Incidence of Type 1 Diabetes in Children Has Fallen to Pre-COVID-19 Pandemic Levels

Citation for published version:

Digital Object Identifier (DOI):
10.2337/dc23-2068

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Peer reviewed version

Published In:
Diabetes Care

Publisher Rights Statement:
Open Access. This article is licensed under a Creative Commons Attribution 4.0 International License (CC BY 4.0), which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Incidence of Type 1 Diabetes in Children Has Fallen to Pre-COVID-19 Pandemic Levels: A Population-Wide Analysis from Scotland

William Berthon\textsuperscript{a}, Stuart J McGurnaghan\textsuperscript{b}, Luke AK Blackbourn\textsuperscript{b}, Louise E Bath\textsuperscript{c}, David A McAllister\textsuperscript{d,e}, Diane Stockton\textsuperscript{d}, Sarah H Wild\textsuperscript{a,d}, Paul M McKeigue\textsuperscript{a}, Helen M Colhoun\textsuperscript{b,d}, on behalf of the Scottish Diabetes Research Network Epidemiology Group\textsuperscript{f}

\textsuperscript{a}Usher Institute, College of Medicine and Veterinary Medicine, The University of Edinburgh, Edinburgh, UK
\textsuperscript{b}Institute of Genetics and Cancer, College of Medicine and Veterinary Medicine, The University of Edinburgh, Edinburgh, UK
\textsuperscript{c}Diabetes Team, Royal Hospital for Children and Young People, Edinburgh, UK
\textsuperscript{d}Public Health Scotland, Glasgow, UK
\textsuperscript{e}Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK
\textsuperscript{f}The Scottish Diabetes Research Network Epidemiology Group, UK
Type 1 diabetes incidence in Scotland’s young people peaked in 2021 at 20% above the 2015-2022 average, but the rise was isolated to 6-14yo and incidence regressed to pre-COVID-19 levels in 2022.

**Running head:**
Type 1 diabetes falls to pre-pandemic rate

**Keywords:**
Type 1 Diabetes; Incidence; Children; Pediatric Diabetes; COVID-19; Population-based studies; Epidemiology; Public Health

**Word count:** 749; 1 Figure
OBSERVATION LETTER

We previously reported in this journal that the incidence of type 1 diabetes among children aged 0-14 years in Scotland during 2020-2021 was 20% higher than the 7-year average across 2015-2021. Among those aged 15-34, we observed a continued slow linear year-on-year rise across the study period [1]. Our report aligned with the findings of a recent meta-analysis showing a rise in 2020 and a peak in 2021 [2]. However, using rt-PCR test data, we found no evidence supporting a direct causal effect of COVID-19 infection itself, consistent with a recent analysis in the prospective, multinational TEDDY cohort of children [3]. These reports of rising type 1 diabetes cases are deeply concerning [4] as they herald increased morbidity, a decline in children’s quality of life, and increased burden on health services. An important question is therefore whether this incidence rise has continued in 2022 amid a less severe pandemic and lifted social restrictions.

In Scotland, healthcare is free at the point of delivery and all new type 1 diabetes diagnoses in primary or secondary care are captured in the nationwide Scottish Care Information - Diabetes (SCI-Diabetes) registry within 24 hours of the diagnosis. Furthermore, the nationwide policy mandates the inpatient admission of all children under 16 with suspected diabetes to a specialist unit on the day of presentation. Using updated data from SCI-Diabetes and hospital admissions, we examined type 1 diabetes incidence in the pediatric population for 2022, assessing differences in age, sex or diabetic ketoacidosis (DKA) presence at admission between 2020-2021 and the surrounding years 2019 and 2022. Data on incident type 1 diabetes cases from 1 January 2015 to 31 December
2022 obtained from SCI-Diabetes for people aged 0-5, 6-14 and 15-34 were combined with daily population estimates for Scotland, derived by fitting a spline function to publicly available midyear estimates. As before [1], adjusted smoothed effects of calendar time were estimated jointly from the counts of daily cases by age group, using the R package mgcv to fit a generalized additive model. Thus, the underlying trend in incidence over time was estimated and plotted relative to the age-group-specific average across the period (Fig. 1). DKA presence at admission was ascertained from the ICD-10 coded Scottish Morbidity Records 01, the nationwide database of general/acute hospital admissions and discharges.

Between 2015 and 2022, the incidence was highest and most variable in 6-14-year-olds. In this group, incidence peaked in early 2021, at about 20% above the 8-year average, but regressed to slightly below it by 2022 (Figure 1). No substantial changes occurred over time in 0-5-year-olds, while a slow but non-significant increase was observed in 15-34-year-olds.

