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Opportunities for earlier diagnosis of type 1 diabetes in children: A case-control study using routinely collected primary care records

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ABSTRACT

Background: The epidemiology of type 1 diabetes mellitus (T1DM) suggests diagnostic delays may contribute to children developing diabetic ketoacidosis at diagnosis. We sought to quantify opportunities for earlier diagnosis of T1DM in primary care.

Methods: A matched case-control study of children (0–16 years) presenting to UK primary care, examining routinely collected primary care consultation types and National Institute for Health and Care Excellence (NICE) warning signs in the 13 weeks before diagnosis.

Results: Our primary analysis included 1920 new T1DM cases and 7680 controls. In the week prior to diagnosis more cases than controls had medical record entries (663, 34.5% vs 1014, 13.6%, odds ratio 3.46, 95% CI 3.07–3.89; $p < 0.0001$) and the incidence rate of face-to-face consultations was higher in cases (mean 0.32 vs 0.11, incidence rate ratio 2.90, 2.61–3.21; $p < 0.0001$). The preceding week entries were found in 330 cases and 943 controls (17.2% vs 12.3%, OR 1.49, 1.3–1.7, $p < 0.0001$), but face-to-face consultations were no different (IRR 1.08 (0.9–1.29, $p = 0.42$)).

Interpretation: There may be opportunities to reduce time to diagnosis for up to one third of cases, by up to two weeks. Diagnostic opportunities might be maximised by measures that improve access to primary care, and public awareness of T1DM.

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1. Introduction

The incidence of type-1 diabetes mellitus (T1DM), a chronic condition characterised by lack of insulin, peaks in children aged 5–7 years and in adolescents [1–4]. The UK has a comparatively high incidence of T1DM, at between 17 and 24 per 100,000 children, but even so the first presentation of a child with new-onset T1DM is an uncommon event for General Practitioners (GPs) [5].

A failure to administer insulin leads inevitably to diabetic ketoacidosis (DKA), the metabolic state characterised by the triad of hyperglycaemia, acidosis and ketonaemia, as a result harm can occur from a relatively short diagnostic delay. DKA has a mortality of 0.15–0.3% and is the leading cause of death in children with T1DM, being implicated in 83% of deaths [6,7]. Children are particularly vulnerable to DKA at the time of initial diagnosis, when 25% suffer DKA compared to 4–5% of children each year subsequently [8].

Epidemiological patterns support the hypothesis that diagnostic delay contributes to DKA at presentation [9]. Children given a diagnosis other than diabetes by their primary care doctor or whose diagnosis is delayed by as little as 24 h have a higher risk of ketoacidosis [10,11]. Children under the age of five years also have higher risk of DKA than older children [8,11]. It is possible that presenting with less obvious clinical patterns, and being less able to communicate symptoms contributes to delay. Children with infections at diagnosis are also high risk for DKA. As well as causing physiological disturbances infection might also confound the diagnostic process [8,11]. Underserved groups, for example children of ethnic minority and of lower socioeconomic status, are at higher risk of DKA at diagnosis [8,11]. Conversely, children with a first degree relative with T1DM, and children with more highly educated parents appear to be at lower risk of DKA, suggesting that access to medical care and diabetes awareness may facilitate timely diagnosis [8].

Clinical guidance issued by the UK's National Institute for Health and Care Excellence (NICE) describes alarm symptoms for T1DM (thirst, polyuria, weight loss, abdominal pain or fatigue) and symptoms of possible DKA (nausea or vomiting, hyperventilation, dehydration and reduced level of consciousness) [12]. Parents report symptoms an average of 16–17 days before diagnosis; a period long enough to potentially make an earlier diagnosis, and therefore reduce the risk of DKA [8]. NICE state that children with suspected T1DM should be referred for same day assessment by a specialist paediatric diabetes team [12]. In the UK, most unwell children are seen in primary care, but the frequency and pattern of consultations leading up to a diagnosis of T1DM is not known. We therefore sought to quantify opportunities for earlier diagnosis by examining children's primary care medical records prior to a diagnosis with T1DM, and comparing these to matched controls.

2. Methods

We conducted a case-control study of children with diabetes and matched controls, using routinely collected medical records from the 13 weeks before diagnosis. Data were provided by the THIN (The Health Improvement Network) database of routinely collected UK primary care records [13,14]. THIN presently covers the anonymised electronic medical records of 12 million patients, approximately 6% of the UK population.

Cases were aged 0–16 years and required at least one year of records prior to diagnosis (children younger than 1 year required data from birth). Cases required diabetes first coded between October 1998 and January 2011, defined by prespecified codes for a diagnosis, attending a specialist diabetes clinic, or diabetic medications. The original dataset included children with diabetes of all types. Cases with T1DM were identified by codes for the type of diabetes and for prescriptions. Cases were excluded if their records had ever been suggestive of type 2 diabetes or maturity onset diabetes of the young—either by inconsistent diagnostic codes for more than one type of diabetes, or by prescriptions [15]. Children with a consistent but unspecified diabetes type were included in the main analysis but excluded in sensitivity analyses. The index date for cases was the first date upon which the patient record indicated diabetes. These dates were then adjusted by taking into account clinical information to reduce bias due to reporting delays (Appendix A). Cases were ineligible if they had subsequent cessation of diabetic treatment or complications of diabetes without a diagnosis or if insulin had been prescribed for them more than 21 days prior to the index-date.

Cases were matched to four controls on: age, sex, registered healthcare provider, and index consultation date (controls had to have a consultation within 21 days of the index date for their matched case). Eligible controls were not diagnosed with diabetes at any point based on the same criteria as cases, and did not have any record of diabetic monitoring or possible or suspected complications of diabetes, e.g. diabetic retinopathy.

Consultation types are coded in the record, but children may have multiple codes on the same day, e.g. a code for a face-to-face visit with the GP and a code for a test and a phone call. In order to avoid double counting, the primary consultation type was determined by a hierarchical code structure (Appendix B). Because our goal was to estimate diagnostic opportunities in primary care, codes judged clinical were prioritized over those thought to be administrative, and practice-based codes were favoured over codes recording non-practice based activity. NICE alarm symptoms and DKA related outcomes were based on the presence or absence of codes suggestive of these symptoms without a hierarchical structure (Appendix C).

Matching on the index date introduced the possibility that controls were abnormally high users of healthcare (because children consulting more often have a higher probability of being selected). This was addressed in a sensitivity analysis where cases were used as their own controls, using 13 weeks preceding a consultation as close as possible to one year earlier to avoid introducing seasonal effects, and with a term for age included in the regressions to account for an extra year of life. This self-controlled analysis was undertaken on both definitions of cases (i.e. both including and excluding cases coded as diabetes of 'unspecified type').

Analyses were undertaken using Stata versions 11 and 14. Univariate associations were examined with the use of non-parametric tests (equality of median test for variables that

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