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Inequalities in glycaemic control in childhood onset type 2 diabetes in England and Wales – A national population-based longitudinal study

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Abstract

Background Not much is known about glycaemic-control trajectories in childhood-onset type 2 diabetes (T2D). We investigated characteristics of children and young people (CYP) with T2D and inequalities in glycaemic control.

Methods We studied 747 CYP with T2D, <19 years old in 2009-2016 (from total population-based National Paediatric Diabetes Audit [>95% diabetes cases in England/Wales]). Linear mixed-effects modelling was used to assess socioeconomic and ethnic differences in longitudinal glycated haemoglobin (HbA_{1c}) trajectories during four years post-diagnosis (3,326 HbA_{1c} datapoints, mean 4.5 datapoints/subject). Self-identified ethnicity was grouped into six categories. Index of Multiple Deprivation (small area-level deprivation measure) was grouped into SES quintiles for analysis.

Results 58% were non-White, 66% were female and 41% were in the most disadvantaged SES quintile. Mean age and HbA_{1c} at diagnosis were 13.4 years and 68mmol/mol respectively. Following an initial decrease between diagnosis and end of year 1 (-15.2mmol/mol 95%CI, -19.2, -11.2), HbA_{1c} trajectories increased between years 1 and 3 (10mmol/mol, 7.6, 12.4), followed by slight gradual decrease subsequently (-1.6mmol/mol, -2, -1.1).

Compared to White CYP, Pakistani children had higher HbA_{1c} at diagnosis (13.2 mmol/mol, 5.6-20.9). During follow-up, mixed-ethnicity and Pakistani CYP had poorer glycaemic control. Compared to children in the most disadvantaged quintile, those in the most advantaged had lower HbA_{1c} at diagnosis (-6.3mmol, -12.6, -0.1). Differences by SES remained during follow-up. Mutual adjustment for SES and ethnicity did not substantially alter the above estimates.

Conclusions About two thirds of children with childhood-onset T2D were non-White, female adolescents, just under half of whom live in the most disadvantaged areas of England and Wales. Additionally, there are substantial socioeconomic and ethnic inequalities in diabetes control.

Keywords: Diabetes Mellitus, Type 2; Glycated Hemoglobin A; Healthcare Disparities; Ethnic Groups; Socioeconomic Factors

Introduction

Considerable evidence indicates that children and young people (CYP) from ethnic minority groups and more disadvantaged backgrounds are at greater risk for childhood-onset type 2 diabetes in high-income countries[1-5]. Type 2 diabetes diagnosed in adolescence presents a different set of challenges for both patient and healthcare provider compared to that diagnosed in adulthood because is a relatively new phenomenon (increasing in incidence due to the ongoing obesity epidemic) and till date both research and healthcare provision in paediatric diabetes has largely focused on type 1 diabetes[2 2,6]. Furthermore, paediatric diabetes centres have limited experience in managing type 2 compared to type 1 diabetes, particularly in administrating the newer therapies used in adults with type 2 diabetes, many of which remain unlicensed in this age group. CYP with this condition are at greater risk for future comorbidities and complications compared to those with type 1 diabetes[2,5,7-9]. These include renal disease (the most common), retinopathy, dyslipidaemia, hypertension, depression and neuropsychiatric disorders and poorer pregnancy outcomes which further exacerbate glycaemic control[8,10-13]. Treatment and management of type 2 diabetes is complicated involving treating several diseases and there is limited evidence on the efficacy of the currently available few drug therapies[6]. This is further complicated by evidence suggesting that CYP with this chronic condition require individually tailored treatments.

Ethnic minorities and those from more deprived backgrounds have an increased risk for poorer management of chronic conditions leading to increased risk for associated comorbidities[14,15]. Reasons could include poorer access to healthcare systems, cultural/ethnic differences and barriers to managing a chronic condition, genetic

predisposition to the disease itself or comorbidities commonly associated with it[16,17]. Ethnic minorities and lower socioeconomic status (SES) CYP with type 1 diabetes are at increased risk for poorer glycaemic control during long-term follow-up which also increases their risk for acute and chronic complications[18,19]. This could be the case in CYP with type 2 diabetes, yet there is very limited evidence on glycaemic control trajectories in childhood-onset type 2 diabetes following diagnosis. Most longitudinal studies originate from North America and none have been total population-based[2]. Studies thus far have been nationally representative sub-samples or regional populations, with small sample sizes and/or follow-up less than 3 years. Furthermore there is a lack of comprehensive evidence on social and ethnic differences in glycaemic control in a national population-based cohort, which is an important gap in the evidence base since type 2 diabetes primarily affects more deprived and ethnic minority CYP. Therefore, the aim was to analyse socioeconomic and ethnic differences in glycaemic control using a population-based national cohort of CYP with type 2 diabetes in England and Wales.

