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RESEARCH LETTER

WILEY

Initial observations on the frequency of diabetic ketoacidosis following pilot screening for type 1 diabetes in the general Italian population

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1 | BACKGROUND/CONTEXT

Diabetic ketoacidosis (DKA) is common at clinical onset of diabetes,[1] and a delayed diabetes diagnosis is a major contributing factor.[2] Following parliament approval in September 2023 and endorsement by the Italian Paediatric Society (SIP) and the Italian Society of Paediatric Endocrinology and Diabetology (ISPED),[3] Italy became the first country to legislate for voluntary screening for type 1 diabetes and celiac disease (law no. 130/23 proposed by the Fondazione Italiana Diabete stating, as a public health measure, universal screening for type 1 diabetes and celiac disease in children). This initiative aims to reduce the incidence of DKA, slow diabetes progression, and diagnose celiac disease earlier. A 2024 pilot study conducted in four Italian regions (Lombardy, Marche, Campania, Sardinia), dubbed the 'D1Ce (Diabetes type 1 and Celiac disease) Screen Study', evaluated the feasibility of general population screening for these conditions by collecting clinical data, conducting widespread screening, and communicating results to families. Positive cases were referred to specialized centres for further monitoring and treatment. However, these regions were engaged in D1Ce Screen in 2023 before project implementation in 2024 through multiple stakeholder participation, including from the Ministry of Health, the Istituto Superiore di Sanità (ISS), experts in type 1 diabetes and celiac disease, laboratories, family paediatricians, and specialized paediatric diabetes and celiac disease centres. Family paediatricians in the regions selected for D1Ce Screen played a vital role in implementation by informing families about the screening process. In this pre-implementation phase in 2023, several online and in-person meetings were organized with paediatricians in the involved regions focusing on the importance of early diagnosis of type 1 diabetes, DKA prevention, and the potential of offering diabetes-modifying therapies. In addition, the ISS established an IT platform providing video tutorials and electronic educational materials for children and parents.[4]

To investigate the impact of the D1Ce Screen project, here we compared the frequency of DKA in regions involved in the D1Ce Screen project with the frequency in regions not involved in the project, evaluating data in the year before D1Ce Screen implementation (2023) and in 2024, when screening was implemented.

2 | METHODS

In January 2025, we conducted a survey of Italian paediatric diabetes centres to analyse DKA frequency at diagnosis of type 1 diabetes in 2023 and 2024. We collected aggregated data on children and adolescents categorised by age group (0.5–5, 6–11, and 12–17 years) together with their sex, presence of DKA or severe DKA at diagnosis (defined as per ISPAD guidelines: blood glucose >11 mmol/L (200 mg/dL), venous pH <7.3 or bicarbonate <15 mmol/L, and ketonaemia/ketonuria for DKA and venous pH <7.1 or bicarbonate <5 mmol/L for severe DKA), and year of observation. All type 1 diabetes diagnoses were confirmed by the presence of at least one autoantibody targeting pancreatic islet cells. The proportion of DKA in the population of children and adolescents with newly diagnosed type 1 diabetes was estimated as the ratio of new type 1 diabetes cases with DKA at onset and the number of new type 1 diagnoses with 95% confidence intervals (95% CI) stratified by age group, sex, year of observation, and by regions participating in D1Ce Screen in 2024 (Lombardia, Marche, Campania, Sardegna) and those not involved in the project (Abruzzo, Calabria, Emilia-Romagna, Friuli, Lazio, Liguria, Piemonte, Sicilia, Toscana, Puglia, Trentino, and Veneto).

The study was conducted in accordance with the Helsinki Declaration, and all data were anonymised. Ethics committee approval was not required, since the General Authorisation to Process Personal Data for Scientific Research Purposes (authorisation 9/2014) exempts retrospective archive studies that use identifier codes preventing subject re-identification.

