients within specific catchment area and relay on diagnostic confirmation in clinical setting, whereas studies using HUDs are based on disease-related contacts of the entire population with the regional healthcare system.

Notably, a recent screening national law introducing screening programs for CD and early stages of T1D may further improve the accuracy of epidemiological estimates in the coming years [32].

It is well known that there is a marked higher prevalence of coeliac disease in individuals with T1D compared to the general paediatric population, due to their autoimmune aetiology. However, CD prevalence in children and adolescents with T1D is characterised by high variability worldwide, ranging between 1.6% in French [33] and 12.3% in Denmark [34]. In our study the prevalence of CD in children with type 1 diabetes was 9.8%, similar to that reported in a recent nationwide Sweden study [13], and slightly higher than estimates from a large international study involving three continents (1.9% in the USA to 7.7% in Australia)[35]. In both studies, CD diagnosis was confirmed by biopsy, which provides the highest diagnostic accuracy.

Our findings on CD incidence among children with newly diagnosed T1D further highlight the strong co-occurrence between the two conditions. The incidence of CD in this group was nearly 37 times higher than that of the general paediatric population, confirming that children with T1D constitute a high-risk subgroup. Moreover, cumulative probability of developing CD reached 10.3% at six years, with 95% of diagnosis occurring within 3 years after the clinical diagnosis of T1D. The markedly higher CD incidence observed among children with T1D may partly reflect differential case ascertainment. Children with T1D undergo routine clinical visits and laboratory evaluations, whereas diagnosis in the general paediatric population is largely symptom-driven; therefore, part of the excess incidence may reflect enhanced surveillance, in addition to the well-established shared autoimmune pathogenesis of the two conditions.

The CD incidence observed in our study was higher than the 5.8 per 1,000 person-years reported in a UK study [36]. This discrepancy may be attributable to differences in the study period, data sources, and population characteristics, as the British study involved individuals up to 18 years of age. Other factors that may contribute to these differences may be related to lifestyle and nutritional habits.

The study has several strengths. The longitudinal population-based design ensures good generalizability and allow the assessment of temporal trends over a long follow-up period. The use of HUDs enabled the estimation of both prevalence and incidence of CD among children with T1D, providing longitudinal evidence that complements existing cross-sectional studies.

Some limitations should be acknowledged. The relatively small number of incident CD cases among children with T1D in the Marche Region limited the ability to assess potential risk factors reported in literature, such as younger age at T1D diagnosis and the female sex. Furthermore, some degree of misclassification may have occurred. However, the use of exemption codes based on clinically confirmed diagnosis likely mitigate this bias. Importantly, our prevalence and incidence estimates, and the observed trends are consistent with previous studies, supporting the robustness of our findings. Finally, differences in the natural history and clinical presentation of T1D and CD may impact the estimation of epidemiological measures. T1D typically has an acute and symptomatic onset, allowing relatively accurate identification of the timing of clinical diagnosis. In contrast, CD often follows an insidious or asymptomatic course, with diagnosis frequently delayed relative to true disease onset.

In conclusion, this study, based on HUDs, found a high prevalence and incidence of coeliac disease in subjects under 15 years of age with type 1 diabetes in a population of Central Italy. The use of administrative databases has proven to be effective in the epidemiological surveillance of chronic diseases in unselected populations, allowing for reliable and up-to-date estimates of prevalence and incidence.

Our findings provide evidence to support the recommendation for systematic CD screening in the population with T1D, particularly useful in asymptomatic children in order to identify cases early and promptly initiate treatment with a gluten-free diet, reducing long-term complications.

5. Authors' contributions

RG, AF, MI conceptualized the study, developed the methodology for data analysis and curation, and drafted the manuscript. AF managed the data and performed the formal statistical analyses. MP and FC were in charge for data extraction and authorized their utilization. RG, AF, MI assisted in the results interpretation. VC contributed to the clinical interpretation and discussion of study results and supervised the manuscript. RG is the guarantor of the overall content of the work.

All authors assisted in manuscript revision, read and approved the final manuscript.

Ethics statement

This observational study fulfils the Italian regulations of ethics committees, which require only standard written informed consent at the time of hospital admission.

Ethical review and approval were waived for this study. We did not mention ethical safeguards simply because not pertinent in our study. All data were anonymized and managed in a manner that protected the privacy and confidentiality of individuals represented in the datasets.

According to Article 9 of the General Data Protection Regulation (European Union Regulation 2016/679), pseudonymized administrative data can be used without specific written informed consent when patient information is collected for healthcare management, quality evaluation, and improvement. All procedures adhered to the 1964 Helsinki Declaration and its subsequent amendments.

Data availability statement

Restrictions apply to the availability of these data. The datasets generated and/or analysed during the current study are property of a third party that is the Regional Health Agency of Marche (ARSMarche) and, although they are anonymized, datasets are not publicly available due to the current regulation on privacy. The description of the administrative databases is available from the website ARSMarche/Flussi.

Other researchers can obtain access to the data through a formal request based on a research project to the Regional Health Agency of Marche.

CRediT authorship contribution statement

Alessandro Fontanarosa: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Marica Iommi:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Data curation, Conceptualization. **Federico Cesanelli:** Writing – review & editing. **Andrea Pompei:** Writing – review & editing. **Marco Pompili:** Writing – review & editing, Resources. **Flavia Carle:** Writing – review & editing, Resources. **Edlira Skrami:** Writing – review & editing. **Valentino Cherubini:** Writing – review & editing, Validation. **Rosaria Gesuita:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2026.113238.

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