Methods

Design, setting and data source

Data for this longitudinal study were obtained from the National Paediatric Diabetes Audit (NPDA) for England and Wales. The audit (initiated 2002) reached near 100% participation covering all 178 paediatric diabetes clinics in 2012. It is comprehensive including demographic and clinical data on almost all CYP <19 years of age with all forms of diabetes and treated at specialist paediatric diabetes clinics. This study focused on data spanning a period of seven years (2009-10 to 2015-16) but excluded data from the 2010-11 audit year which could not be linked due to administrative reasons. We excluded data from 2002-2008 due to the small number of CYP with type 2 diabetes and the low national coverage during the audit's initial years. The National Institute of Health and Care Excellence (NICE) recommends a patient with any form of diabetes be offered integrated healthcare by a multidisciplinary team at a clinic, with HbA_{1c} levels, height and weight recorded at each visit[20]. All demographic and clinical parameters are recorded systematically across clinics enabling comparison. For this analysis, we derived an incident cohort with inclusion criteria comprising a diagnosis of type 2 diagnosis, age<19 years on the first day of the audit, a minimum of one visit to a clinic during any audit year and valid information on date of diagnosis and sex. 1,053 CYP met the inclusion criteria during the study period and were eligible to be included in the study.

Outcome and independent variables

Glycaemic control – measured by HbA_{1c} levels – was the main outcome of interest. HbA_{1c} values recorded as percentages were converted to mmol/mol using the formula: (HbA_{1c} value in percentage-2.15) x 10.929. HbA_{1c} values within the range of 20 to 200mmol/mol and recorded within an audit year as reported by the clinics to

the NPDA were considered as valid. All valid HbA_{1c} values recorded for a subject during the study period were included in the analysis (i.e. multiple HbA_{1c} datapoints recorded for any single individual within an audit were treated independently). As per NICE recommendations (prior to 2015), HbA_{1c} values <58mmol/mol and ≥80mmol/mol were categorised as good and poor control respectively[20].

Independent variables included age at diagnosis, sex, diabetes duration, ethnicity and SES. Age at diagnosis was calculated by subtracting the date of birth from the date of diagnosis. Duration of diabetes was calculated by subtracting date of diabetes diagnosis from the date of clinic visit. BMI was calculated as weight (in kilograms) divided by height (in metres) squared. Overweight and obesity in children was determined by using age- and sex-specific cut-offs proposed by the International Obesity Task Force[21]. Age and sex appropriate BMI standard deviation scores or Z-scores were calculated from the UK 1990 growth reference[22].

Patients (or their parents) self-reported their ethnicity using one of fifteen categories recommended by the Information Standards Board for Health and Social Care (including the option to decline stating their ethnicity, the 'Not Stated' category). The fifteen ethnic categories were collapsed into six broader groups (listed in Supplemental Table 1): White (British, Irish and any other White background), Mixed (any form of mixed ethnic background), Asian Pakistani, Asian and 'other' (comprising subjects of all other Asian backgrounds but mostly South Asian in origin and any other ethnic background including Chinese and Arabic), Black (subjects of Caribbean and African origin), and 'Not Stated'. We implemented a two stage process while cleaning the ethnicity variable to ensure that each subject had the same ethnic group entered throughout follow-up,: First, the last recorded entry for ethnicity was used in the analysis (assuming subjects that identify their ethnicity at

older ages reflect their true choice and data validity and completion is better in the most recent years). Second, if there was a discrepancy in the entry for ethnicity between the last and previous visits, then the most commonly entered category was chosen (for example, if a subject identified as White in all visits, but as Black in the final visit, then White was chosen as it was the most commonly entered ethnic category).

Indices of Multiple Deprivation (IMD) 2010 were derived from postcodes for England, and the Welsh Indices of Multiple Deprivation 2008 for Wales[23]. These indicators of deprivation of small area of residence were used as a measure of SES. Although the two countries use slightly differing indices to define deprivation, adjustment was made to align the two techniques[24]. The IMD is a multidimensional index which measures the relative deprivation experienced by an individual living in an area with an average of 1,500 individuals. Scores are derived from a weighted combination of several indicators across seven distinct domains including income, employment, education skills and training, health, barriers to housing and services, living environment and crime. IMD rank scores were grouped into quintiles for analysis, with the first and fifth quintiles corresponding to the least and most disadvantaged respectively.

Treatment regimen was categorised into diet and exercise, oral hypoglyceamics and oral hypoglycaemics plus insulin injections.

Data analysis

Associations between ethnicity, SES and other covariates were analysed using univariable linear regression or Chi square tests for differences of proportions for continuous and categorical variables respectively. Continuous variables are

presented as mean values with standard deviations and categorical variables as frequencies.

Longitudinal analysis – Longitudinal change in HbA_{1c} trajectories were analysed using linear mixed effects modelling (growth curve analysis). This method enables comparison of population average HbA_{1c} levels and change over time by independent variables (SES, ethnicity and treatment regimen) while controlling for covariates. We ran three sets of linear mixed effects models: In set 1, SES was the main exposure of interest with subsequent models adjusted for covariates (age at diagnosis and sex). In set 2, ethnicity was the main exposure of interest and subsequent models were adjusted for covariates including SES. Models in set 3 were based on a smaller study population not missing data on treatment regimen and included models adjusted for all covariates of interest.