Two logistic regression models were constructed to assess factors associated with DKA or severe DKA at onset, with year of observation, sex, age group, and involved/uninvolved regions and second-order interaction terms as explanatory variables. Results are reported as forest plots with odds ratios (OR) and 95% CIs. The likelihood ratio (LR) test and Hosmer–Lemeshow test were used to select the most parsimonious model and to evaluate the model's goodness of fit.

3 | RESULTS

Fifty-eight of 59 Italian paediatric diabetes centres participated in the study, following a median (IQR) of 150 (87–426) children and adolescents in each centre. Over the 2-year observation period, 2398 children and adolescents under 18 years were diagnosed with type 1 diabetes. DKA and severe DKA (as a subset of DKA cases) were observed in 821 cases (34.2%, 95% CI: 32.3–36.2) and 316 cases (13.2%, 95% CI: 11.9–14.6), respectively.

New cases of type 1 diabetes and proportion of DKA at diagnosis by year of onset, age group, and included/not included region are reported in Table 1. Percentages of DKA and severe DKA at diagnosis of type 1 diabetes by age group and year of diagnosis are shown in Figure S1. DKA and severe DKA were more common in regions not involved in the D1Ce Screen project than in those not involved in the project in both 2023 (DKA OR 0.76, 95% CI: 0.60–0.97; severe DKA OR 0.46, 95% CI: 0.31–0.68) and 2024 (DKA OR 0.69, 95% CI: 0.53–0.90; severe DKA OR 0.55, 95% CI: 0.37–0.81). There were no significant differences in DKA or severe DKA frequencies over the 2 years of observation in participating and non-participating regions or the entire population.

With year of observation, sex, age group, and involved/uninvolved regions included as explanatory variables, logistic regression models showed that the odds of DKA were 26% lower (OR 0.74, 95% CI: 0.62–0.88, $p < 0.001$) and the odds of severe DKA were 49% lower (OR 0.51, 95% CI: 0.39–0.67, $p < 0.001$) in regions involved in the D1Ce Screen project than in non-participating regions, respectively (Figure 1, Table S1). The probability of DKA was significantly higher in the two younger age groups than in the two older ones; no differences were observed in terms of year of onset and sex for both DKA and severe DKA.

TABLE 1 New diagnoses of type 1 diabetes and the proportion of DKA and severe DKA at type 1 diabetes diagnosis by year of onset, age group, and regions included and not included in the D1Ce Screen study.

	2023			2024		
Regions included in the D1Ce Screen study	**New T1D cases (*n*)**	**DKA (%)**	**Severe DKA (%)**	**New T1D cases (*n*)**	**DKA (%)**	**Severe DKA (%)**
Age groups						
0.5–5	118	31.4	5.9	88	27.3	9.1
6–11	213	30.0	8.9	174	27.6	9.8
12–17	127	31.5	8.7	150	30.7	8.7
Total	458	30.8	8.1	412	28.6	9.2
Regions not included in the D1Ce Screen study	**New T1D cases (*n*)**	**DKA (%)**	**Severe DKA (%)**	**New T1D cases (*n*)**	**DKA (%)**	**Severe DKA (%)**
Age groups				Total	Total	Total
0.5–5	230	41.3	20.9	209	45.9	19.1
6–11	359	35.9	12.8	312	34.3	16.3
12–17	201	33.3	15.9	217	31.3	11.1
Total	790	36.8	15.9	738	36.7	15.6
Both regions						
Total	1248			1150		

