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#### ORIGINAL ARTICLE



# Treatment adherence and BMI reduction are key predictors of HbA1c 1 year after diagnosis of childhood type 2 diabetes in the United Kingdom

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NIHR Translational Research Collaboration for Rare Diseases (NIHR RD-TRC) **Background/Objective:** Type 2 Diabetes (T2DM) is increasing in childhood especially among females and South-Asians. Our objective was to report outcomes from a national cohort of children and adolescents with T2DM 1 year following diagnosis.

**Methods:** Clinician reported, 1-year follow-up of a cohort of children (<17 years) diagnosed with T2DM reported through the British Paediatric Surveillance Unit (BPSU) (April 2015-April 2016).

**Results:** One hundred (94%) of 106 baseline cases were available for review. Of these, five were lost to follow up and one had a revised diagnosis. Mean age at follow up was 15.3 years. Median BMI standard deviation scores (SDS) was 2.81 with a decrease of 0.13 SDS over a year. HbA1c <48 mmol/mol (UK target) was achieved in 38.8%. logHbA1c was predicted by clinician reported compliance and attendance concerns ( $\beta = 0.12$ , P = <0.0001) and change in body mass index (BMI) SDS at 1-year ( $\beta = 0.13$ , P=0.007). In over 50%, clinicians reported issues with compliance and attendance. Mean clinic attendance was 75%. Metformin was the most frequently used treatment at baseline (77%) and follow-up (87%). Microalbuminuria prevalence at 1-year was 16.4% compared to 4.2% at baseline and was associated with a higher HbA1c compared to those without microalbuminuria (60 vs 49 mmol/mol, P = 0.03).

**Conclusions:** Adherence to treatment and a reduction in BMI appear key to better outcomes a year after T2DM diagnosis. Retention and clinic attendance are concerning. The prevalence of microalbuminuria has increased 4-fold in the year following diagnosis and was associated with higher HbA1c.

#### **KEYWORDS**

adolescent, children, complications, obesity, type 2 diabetes

# 1 | INTRODUCTION

Type 2 diabetes (T2DM), once thought of as a condition of adulthood, is an emerging disease in childhood and adolescence. Globally, the highest incidence of T2DM in youth is in the United States, with 12.5 cases per 100 000 per year.<sup>1</sup> Recently, we reported the 2015-2016 UK incidence of T2DM in youth as 0.72 per 100 000 per year, with significant increases across a decade among South-Asians and females.<sup>2</sup> Our study, demonstrated that non-white ethnicity, female

gender, family history, and obesity were strongly associated with disease similar to reports from other countries.<sup>3</sup>

T2DM in youth has an aggressive clinical course (compared with the disease in adults) as it is associated with an accelerated loss of Bcells and rapid development of diabetes-related complications.<sup>4,5</sup> Diabetes-related complications are more common in children with T2DM compared to type 1 diabetes (T1DM). A study from Australia demonstrated higher rates of nephropathy (28% vs 6%) and hypertension (36% vs 16%) in those with T2DM compared to those with

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T1DM despite a shorter duration of disease.<sup>6</sup> A large observational study from the United States, with over 2000 children and adolescents, demonstrated higher odds of nephropathy, retinopathy, and peripheral neuropathy in those with T2DM compared to those with T1DM.<sup>7</sup> The trend of a higher prevalence of T2DM in youth and the rapid development of diabetes-related complications in this population is worrying for the decades ahead. Therefore, prevention, early detection in "at risk" populations and effective treatment strategies are crucial to tackle this disease.

The current guidance from International Society for Pediatric and Adolescent Diabetes (ISPAD) recommends lifestyle changes should be advised at diagnosis and first line treatment with metformin and insulin either alone or in combination.<sup>8</sup> In the previous 2005 cohort of children with T2DM, 94% of cases were commenced on some combination of insulin, metformin, and/or lifestyle changes.<sup>9</sup> Challenges to improving outcomes in T2DM in youth are numerous. Much of the evidence for management of T2DM is from adult experience. Clinicians need to be cognizant of licensing restrictions and the paucity of evidence and experience in drug usage in children. T1DM cases are evenly distributed across socioeconomic groups; however this is not the case with T2DM in youth; in the United States and Europe cases come from predominantly lower socioeconomic and educational backgrounds.<sup>10</sup> Treatment adherence and lack of engagement with diabetes services are key barriers to effective care. One study in Japan reported over 50% of cases of T2DM among youth was lost to follow up.<sup>11</sup>

The purpose of this study is to report on clinical outcomes from a national cohort of children and young people with T2DM 1-year on from diagnosis.