Each set of modelling comprised four models: Model 1: Random intercept only (unconditional growth model) to define the intraclass correlation coefficient (ICC); Model 2: Random intercept and random slope model (which in each set had a better statistical fit and was used in all subsequent models); Model 3: adjusted for our primary predictor; SES or ethnicity; and Model 4: additionally adjusted for other covariates (sex, age at diagnosis and treatment type). In all models we approximated time trends including a cubic term for time since diagnosis (duration in years) as this provided a better statistical fit compared to having only linear and quadratic terms. We separately assessed whether SES and ethnicity interact with duration on mean HbA_{1c} trajectories by testing for interactions between SES/ethnicity and diabetes duration. Models included individuals with any amount of HbA_{1c} data up to four years following diagnosis (i.e. they could have differ in their follow-up time). Additionally, models were restricted to four years follow-up following diagnosis since HbA_{1c}

datapoints were considerably fewer after this. Model parameters were estimated by maximum likelihood and a heterogeneous autoregressive covariance structure was used in all models. We used generalized likelihood ratio statistics, −2 log-likelihood (−2 LL), Aikake information criterion (AIC), and sample-adjusted Bayesian information criterion (BIC) to compare model fit between subsequent nested models, and Wald statistics to test hypotheses about model parameters. In all models ethnicity, SES, age at diagnosis (continuous) and sex were entered as time-invariant predictors whereas treatment regimen was entered as time-variant.

HbA_{1c} trajectories were plotted at the group level (i.e. SES or ethnicity) to visualise model fit and were based on model 4 above (adjusted for all covariates). All statistical analyses were conducted using STATA 14 (College Station, TX, USA).

Sensitivity analysis: We investigated whether subjects excluded due to missing data on treatment regimen differed from those included in the models with data on treatment regimen. The two groups were compared on all covariates using univariable linear regression or chi-squared tests for differences of proportions for continuous and categorical variables, respectively.

Ethics

Ethical approval was not required by the University College London (UCL) Research Ethics Committee. The NPDA has section 251 approval granted by the Confidentiality Advisory Group to collect patient identifiable information for the purpose of audit. For this study all participants were anonymised making them unidentifiable. The study is registered with the R&D office, Institute of Child Health, UCL, (Project number 14PP08).

Results

Of the 1,053 CYP identified with type 2 diabetes, 306 subjects had missing data on various covariates (24 missing data on diabetes duration, 3 missing age at diagnosis, 74 missing HbA_{1c}, 11 missing SES and 134 missing ethnicity, Supplemental Figure S1). A further 60 subjects only had data 4 years post-diagnosis leaving a final study population of 747 CYP (with 3,326 HbA_{1c} datapoints) for our primary analysis.

Models in set 3 adjusted for treatment regimen were based on a sub-sample of 557 CYP (with 2,851 HbA_{1c} datapoints). There were no significant differences between the sub-sample with data on treatment regimen and those excluded because of missing data (N=190) when compared on sex, age at diagnosis, SES and duration of diabetes. However, we did find significant but minor differences in the distribution of ethnic groups between the two populations (for example, the 'not stated' and White groups had higher proportions with missing data on treatment regimen).

Tables 1 and 2 summarise cohort characteristics by SES and ethnicity respectively. Sixty-seven percent of subjects were female and 71% were obese. Forty one percent were from the most disadvantaged SES quintile. Mean age at diagnosis was 13.4 years. CYP in the least disadvantaged SES quintiles had lower HbA_{1c} levels at diagnosis compared to those in the most deprived quintiles but differences were not statistically significant (Table 1). Pakistani CYP had a significantly higher median SES score compared to White CYP (Table 2) and had the largest proportion of subjects in the most deprived SES quintile (64% compared to 37% for White CYP, Table 2). There were no significant differences in distribution of proportions of sex, overweight/obesity and treatment regimen at diagnosis between ethnic groups.

Overall, 71% and 20% of subjects were obese and overweight respectively. 14% of

subjects had poor glycaemic control one year post-diagnosis which increased to 31% four years post-diagnosis (Tables 1 & 2).

Longitudinal analysis

Mean HbA_{1c} at diagnosis (model intercept) for the cohort was 64.9mmol/mol (95% CI 62.5-67.2). There were significant linear, quadratic and cubic terms for duration of diabetes. This implies on average, all subjects experienced a decrease in HbA_{1c} levels between diagnosis and one year following diagnosis (negative linear term, -15.2mmol/mol, Supplemental Figure S2). This was followed by a substantial increase between one and three years post-diagnosis (positive quadratic term, 10.8mmol/mol) and finally a much smaller decrease approximately three years post-diagnosis (negative cubic term, -1.7mmol/mol) in HbA_{1c} levels.

CYP from the two least disadvantaged SES quintiles had significantly lower HbA_{1c} at diagnosis (-7.2mmol/mol, -13.4, -1 for CYP in the least deprived quintile, Table 3) compared to most deprived CYP. A test for interaction between diabetes duration and SES was not statistically significant indicating the observed differences in HbA_{1c} at diagnosis by SES persisted equally throughout follow-up (Figure 1A).

Table 4 and Figure 1B show results from modelling ethnic differences in glycaemic control. All ethnic minority groups had higher HbA_{1c} at diagnosis compared to White CYP but differences were significant only in Pakistani CYP (14.8mmol/mol, 7.2-22.4, higher HbA_{1c}). The test for interaction between ethnicity and diabetes duration was statistically significant (p=0.004) indicating that ethnic-specific HbA_{1c} trajectories varied by time. Adjustment for SES made little difference to the ethnicity-HbA_{1c} estimates. During follow-up, the mixed-ethnicity and Pakistani groups (linear interaction terms -16.1mmol/mol, -32.2, -0.1 and -27.5mmol/mol, -40.6, -14.3 respectively, Model 4, Table 4) had substantial and additional decreases in HbA_{1c}

levels compared to the White group. However, these were offset by large increases in HbA_{1c} in the same two groups towards the end of follow-up (positive quadratic interaction terms, Model 4, Table 4 and Figure 1B).