We examined the characteristics of diagnosed 6-14-year-olds for each year from 2019 to 2022. The mean age [95% CI] at onset was 10.7 [10.4-11.0], 10.7 [10.4-11.0], 10.4 [10.1-10.6] and 10.6 [10.3-10.9]. The percentage of males [95% CI] was 45.8% [39.7-52.0], 51.9% [46.1-57.8], 51.2% [45.9-56.5] and 52.4% [46.2-58.7]. The percentage of new onset cases with a DKA ICD-10 code on hospital admission records [95% CI] was 31.2% [25.5-37.0], 31.4% [26.0-36.9], 31.4% [26.5-36.3] and 34.1% [28.2-40.1].

Subdividing children aged 0-14 into two subgroups has revealed that the sharp increase in type 1 diabetes incidence seen in 2021 was restricted to 6-14-year-olds and did not persist into 2022. This finding should provide substantial
reassurance to parents and service providers. In that group, there was no significant difference in age, sex or DKA presentation among incident cases between 2020-2021 and surrounding years.

A limitation of our analysis is that the cessation of nationwide free rt-PCR testing for COVID-19 in January 2022 precluded re-examining the infection’s direct effect on type 1 diabetes incidence. However, as previously noted, serology and rt-PCR surveillance data indicated a cumulative proportion of prior pediatric COVID-19 infection of about 25% by June 2021 when type 1 diabetes incidence had peaked, and a rise to about 60% by January 2022. This time course is not consistent with a direct causal effect. Additionally, vaccination in Scotland was not introduced until April 2022 in 5-11-year-olds. Alternative explanations include altered infection rates or timings in children for pathogens that may have a causal role in type 1 diabetes. Recent reports from Germany suggest that the rise in incidence there during the pandemic was greatest in the youngest children below 6 years. However, a decrease in older children was also noted in 2022 [5]. Continued monitoring of type 1 diabetes incidence remains paramount, and it will be of interest to see whether similar patterns are observed in other countries.
ACKNOWLEDGEMENTS

Personal Thanks We acknowledge with gratitude the contributions of people with diabetes, NHS staff and organizations (the Scottish Care Information-Diabetes development team and Steering Group, the Scottish Diabetes Group, the Scottish Diabetes Survey Group, the diabetes managed clinical networks) involved in providing data, setting up, maintaining, and overseeing collation of data for people with diabetes in Scotland. Data linkage is performed by colleagues at Public Health Scotland.

Funding and Assistance No specific funding was received for this study. H.M.C. is supported by an endowed chair from the AXA Research Fund. Authors were not precluded from accessing data in the study and they accept responsibility for submitting the article for publication.

Conflict of Interest There are no conflicts of interest to declare in direct relation to this work. P.M.M. declares stock ownership in the following: Bayer and Roche Pharmaceuticals. H.M.C. declares grants from Juvenile Diabetes Research Foundation International, Diabetes UK, IQVIA, Chief Scientist Office, Medical Research Council (UKRI) and EU Commission; honoraria from Novo Nordisk; advisory board fees paid through her institution from Novo Nordisk and Bayer; and stock ownership in Bayer and Roche. No other authors have any conflicts to declare. All authors have completed the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest.

Author Contributions and Guarantor Statement H.M.C. and P.M.M. conceived and designed the study and made the decision to submit the work for publication. S.J.M. and L.A.K.B. contributed to retrieving or pre-processing data
for the study. H.M.C. and W.B. undertook literature searches. H.M.C. and W.B. contributed to data interpretation. W.B. accessed and analyzed the data. H.M.C. accessed and verified the analysis. H.M.C. and W.B. wrote the first draft of the manuscript. All authors contributed to reviewing and editing the manuscript for intellectual content. All authors approved the final version of the manuscript. H.M.C. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
REFERENCES


FIGURE LEGEND

**Figure 1.** Fitted curves for relation of type 1 diabetes incidence in Scotland to calendar time from 2015 through 2022, adjusted for age, seasonality, weekday/weekend, and stratified by age. Ribbon edges are 1 SE above and below the fitted curve. A rate ratio of 1.0 corresponds to the 8-year average within each age group.
Incidence rate of type 1 diabetes over time in Scotland expressed as the ratio relative to the 8-year average within each age group.

Age at diagnosis: 0-5 years old

Age at diagnosis: 6-14 years old

Age at diagnosis: 15-34 years old

Fitted curves for relation of type 1 diabetes incidence in Scotland to calendar time from 2015 through 2022, adjusted for age, seasonality, weekday/weekend, and stratified by age. Ribbon edges are 1 SE above and below the fitted curve. A rate ratio of 1.0 corresponds to the 8-year average within each age group.