## 2 | METHODS

A prospective monthly surveillance of over 3400 consultant pediatricians in the United Kingdom and the Republic of Ireland (ROI) using the British Paediatric Surveillance Unit (BPSU) based at the Royal College of Paediatrics and Child Health (RCPCH), UK, was undertaken to identify new cases of T2DM in children under the age of 17 years between April 2015 and April 2016, with planned follow-up at 1-year following diagnosis. The initial study calculated the incidence and characterized the presentation of cases of T2DM.<sup>2</sup> In summary, during this period, an orange report card containing a list of conditions (including T2DM) was sent monthly, by post or electronically, to all consultant pediatricians in the United Kingdom and ROI. Respondents reported cases they saw in the previous month for conditions named on the card or ticked "Nothing to report." The BPSU forwarded the reporting clinician's details to the research team who sent a proforma requesting the child's clinical details. The case questionnaires were reviewed by J.H.S., T.B., and T.C. to examine if they satisfied the diagnostic criteria for T2DM.

Diabetes mellitus was defined according to American Diabetic Association<sup>12</sup> definition with fasting glucose above 7 mmol/L, a random glucose of above 11.1 mmol/L or stimulated glucose level of above 11.1 mmol/L following a standard oral glucose tolerance test (OGTT) or DCCT (Diabetes Control and Complications Trial)standardized HbA1c greater than 48 mmol/mol or 6.5%. T2DM was distinguished from other types of diabetes using the following criteria (a) presence of raised fasting insulin level (>132 pmol/L) or raised random C peptide level (>0.6 nmol/L)<sup>13,14</sup> or (b) the child was managed off insulin therapy for greater than 9 months in the absence of typical T1DM auto-antibodies. Exclusion criteria included: T1DM (positive auto-antibodies and/or persisting insulin requirement from diagnosis), monogenic diabetes, formerly known as Maturity Onset Diabetes of the Young (MODY), diabetes developing in a person with a known diabetes associated syndrome, such as Prader-Willi or Bardet-Biedl syndromes, diagnosis of diabetes while on medical therapy with a known diabetogenic medication, pancreatic failure, or Cystic Fibrosis Related Diabetes.

A follow-up questionnaire was sent to clinicians who reported confirmed cases of T2DM (n = 106), 12 months after the case was notified (between April 2016 and April 2017). These returned follow-up questionnaires were further scrutinized by the same reviewers (J.H.S., T.B., and T.C.) to see if they still met the diagnostic criteria for T2DM.

Clinicians were asked to provide evidence of comorbidities including hypertension (defined as systolic blood pressure above the 95th centile for sex, age, and height centile<sup>15</sup>), renal disease (macro/ microalbuminuria defined as above local cut offs of normal range), polycystic ovarian syndrome (evidenced by oligo or secondary amenorrhea, ultrasound showing multiple ovarian follicles, or biochemical picture of LH (Luteinizing Hormone):FSH (Follicle-stimulating hormone) ratio greater than three, low Sex Hormone Binding Globulin<sup>16</sup>), neuropathy, or retinopathy.

Clinicians were asked "Have you concerns regarding patient compliance with treatment and attendance?" with the options to respond either "Yes or No." If responders answered "Yes," there was free text space to comment further. The clinician could also record evidence of social care involvement with the child and their family. The number of clinical encounters (with either a doctor or allied health professional e.g., dietitian, nurse specialist, or psychologist) offered and attended since diagnosis were recorded. Percentage clinic attendance was calculated by dividing the number of clinical appointments attended by the number of clinical appointments offered multiplied by 100.