In all regression models, neither sex or age at diagnosis were associated with glycaemic control.

Supplemental Table S2 shows socioeconomic and ethnic effects on glycaemic control adjusted for treatment regimen. The previously observed higher HbA_{1c} in Pakistani and more disadvantaged groups were still evident but marginally attenuated (Model 4, Supplemental Table S2). Subjects on oral hypoglycaemics and insulin injections had significantly higher HbA_{1c} at diagnosis compared to those on oral hypoglycaemic only (10.5mmol/mol, 7.6-13.3, Model 4, Supplemental Table 2).

Discussion

In England and Wales, CYP with type 2 diabetes from socioeconomically disadvantaged areas had significantly higher HbA_{1c} at diagnosis compared to those from less disadvantaged areas and differences persisted throughout follow-up. Pakistani CYP had significantly higher HbA_{1c} at diagnosis, and both Pakistani and mixed-ethnicity CYP had significantly poorer glycaemic control during follow-up. This total population study confirms that childhood-onset type 2 diabetes largely affects overweight female adolescents from disadvantaged and ethnic minority backgrounds.

Longitudinal studies on glycaemic control in childhood-onset type 2 diabetes are limited with most studies originating from North America. The two larger studies that reported extensively on type 2 diabetes in CYP are the Treatment Options for Type 2 Diabetes in Adolescent and Youth (TODAY), a randomised control trial (RCT) focusing on the efficacy of treatment regimens and the SEARCH for Diabetes in Youth study based on a nationally representative sample of subjects from five states in the US[25,26]. Both studies reported higher HbA_{1c} at diagnosis and during follow-up in ethnic minority groups. However, comparisons are limited as the TODAY study is a RCT which reported that ethnic minorities (Black and Hispanics) were more likely to achieve failure (defined as loss of glycaemic control [HbA_{1c}≥9%] over a 5 year-follow-up without adjustment for SES. The SEARCH study (based on a smaller sample of subjects, N=373) primarily reported ethnic differences in HbA_{1c} between diagnosis and one year after diagnosis[26]. Neither study reported HbA_{1c} trajectories by SES or ethnicity and both are based on regional or nationally representative samples but are not total-population based studies. As expected the ethnic groups

analysed in these studies are more relevant to the US. Comparisons are further limited as the healthcare system in the US is based on the type of insurance coverage. Other studies that explored glycaemic control in CYP with type 2 diabetes have been much smaller in size, based on regional diabetes registries, with shorter follow-up, cross-sectional in design and/or reported HbA_{1c} at specific time points such as diagnosis, 1 year after diagnosis or the mean value during follow-up[5,27-29]. The only UK study that reported glycaemic control in CYP with type 2 diabetes was based on a smaller sample (N=73) with cases identified via the British Paediatric Surveillance Unit (which provides a nationally representative sample)[30]. Comparisons are limited as the study had a short follow-up of one year post-diagnosis and used the older recommendations for targeted glycaemic control. Mean HbA_{1c} at diagnosis and the time course for the observed initial but transient reduction in HbA_{1c} between diagnosis and 12 months observed in this study has been reported in other smaller studies[27,31]. This is most likely a response to initial treatment, diabetes education and lifestyle changes. However, the rise in HbA_{1c} in all groups in the subsequent two years is consistent with evolving beta-cell failure together with reduced adherence to treatments and the initial lifestyle changes, together with increasing insulin resistance that occurs during adolescence[32]. This evolution of disease processes in type 2 diabetes in this age group and concurrent rise in HbA_{1c} from twelve months onwards indicate that either current treatment strategies are potentially ineffective, compliance is poor or diabetes presenting in adolescence represents a more serious phenotype of the disease compared to that diagnosed in adulthood. Additionally, recommended lifestyle changes such as weight reduction seem to be limited (as observed by the largely stable BMI trajectory over time since diagnosis in this cohort – data not shown). Including BMI in the models did not affect

the observed ethnicity- and SES-estimates for HbA1c and hence were not reported in the final models.

The main strength of this study is that it describes the natural history of glycaemic control in a large well-described population based cohort with >95% of childhood-onset type 2 diabetes cases in England and Wales. Other strengths include the longitudinal prospective population-based design, self-identified ethnicity, follow-up from diagnosis onwards, and relatively low missing data on most covariates (sex, age at diagnosis, duration and SES with <3% missing data). All data are recorded systematically across all paediatric clinics which then submit data to a centralized database helping minimize selection bias. Mixed effect modelling allows for the inclusion of a large number of data points including subjects with just one HbA_{1c} measurement even when the data are 'unbalanced' (subjects with differing number of data points measured at different time points).