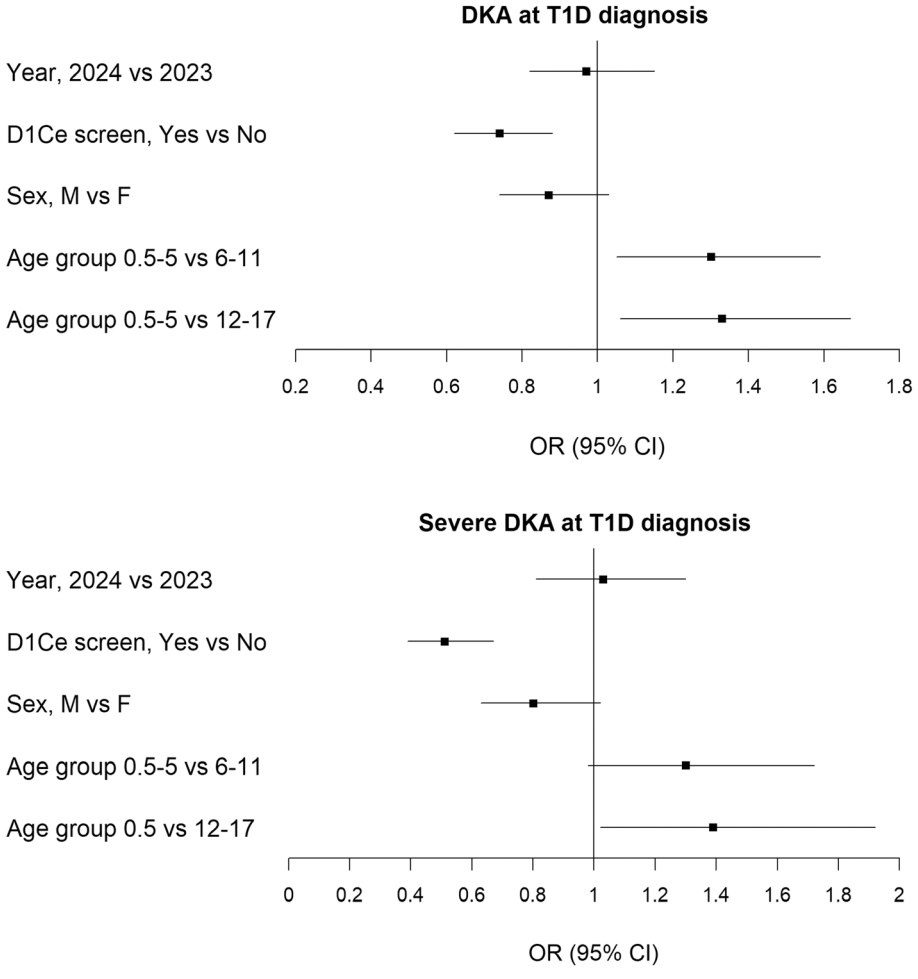

FIGURE 1 Factors associated with DKA or severe DKA at diagnosis of type 1 diabetes. Results of multiple regression analysis.

4 | CONCLUSIONS

The D1Ce Screen project marks the first step in the implementation of the diabetes screening law in Italy. Here we report preliminary results of this initiative. Individuals in regions involved in the project were 26% less likely to present with DKA at diagnosis of type 1 diabetes and 49% less likely to present with severe DKA. The reduced risk of DKA was apparent both in 2023, when the D1Ce Screen project was being planned and discussions with important stakeholders such as family paediatricians had already begun, and in 2024, when the pilot project started in earnest. Therefore, the observed reduced risk of DKA at diagnosis in the D1Ce Screen regions cannot be attributed to the direct results of screening (i.e., autoantibody detection), as the effect was seen in 2023 before pilot program implementation and before positive autoantibody results were being communicated to affected individuals and their families. In addition, this study shows that, in 2023 and 2024, there was a slight reduction in DKA in Italy (about 18%) compared with recent observations.[5,6]

This study aimed to provide an early assessment of the potential direct impact of screening by comparing regions actively participating in the D1Ce Screen pilot project in 2024 with those not participating, using 2023 data from both regions as baseline. To achieve this, our multiple logistic regression model (Figure 1, Table S1) included the year of observation and region involvement as explanatory variables, allowing us to evaluate whether there were independent effects of year and region on DKA occurrence. These results show that, over this period of observation, there was no observable direct effect from D1Ce Screen implementation in this early and limited phase of the initiative.