BMI standard deviation scores (SDS), also known as z scores, at diagnosis were calculated from weight, height, age, and gender using the 1990 UK growth standard curves<sup>17</sup> and overweight and obesity were defined as described in Cole et al<sup>18</sup> as follows: SDS greater than or equal to 1.30 and greater than or equal to 2.37, for boys; greater than or equal to 1.19 and greater than or equal to 2.25 for girls respectively. Ethnic groups were recorded by the reporting clinician as per the ethnicity categories defined by the UK Office for National Statistics.<sup>19</sup>

#### 2.1 | Ethical approval

This study was approved by the National Research Ethics Service Committee South West, Central Bristol, UK [14/SW/1143] and approved by Health Research Authority [15/CAG/0102].

#### 2.2 | Statistical analysis

HbA1c, BMI SDS, BMI SDS change at 1 year, and weight change were not normally distributed and thus non-parametric tests were used and median and interquartile range (IQR) reported to summarize data distributions. Mann-Whitney *U* tests were used to compare HbA1c across the binary variables of gender (Male/Female), child protection involvement (Yes/No), compliance and attendance concerns reported (Yes/No), microalbuminuria (Yes/No), treated with insulin (Yes/No), and evidence of BMI SDS improvement (Yes/No). Kruskal-Wallis test was used to compare HbA1c across ethnic groups and for weight change across different HbA1c categories. HbA1c was categorized according to risk stratification: less than 39 mmol (below risk stratification for prediabetes ie, normal<sup>20,21</sup>), 39 to 47 mmol/mol (increased risk of diabetes<sup>20</sup>), greater than 48 mmol/mol (diabetic range<sup>20</sup>) and greater than 80 mmol/mol (poorly controlled diabetes<sup>22</sup>).

The association of BMI SDS with ethnic groups was examined by using multiple linear regression model adjusted for potential confounding variables including number of clinic appointments attended, clinician reported compliance concerns, and formal social involvement.

Multiple linear regression analysis was used to investigate associations between HbA1c (outcome) and potential risk factors (predictors) including age, gender, ethnicity, social care involvement, compliance, and attendance concerns reported, number of clinic appointments attended, BMI SDS, and BMI SDS change over 1 year. Because the HbA1c was not normally distributed, the log10 transformed HbA1c was used as the response. The histograms of HbA1c and log HbA1c are shown in Figures S1 and S2 (Supporting Information) respectively. Estimated coefficients were back transformed using the equation, 100 ( $10^{\beta}$  – 1), where  $\beta$  is the estimated coefficient, to represent percentage change in HbA1c per unit increase in the corresponding predictor, while other predictors remain unchanged. Tests were performed to assess collinearity between predictor variables. A 5% level of significance was used for all tests. All analyses were performed using statistical software, IBM spss Statistics for Windows (IBM Corp, Armonk), Version 24.0.

# 3 | RESULTS

### 3.1 | The cohort

There were 106 cases of T2DM between April 2015 and April 2016. One hundred follow-up questionnaires were received from notifying clinicians giving a response of 94% (see Figure 1.). Five cases were completely lost to follow up (i.e., no clinic appointment attended since diagnosis) and therefore the notifying clinician could not report any ongoing clinical details. One case was reclassified as diabetes related to bone marrow transplantation. Therefore, at follow-up, 94 cases of T2DM were available for review.

#### 3.2 | Patient characteristics

The mean age at follow-up was 15.3 years (range 9.3-18.4 years). Sixty-seven per cent were female. Ethnic breakdown was white (45%), mixed ethnicity (4%), Asian (33%), Black, African, Caribbean or Black British (BACBB) (14%), Unknown (3%), and other (1%). 3