We were unable to control for family history of diabetes, physical activity and diet which could potentially be associated with glycaemic control as this information is not collected. The majority of CYP begin transitioning to adult healthcare services from around age 16 and as type 2 diabetes is largely diagnosed in adolescence, a follow-up >4 years is not possible due to the paucity of HbA_{1c} data from the fourth year on. The apparent better glycaemic control observed towards the end of follow-up is more likely an artefact due to the modelling strategy and paucity of data and should be interpreted with caution. Models adjusted for treatment regimen should be interpreted with caution as this variable was more likely to be missing during the initial years of the audit. However, the reported associations are in the expected direction. Lastly, it is possible that the 'not stated' ethnic group includes CYP missing information on ethnicity.

There is considerable focus on social determinants of health (SDOH) as a potential explanatory factor for both the aetiology of type 2 diabetes and glycaemic control in youth. As in our study, others showed substantial proportions (≥40%) of subjects come from the most deprived families[5,33,34]. The conceptual model for SDOH in youth with T2D proposes social determinants such as low family income, low parental education and higher levels of stress (in parents/caregivers and youth) are more prevalent in some ethnic minorities leading to both onset of type 2 diabetes and poorer glycaemic control acting via mediators like poorer lifestyle choices, healthcare access, family knowledge and coping skills and management of chronic diseases[35]. Attitudes of healthcare providers when treating CYP from diverse ethnic and socioeconomic backgrounds could be another explanatory factor though not as significant as those above and harder to assess in observational studies like ours. Another explanation could be physiological differences between ethnic groups (like higher rates of insulin resistance in non-White Europeans). There is evidence for higher HbA_{1c} in both type 2 diabetic and non-diabetic people of non-White European origin. In several studies, the observed ethnic differences in glycaemic control remain after adjustment for a number of social and clinical factors[36,37]. Additionally, inter-individual variation in HbA_{1c} is linked to non-glycaemic factors including sex, visceral fat, hormones and differences in biological variation of haemoglobin glycation[36,38]. Thus there is an ongoing debate on whether HbA_{1c} is ideal for comparing glycaemic control across ethnic groups and as a diagnostic test for diabetes[36]. Nonetheless, the body of evidence linking poorer glycaemic control with higher risk for micro- and macro-vascular complications is undisputed. Our results are concerning as they highlight a potential and substantial increase in the burden of

diabetes-related complications in the near future as poorer glycaemic control starts considerably earlier in those with childhood-onset type 2 diabetes. Ethnic minority adults with type 2 diabetes are at increased risk for complications including cardiovascular disease[39].

In addition to reducing the social inequalities that drive inequalities in child health, reducing inequalities in glycaemic control in CYP with type 2 diabetes will require substantial interventions beyond the healthcare sector. Whilst it is important to address issues post-diagnosis like improving access to healthcare especially for the more disadvantaged groups, and closer monitoring of CYP with poorer glycaemic control, a focus on population level prevention is also required. As type 2 diabetes is a condition closely linked to poorer childhood socio-economic circumstances associated with areas with greater deprivation, there is a critical need to address the larger issues which can support healthier lifestyles for disadvantaged families and subsequently reduce risk for type 2 diabetes. For example, public health interventions can be designed to maximise income support for poor families; to make healthy food more accessible in disadvantaged neighbourhoods; and to encourage physically active lifestyles by improving access to play grounds, recreational areas and other facilities, in addition to targeted support for high risk groups, following the principle of proportionate universalism[40].

We found substantial evidence for socioeconomic and ethnic inequalities in a large population-based cohort of CYP with type 2 diabetes. There is urgent need to further investigate which modifiable factors drive these inequalities to prevent diabetes associated complications in these groups.

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Table 1 Characteristics of 747 youth with type 2 diabetes by socioeconomic status and registered in the National Paediatric Diabetes Audit (NPDA), England & Wales, 2009-2015. Values are means (SD) unless otherwise stated.

*mean of 2,358 BMI values (for 804 individuals) recorded between diagnosis and 4 years post-diagnosis

	Socioeconomic Status (geographic area-level deprivation)						
	Quintile 1 Most advantaged	**Quintile 2**	**Quintile 3**	**Quintile 4**	**Quintile 5** Most disadvantaged	***All***	***P***
N (%)	42 (6)	84 (11)	118 (16)	195 (26)	308 (41)	*747 (100)*	
Females (%)	74	70	72	61	66	*67*	0.21
Age at diagnosis (years)	13.6 (1.9)	12.9 (3.3)	13.5 (2.2)	13.7 (2.3)	13.3 (2.2)	*13.4 (2.3)*	0.71
Deprivation score (median)	5.3	10.9	17.5	28.5	48.8	*30.1*	
BMI categorical (%)							0.34
Overweight	18	11	16	22	21	*20*	
Obese	68	75	74	71	71	*71*	
BMI Z-score[*]	2.1 (1.1)	2.7 (1.2)	2.6 (0.9)	2.6 (1)	2.6 (1)	*2.6 (1)*	0.23
HbA_{1c} (mmol/mol)[†]	57.7 (21.8)	57.5 (20)	62.7 (24.5)	61.9 (25.7)	65.5 (26.8)	*62.9 (25.5)*	0.03
HbA_{1c} (%)[†]	7.4 (4.1)	7.4 (4)	7.9 (4.4)	7.8 (4.5)	8.1 (4.6)	*7.9 (4.5)*	0.03
HbA_{1c} at diagnosis[‡]	56.5 (22.8)	64.1 (19.2)	73.1 (26.4)	67.2 (25.7)	68.6 (27.2)	*67.9 (25.9)*	0.4
HbA_{1c} at diagnosis[‡] **(%)**	7.3 (4.2)	8 (3.9)	8.8 (4.6)	8.3 (4.5)	8.4 (4.6)	*8.4 (4.5)*	0.4
Glycaemic control at end of follow-up (%)[§] Good (<58mmol/mol)	67	46	50	49	41	*47*	
Poor (≥80mmol/mol)	25	27	28	28	38	*31*	0.83
Glycaemic control one year post-diagnosis (%)[‖] Good (<58mmol/mol)	77	61	67	64	63	*65*	
Poor (≥80mmol/mol)	9	12	16	12	16	*14*	0.85
Treatment regimen at diagnosis (%)[¶]							
Diet & exercise	21	38	31	40	46	*39*	
Oral hypoglycaemics	71	62	60	51	44	*52*	
Oral hypoglycaemics & insulin	7	-	9	9	10	*9*	0.52