This study was not intended to assess the determinants of changes in DKA frequency but to explore effects potentially related to the first phase of implementation of type 1 diabetes screening. The early diagnosis of type 1 diabetes is crucial for preventing DKA,[7] which is often caused by delays in diagnosis. The initial symptoms of type 1 diabetes, such as fatigue or increased thirst, can be non-specific or develop gradually, making it challenging to distinguish children with type 1 diabetes from the many who exhibit similar symptoms due to minor, undifferentiated illnesses. Common reasons for a delayed diagnosis include misdiagnosis by attributing symptoms to common illnesses and delays in the diagnostic and referral pathways before a child is seen by a specialist team.[8]

It is plausible to speculate that the active participation of family paediatricians from early 2023 onwards, as key players in the D1Ce Screen projects, may have been a significant factor in increasing their attention to the signs and symptoms of the disease and thus to the early diagnosis of type 1 diabetes, thus reducing the risk of DKA in these regions. It is also conceivable that there may have been a general increase in awareness about diabetes, including in paediatric diabetologists and paediatricians in regions not directly involved in the project but certainly aware of the new law. This could be one possible explanation for the broader, albeit non-significant, decrease in DKA across regions noted in our survey. If such a spillover awareness effect exists, it would indeed make the specific impact of the D1Ce interventions harder to isolate and could potentially lead to an underestimation of the true effect in participating regions when compared with non-participating regions that also experienced some awareness benefit.

Recent systematic reviews[9–11] have suggested that DKA incidence may be falling in some settings due to improved awareness and practitioner behaviour, though trends vary by region and methodological variability challenges definitive conclusions. In Italy, the 8-year Parma campaign was associated with a 78% decrease in DKA incidence,[12] but that was a smaller local initiative compared with the current study.

This survey was based on a very high participation of Italian paediatric diabetes centres (98%), providing a comprehensive overview of new diagnoses of type 1 diabetes across the country in light of the launch of the screening programme. However, as a preliminary observational study using aggregated data, we cannot definitively establish causality nor account for unintended confounding. While our approach adjusted for age, sex, year, and region participation, other unmeasured confounders such as healthcare access, population density, urban and rural disparity, general paediatrician education, national awareness campaigns, or COVID-related changes in health behaviour may have influenced the observed outcomes. ISPED now intends to monitor the effects of the screening programme on early-onset DKA through the longitudinal study of involved children and family paediatricians by examining a larger, unselected population and considering factors not collected here, such as the socioeconomic and demographic characteristics of participants.

In conclusion, the introduction of screening for type 1 diabetes in clinical practice has the potential to reduce the frequency of DKA at type 1 diabetes diagnosis both by identifying individuals in presymptomatic phases and, as our early findings suggest, possibly by contributing to decreased DKA at clinical presentation through increased practitioner and general population awareness. This early snapshot of programme efficacy now needs assessing over the longer term and separating out from true screening effects.

AUTHOR CONTRIBUTIONS

Valentino Cherubini, Andrea Enzo Scaramuzza and Ivana Rabbone conceptualized and designed the study, designed the data collection instrument, collected data, wrote the article and contributed to discussions. Riccardo Bonfanti, Dario Iafusco, Enza Mozzillo, Carlo Ripoli and Marco Marigliano supervised data collection and analysis and critically revised and reviewed the manuscript. Rosaria Gesuita performed statistical analysis, wrote the article and contributed to discussions. Umberto Agrimi, Emanuele Bosi, Antonio D'Avino, Flavia Pricci, Marco Silano, Francesca Ulivi and Olimpia Vincentini are members of the D1Ce study group and discussed critically the results and the final draft of the article. Members of Diabetes Study Group of the Italian Society for Paediatric Endocrinology and Diabetes collected data and discussed and commented on data analyses. Andrea Enzo Scaramuzza is the corresponding author of this work and, as such, had full access to all the data in the study and has final responsibility as guarantor.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.16611.

DATA AVAILABILITY STATEMENT

Data are available upon reasonable request from the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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