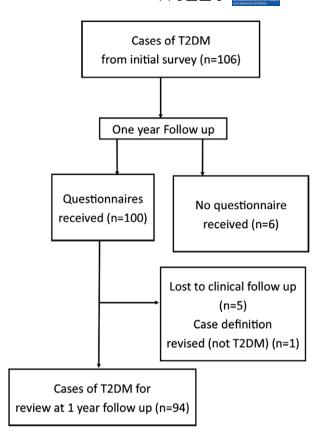


FIGURE 1 Case classification at 1 year follow-up

#### 3.3 | Patient outcomes

The median (IQR) weight change over the year was +2.5 kg (-1.5 to 6.0). A reduction in body weight of 5% or more from baseline weight was achieved in 14% of cases. At 1 year follow-up, the overall median (IQR) BMI SDS was 2.81 (2.30-3.23); 2.91 for girls (2.39-3.30) and 2.7 (2.25-2.97) for boys (with no evidence for a difference between sexes, P = 0.18). There was a decrease in BMI SDS at 1-year follow-up (median = -0.13; IQR = -0.30 to 0.10), and 58% demonstrated some reduction in BMI SDS. Eleven cases (10.5%) were able to reduce their BMI SDS score by more than 0.5 SDs, this being a level in obese adolescents likely to reflect an actual reduction in percentage fat mass.<sup>23</sup> At follow-up 74.2% were obese and 19.8% overweight. There was evidence that Asian cases had lower BMI SDS at follow-up (-0.49 lower BMI SDS compared to white children, P = 0.009) which is similar to that reported at baseline.<sup>2</sup>

The median (IQR) HbA1c at follow-up (mean approximately 14 months post diagnosis) was 53 mmol/mol (42.5-68.5) or 7%. There was no HbA1c data collected at diagnosis. At 1 year, an HbA1c below 39 mmol/mol was attained in 15.1%, between 39 and 47 mmol/mol in 23.7%, between 48 and 79 mmol/mol in 45.2% and above 80 mmol/mol in 16.1% of cases. There was some evidence that BMI SDS change at 1-year differs for those with HbA1c <39 mmol/mol (resolution of diabetes) from those with HbA1c >39 mmol/mol; median = -0.33, IQR = -0.87 to 0.03 vs median = -0.08, IQR = -0.25 to 0.12 respectively (P = 0.012).

There was no difference in median HbA1c between those who had any reduction in BMI SDS vs those who did not (53 vs 54 mmol/ mol, P = 0.33). There was no difference in median HbA1c between

ethnic groups White (52 mmol/mol), Mixed (54 mmol/mol), Asian (54 mmol/mol), and BACBB (53 mmol/mol) (P = 0.96). There was no difference in HbA1c between males, median = 54 mmol/mol and females, median = 52 mmol/mol, P = 0.4. There was a trend for those with formal social care involvement to have a higher HbA1c, but it did not reach significance (73 vs 53 mmol/mol respectively, P = 0.063). There is strong evidence that there was a difference between those with and those without reported compliance and attendance concerns (61.5 vs 45.5 mmol/mol respectively, P < 0.0001).

Results demonstrated that compliance or attendance concerns ( $\beta$  coefficient = 0.12, *P* = <0.0001) and BMI SDS change at 1 year ( $\beta$  coefficient = 0.13, *P* = 0.007) were associated with HbA1c when adjusted for sex, age, ethnicity, child protection concerns, clinic appointments attended, and current BMI SDS (see Table 1.). Clinician reported compliance or attendance concerns were associated with a 32.1% higher HbA1c compared to those without these concerns. One-unit increase in BMI SDS was associated with 34.9% increase in HbA1c.

#### 3.4 | Treatment

The most common treatment at diagnosis and at 1-year was metformin. Metformin was used as a monotherapy in 54/105 (51.4%) at diagnosis and 59/94 (62.8%) at 1-year (see Table 2), although 77% used metformin within their treatment regime at diagnosis and 87% at follow-up. The median (IQR) daily dose of metformin at follow-up was 1.5 g (1.0-2.0). The number treated with diet alone fell from 17% (18/105) to 11.7% (11/94).

The number treated with insulin, either alone or in combination with oral medication fell from 33/105 (31.4%) to 21/94 (22.3%) of cases at 1-year follow-up. Of the 21 cases, where reported or able to calculate, the dose range was 0.2 to 0.8 units/kg/day. Fourteen were using once daily long acting insulin, 6 were on basal-bolus regimens and 1 case on twice daily mixed insulin. As might be expected, those treated with insulin had a higher HbA1c (60 vs 44 mmol/mol, P = 0.017).