†mean of 3,326 $HbA1_c$ values recorded between diagnosis and 4 years post-diagnosis

‡165 $HbA1_c$ values recorded during the first two months following diagnosis

§Proportions for good or poor glycaemic control for 207 CYP at four years post-diagnosis

‖Proportions for good or poor glycaemic control for 451 CYP at one year post-diagnosis

¶treatment data available for 198 CYP at diagnosis

Table 2 Characteristics of 747 youth with type 2 diabetes by ethnicity and registered in the National Paediatric Diabetes Audit (NPDA), England & Wales, 2009-2015. **Values are means (SD) unless otherwise stated.**

	Ethnicity							
	White	**Mixed-ethnicity**	**Asian/Other**	**Pakistani**	**Black**	**Not Stated**	***All***	***P***
N (%)	316 (42)	37 (5)	129 (17)	90 (12)	55 (7)	120 (16)	*747 (100)*	
Females (%)	71	59	61	66	73	60	*67*	0.11
Age at diagnosis (years)	13.3 (2.4)	13.2 (1.6)	13.5 (2.1)	13.4 (2.1)	13.2 (2.5)	13.7 (2.8)	*13.4 (2.3)*	0.68
Deprivation score (median)	28	29	30	45	31	26	*30*	
BMI categorical (%)								NS
Overweight	12	22	32	20	24	20	*19*	0.43
Obese	80	75	56	70	67	71	*71*	
BMI Z-score[*]	2.8 (0.1)	2.6 (1)	2.3 (0.9)	2.6 (0.8)	2.7 (0.9)	2.5 (1.1)	*2.6 (1)*	<0.001
HbA_{1c} (mmol/mol)[†]	60.2 (22.8)	75.8 (31.6)	60.1 (23.4)	64.4 (25.4)	66.6 (30.1)	65.3 (27.5)	*62.8 (25.4)*	0.02
HbA_{1c} (%)[†]	7.7 (4.2)	9.1 (5)	7.6 (4.3)	8 (4.5)	8.2 (4.9)	8.1 (4.7)	*7.9 (4.5)*	0.02
$HbA1_c$ at diagnosis[‡]	62.4 (22.8)	72.2 (34.5)	66.5 (21.6)	78.1 (30.5)	82.5 (25.9)	69.2 (27.7)	*67.7 (25.9)*	0.10
$HbA1_c$ at diagnosis[‡] **(%)**	7.9 (4.2)	8.8 (5.3)	8.2 (4.1)	9.3 (4.9)	9.7 (4.5)	8.5 (4.7)	*8.3 (4.5)*	0.10
Glycaemic control at end of follow-up (%)[§] Good (<58mmol/mol)	45	11	52	50	46	55	*47*	
Poor (≥80mmol/mol)	30	89	30	32	33	19	*31*	NA
Glycaemic control one year post-diagnosis (%)[‖] Good (<58mmol/mol)	63	60	65	66	71	68	*65*	
Poor (≥80mmol/mol)	13	24	14	11	14	13	*14*	NA
Proportion in most deprived SES quintile	37	41	43	64	37	36	*41*	<0.0001
Treatment regimen at diagnosis (%)[¶]								

Diet & exercise	32	67	34	45	33	53	*39*	0.11
Oral hypoglycaemics	62	33	47	45	58	38	*52*	
Oral hypoglycaemics & insulin	6	-	19	10	8	9	*9*	

*mean of 2,388 BMI values (for 669 individuals) recorded between diagnosis and 4 years post-diagnosis

†mean of 3,372 $HbA1_c$ values recorded between diagnosis and 4 years post-diagnosis

‡173 $HbA1_c$ values recorded during the first two months following diagnosis

§Proportions for good or poor glycaemic control for 207 CYP at four years post-diagnosis

‖Proportions for good or poor glycaemic control for 459 CYP at one year post-diagnosis

¶treatment data on 198 CYP

Table 3. Linear mixed-effects models for socioeconomic differences in glycaemic control (HbA_{1c}) in 747 children and young people with type 2 diabetes in England and Wales, 2008-2015