TABLE 1	Multiple linear	regression	model c	of predictors	of logHbA1c
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Glucagon-like peptide 1 (GLP-1) agonists were not used at diagnosis but four cases were using them at follow-up (3 liraglutide dose range 1.2-1.8 mg daily, 1 dulaglutide 1.5 mg weekly). No cases were given sulfonlyureas either at diagnosis or at follow-up.

Of those with an HbA1c below 39 mmol/mol, management included; diet and lifestyle alone (n = 4), metformin (n = 9), and metformin and insulin (n = 1).

#### 3.5 | Comorbidity

The comorbidities reported at baseline and at follow-up are shown in Table 3. The reporting of comorbidities was incomplete, reflected in the variable denominator used for calculating the percentage with each condition. Absolute numbers of those with hypertension, retinopathy, and dyslipidemia were reduced at 1 year. Of the 20 cases with hypertension at baseline, only two remained hypertensive at follow-up. There was no difference in HbA1c, BMI SDS change at 1 year or percentage weight change between those who remained hypertensive and those in which it had resolved. Of the 12 cases of hypertension at 1 year follow-up. 2 were on antihypertensive agents. Only 1 case was reported to be on a statin. Of the 11 with PCOS (Polycystic Ovary Syndrome), 10 were on metformin and 1 was treated with Drospirenone (Yasmin). Three cases had evidence of microalbuminuria at baseline, 11 at their most recent follow-up. There is evidence that those with microalbuminuria had higher HbA1c compared to those without (median 60 vs 49 mmol/mol. P = 0.033). However, there was no difference in HbA1c between those with each of the other comorbidities and those without; including hypertension (P = 0.76), retinopathy (P = 0.16), and PCOS (P = 0.08).

At follow-up 4.3% (4/94) of cases were under formal social care involvement (Child protection or child in need). Clinicians reported issues with compliance/adherence to medication and treatment plan in 53% of cases. The mean clinic attendance was 75% (S.D. 28) with mean appointments attended 3.8 per year (SD 1.6, minimum 1, maximum 10).

	Unstandardized coefficients		% change in HbA1c per one unit increase in predictor		
Model	β	SE	- · · · · · · · · · · · · · · · · · · ·	t	Sig.
Constant	1.63	0.17		9.86	0.00
Ethnic group "Mixed"	0.01	0.07	2.33	0.14	0.89
Ethnic group "Asian"	0.02	0.03	3.75	0.48	0.64
Ethnic group "BACBB"	0.02	0.04	5.20	0.54	0.59
Compliance concerns reported by clinician	0.12	0.03	32.13	4.26	0.00
Number of clinic appointments attended	0.004	0.009	0.93	0.42	0.68
Formal social care involvement	0.09	0.07	22.74	1.24	0.22
BMI SDS change at 1 year follow-up	0.13	0.05	34.90	2.75	0.007
BMI SDS at 1 year follow-up	-0.03	0.02	-5.81	-1.20	0.23
Sex	0.05	0.03	11.94	1.62	0.11
Age at follow-up	0.01	0.01	1.39	0.729	0.47

Abbreviations: BACBB, Black, African, Caribbean or Black British; SDS, standard deviation scores. Dependent variable =  $\log^{10}$  HbA1c.

 $R^2 = 0.31, P = 0.001.$ 

#### TABLE 2 Treatment of T2DM at diagnosis and at 1-year follow-up

Treatment	Baseline treatment (%)	1 year follow-up (%)
Diet and lifestyle alone	18/105 (17.1)	11/94 (11.7)
Insulin alone	6/105 (5.7)	1/94 (1.1)
Metformin alone	54/105 (51.4)	59/94 (62.8)
Insulin and metformin	27/105 (25.7)	18/94 (19.1)
GLP-1 agonist + insulin + metformin	0/105 (0)	1/94 (1.1)
GLP-1 agonist + metformin	0/105 (0)	3/94 (3.2)
DPP-4 inhibitors + insulin + metformin	0/105 (0)	1/94 (1.1)

Abbreviations: DPP-4, Dipeptidyl Peptidase-4; GLP, glucagon-like peptide; T2DM, type 2 diabetes.