	Model 1	**Model 2**	**Model 3**	**Model 4**
Fixed effects	Random intercept or unconditional growth model	Random intercept + random slope model	Model 2 + socioeconomic status	Model 3 + sex & age at diagnosis
Constant/intercept (HbA_{1c} mmol/mol)	**64.9 (62.5, 67.2)**	**64.9 (62.6, 67.2)**	**66.9 (64, 69.8)**	**71.9 (60.1, 83.7)**
Slope coefficients				
Duration since diagnosis (years)				
Linear	**-15.2 (-19.2, -11.2)**	**-16.3 (-20.3, -12.3)**	**-16.5 (-20.5, -12.5)**	**-16.4 (-20.4, -12.4)**
Quadratic	**10 (7.6, 12.4)**	**10.8 (8.4, 13.2)**	**10.9 (8.5, 13.3)**	**10.9 (8.5, 13.3)**
Cubic	**-1.6 (-2, -1.1)**	**-1.7 (-2.1, -1.3)**	**-1.7 (-2.1, -1.3)**	**-1.7 (-2.1, -1.3)**
Socioeconomic Status				
Quintile 5 (most disadvantaged)			Reference	Reference
Quintile 1 (least disadvantaged)			**-7.3 (-13.5, -1.1)**	**-7.2 (-13.4, -1)**
Quintile 2			**-6.1 (-11.1, -1)**	**-6 (-11, -1)**
Quintile 3			-1.8 (-5.9, 2.4)	-1.6 (-5.8, 2.6)
Quintile 4			-2.5 (-6, 1.0)	-2.6 (-6.1, 0.8)
Sex Male				Reference
Female				-3.2 (-6.4, 0.1)
Age at diagnosis (years)				0.1 (-0.7, 0.7)
Interclass Correlation Coefficient (ICC)	0.66	0.67	0.67	0.67
Model fit				
Aikake information criterion (AIC)	28722.03	28491.91	28490.65	28490.92
Bayesian information criterion (BIC)	28758.69	28540.78	28563.97	28576.45
-2LL	28710	28474	28466	28462
Likelihood ratio test for model comparison (*p*-value)	Not Applicable	p<0.0001	p<0.05	p=0.15

Table 4. Linear mixed-effects models for socioeconomic and ethnic differences in glycaemic control (HbA_{1c}) in 747 children and young people with type 2 diabetes in England and Wales, 2008-2015

	Model 1	**Model 2**	**Model 3**	**Model 4**
Fixed effects	Random intercept/or unconditional growth model	Random intercept + random slope model	Model 2 + ethnicity	Model 3 + socioeconomic status, sex & age at diagnosis
Constant/intercept (HbA_{1c}, mmol/mol)	**64.9 (62.5, 67.2)**	**64.9 (62.6, 67.2)**	**61.7 (58.2, 65.2)**	**68.8 (56.6, 80.9)**
Slope coefficients				
Duration since diagnosis (years)				
Linear	**-15.2 (-19.2, -11.2)**	**-16.3 (-20.3, -12.3)**	**-11.3 (-17.3, -5.2)**	**-11.3 (-17.4, -5.3)**
Quadratic	**10 (7.6, 12.4)**	**10.8 (8.4, 13.2)**	**7 (3.4, 10.7)**	**7 (3.4, 10.7)**
Cubic	**-1.6 (-2, -1.1)**	**-1.7 (-2.1, -1.3)**	**-1 (-1.6, -0.4)**	**-1 (-1.6, -0.4)**
Ethnicity				
White			Reference	Reference
Mixed-ethnicity			8.7 (-1.2, 18.5)	8.1 (-1.7, 18)
Asian/Other			1.2 (-5.3, 7.8)	0.6 (-6, 7.1)
Pakistani			**14.8 (7.2, 22.4)**	**13.2 (5.6, 20.9)**
Black			8.8 (-1.4, 19)	8.8 (-1.4, 18.9)
Not stated			0.7 (-6.3, 7.7)	0.5 (-6.5, 7.6)
Socioeconomic Status				
Quintile 5 (most disadvantaged)				Reference
Quintile 1 (least disadvantaged)				**-6.3 (-12.6, -0.1)**
Quintile 2				**-5.8 (-10.9, -0.7)**
Quintile 3				-1.6 (-5.8, 2.6)
Quintile 4				-2.7 (-6.2, 0.8)
Sex Male				Reference
Female				-2.9 (-6.2, 0.3)
Age at diagnosis (years)				0.1 (-0.7, 0.7)
Interaction between ethnicity & linear duration				
Mixed-ethnicity			**-16.2 (-32.4, -0.1)**	**-16.1 (-32.2,- 0.1)**
Asian/Other			-2.4 (-13.6, 8.8)	-2.4 (-13.6, 8.8)
Pakistani			**-27.7 (-40.8, -14.5)**	**-27.5 (-40.6, -14.3)**
Black			-9.5 (-26.3, 7.2)	-10 (-26.7, 6.7)
Not stated			1.7 (-10.7, 14)	1.5 (-10.8, 13.9)