TABLE 3 Comorbidities reported at baseline and 1-year follow-up

Complications reported	Baseline (%)	1 year follow-up (%)
Hypertension	20/95 (21.1)	12/86 (14)
Retinopathy	6/105 (5.7)	2/94 (2.1)
Microalbuminuria at last follow-up	3/71 (4.2)	11/67 (16.4)
PCOS	11/70 (15.7)	10/63 (15.9)
Nephropathy clinically suspected	3/71 (4.2)	3/94 (3.2)
Dyslipidemia	9/105 (8.6)	1/94 (1.1)

Note the denominator reported in the table for each complication reflects the number of cases with results or responses.

## 4 | DISCUSSION

Young people with T2DM are at significant risk of diabetes-related complications and therefore early engagement, treatment, and achieving optimal glycemic control are crucial to achieve better long term clinical outcomes. The key messages from our study are that adherence to treatment and a reduction in BMI is strongly associated with a lower HbA1c. This can be a reassuring and simple message to young people with T2DM; adhere to treatment and you will see an improvement in your HbA1c and help reduce long term complications. Furthermore, reducing your BMI should remain the key target and is associated with improved glucose control. Greater BMI loss (0.33 BMI SDS) was attained by those with an HbA1c in "normal euglycemic" range (<39 mmol/mol) and for each one-unit increase in BMI SD score the HbA1c increases by over a third suggesting that weight reduction strategies are important to restore normal glycemic parameters. This is similar to recommendations that a reduction in BMI SDS score by more than 0.5 SDs, is likely to reflect an actual reduction in percentage fat mass.<sup>23</sup> In 2005, the BPSU conducted a survey of type 2 diabetes in the UK children<sup>9,24</sup> using the same methodology as this study (ie, follow-up questionnaire sent 1 year on from diagnosis). This allows for direct comparison of a range of clinical outcomes across the decade. Compared to the cohort from 2005, where BMI SDS fell by 0.11 a year after diagnosis<sup>9</sup> this group had a similar reduction of 0.13 suggesting we are no further forward in attaining significant weight improvement and should perhaps consider recent evidence from DiRECT trial on the utility of low calorie diets after diagnosis.<sup>25</sup> Weight loss was demonstrated in the TODAY cohort, to be associated with better cardiometabolic outcomes including HbA1c,<sup>26</sup> though interestingly there was no effect from intensive lifestyle interventions on weight-related outcomes.<sup>27</sup>

Over half of those diagnosed with T2DM had adherence concerns at 1-year follow-up, and on average those with T2DM are not attending a quarter of appointments offered. It is a worry that 5% of cases did not attend any follow-up after diagnosis, though significant loss to follow up has been described previously.<sup>11</sup> Although a previous study has shown that clinic attendance and HbA1c are associated,<sup>28</sup> we did not demonstrate this association in our study when we adjusted for other covariables. The challenge is engaging young people with T2DM in the diabetes clinical services and their management plan. The National Paediatric Diabetes Audit (UK) (NPDA)<sup>29</sup> reported only 2.2% of cases treated in pediatric diabetes units are T2DM, and much of the expertise from clinicians, nurse specialists, and allied health professionals and the service is focused on those with T1DM. Therefore, creativity in approach, better training for diabetes teams, and adolescent accessible services must be championed for this subset of patients. In those with T2DM, a lower HbA1c has been reported by involving peer-to-peer support<sup>30</sup> and community health workers<sup>31</sup> in diabetes management. T2DM in children has been described as a disease of poverty,<sup>32</sup> in addition to this a disproportionate number of our cohort had active child protection interventions in place. Therefore, close liaison with social care teams is essential to support these children and their families in managing all aspects of the disease and its impact on the family. Positive experiences have been reported in having a social worker part of the team working with voung people with T2DM.<sup>33</sup>

The median HbA1c was higher in 2015 compared to 2005 (53 vs 48 mmol/mol); although a modest increase, it reflects a HbA1c above the target range for this cohort.<sup>34</sup>

Our study showed no significant gender disparity with regard to HbA1c, though there was a trend for higher HbA1c in boys in the multiple regression model (see Table 1,  $\beta$  = 0.05, *P* = 0.11). At a population level, in non-diabetic adolescents, HbA1c has been reported to be higher in boys than girls.<sup>35</sup> A recent study from the United Kingdom demonstrated higher HbA1c among young adult males with T2DM compared to females.<sup>36</sup> Furthermore, we did not demonstrate

that ethnicity was associated with HbA1c. This is not consistent with studies from the United States, for example the SEARCH<sup>37</sup> study reported higher HbA1c among non-white ethnic groups.

In terms of treatment, the majority are following the IPSAD guidance on initial treatment with metformin and/or insulin. Insulin was often started at diagnosis when the patient was either not metabolically stable (or when the diagnosis of T2DM was not confirmed). There was a subsequent fall in those treated with insulin with transition to other treatment regimens once the patient was clinically stable and the diagnosis of T2DM was evident. The median dose of metformin of 1.5 g daily is within the recommended range (1 g BD maximum) as recommended by IPSAD. Compared to 2005, the notable change in management is the use of GLP-1 agonists. In 2005, GLP-1 agonists were only just being introduced into adult T2DM care, however in 2015 4% of our cohort were reportedly on these drugs. In adults, GLP-1 agonists (e.g., liraglutide) have shown to be efficacious and safe in reducing HbA1c (compared to placebo) with fewer episodes of hypoglycemia compared to sulfonylurea (glimepiride).<sup>38</sup> In children, the experience of using GLP-1 agonists is limited. However, studies have shown it safe and effective compared to placebo in a pediatric population.<sup>39</sup>

The rise in cases of microalbuminuria is concerning with a 4-fold increase over 1 year. Those with microalbuminuria had higher HbA1c levels, suggesting early-onset nephropathy may associate with poorer early diabetes control. A recent paper from Scandinavia, sub-dividing T2DM into five clusters did identify that cluster 3 (Severe Insulin Resistant Diabetes [SIRD]) associated more with accelerated kidney disease and this group may be over-represented in our cohort providing an alternate basis for the rapid increase in prevalence as insulin resistance appears intimately linked to kidney damage.<sup>40,41</sup> The rapid development of microalbuminuria has been documented previously with one study demonstrating 6.3% prevalence of microalbuminuria at baseline (median disease duration of 7 months) and 16.6% by 36 months.<sup>42</sup>

It is worrying that 28% of cases had no screen for microalbuminuria reported. Interestingly, prevalence of hypertension (21%-14%) and dyslipidemia (9%-1%) fell over the year and may reflect an improvement in overall cardiometabolic health with treatment for T2DM.

The study relies on the accuracy and objectivity of clinician responses. The clinician reported concerns about compliance with treatment cannot be quantified (as clinic attendance can be) and to do this would require more intensive assessment of the patient's compliance to medication. This is beyond the scope of our study methodology but warrants further investigation in future studies. It is interesting that clinic attendance (which was measured) was not associated with HbA1c, suggesting that engagement and adherence to management plans is more complex than just turning up for appointments. Only 6 (6%) cases of 106 at baseline failed to return a completed questionnaire. In the 2005 follow-up study the figure was 4%.

T2DM diagnosed in childhood provides a management challenge for clinicians. With the continued rise in cases in this population and the aggressive nature of the disease, it is essential that we learn how best to engage with these children and their families to ensure we have better outcomes in the next 10 years.

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#### Author contributions

T.C. collected the data, analyzed the data and led the writing of the manuscript. J.H.S., T.B. and R.L. devised the study. T.C., J.H.S., T.B. reviewed the cases. O.M. advised on the statistical analysis. J.H.S., R.L., O.M. and T.B. contributed to the revision of the manuscript. Data on Birmingham children were collected with the support of the NIHR Wellcome Clinical Research Facility staff. The authors would like to thank the staff at the BPSU and the pediatricians who reported cases and returned data.

#### Disclaimer

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#### SUPPORTING INFORMATION

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

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