Interaction between ethnicity & quadratic duration				
Mixed-ethnicity			**13.9 (4.1, 23.8)**	**13.9 (4.1, 23.7)**
Asian/Other			2.1 (-4.6, 8.7)	2.2 (-4.5, 8.8)
Pakistani			**16.8 (8.8, 24.8)**	**16.7 (8.7, 24.8)**
Black			6 (-3.6, 15.6)	6.2 (-3.4, 15.8)
Not stated			1.2 (-6.3, 8.6)	1.3 (-6.2, 8.8)
Interaction between ethnicity & cubic duration				
Mixed-ethnicity			**-2.3 (-4, -0.7)**	**-2.3 (-4, -0.7)**
Asian/Other			-0.5 (-1.6, 0.6)	-0.5 (-1.6, 0.6)
Pakistani			**-2.7 (-4.1, -1.3)**	**-2.7 (-4.1, -1.3)**
Black			-1 (-2.6, 0.6)	-1 (-2.6, 0.5)
Not stated				
Interclass Correlation Coefficient (ICC)	0.66	0.67	0.67	0.67
Model fit				
Aikake information criterion (AIC)	28722.03	28491.91	28487.41	28488.33
Bayesian information criterion (BIC)	28758.69	28540.78	28658.48	28696.05
-2LL	28710.04	28475.9	28431.42	28420.32
Likelihood ratio test for model comparison (*p*-value)	Not Applicable	p<0.0001	p<0.001	p=0.08

Figure 1A. Linear adjusted and predicted HbA_{1c} trajectories by socioeconomic status (SES) in 747 children and young people diagnosed with type 2 diabetes in England and Wales

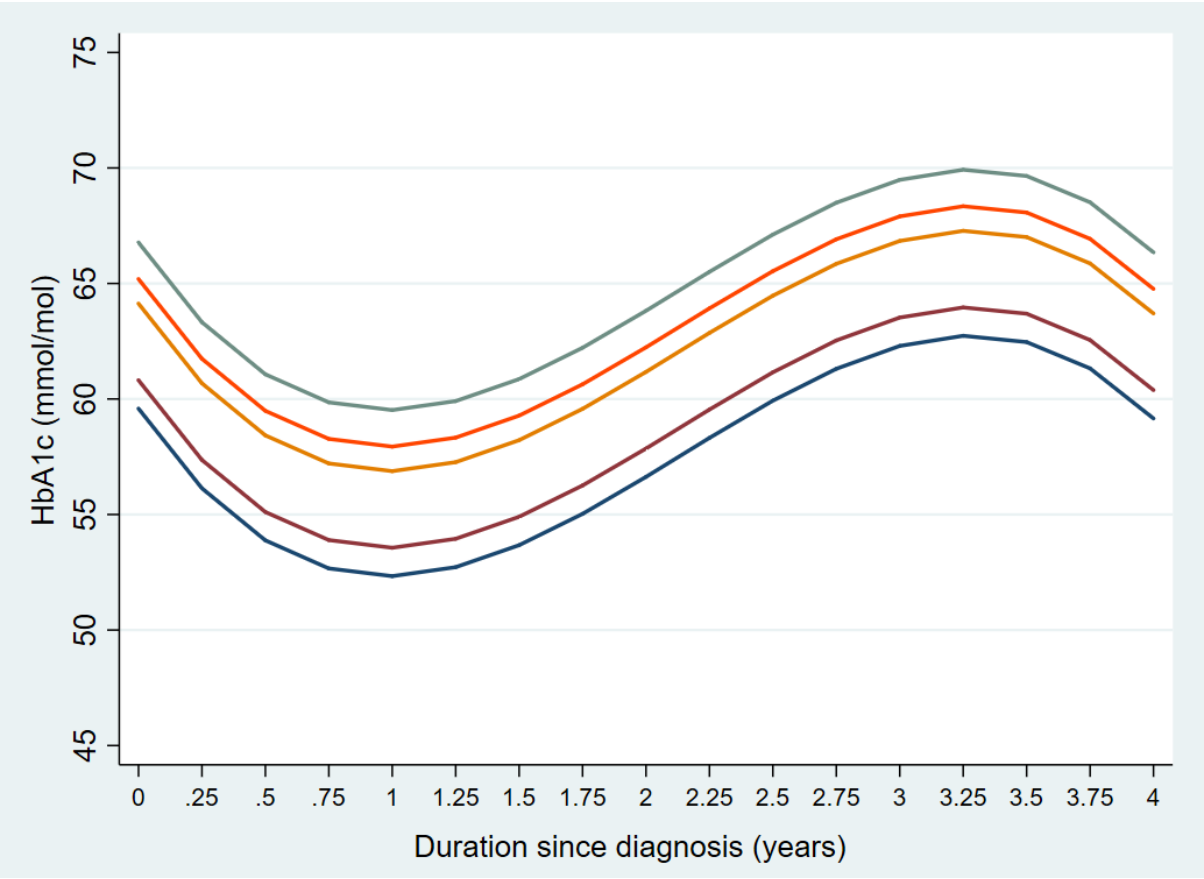

Figure 1A Legend:

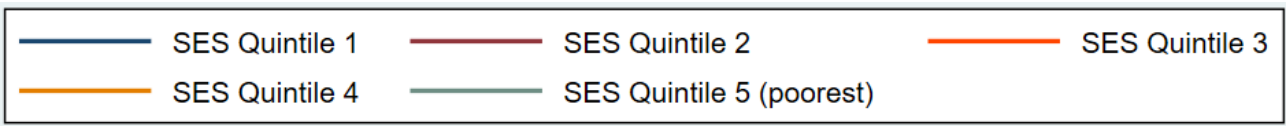

Figure 1B. Linear adjusted and predicted HbA_{1c} trajectories by ethnicity in 747 children and young people diagnosed with type 2 diabetes in England and Wales

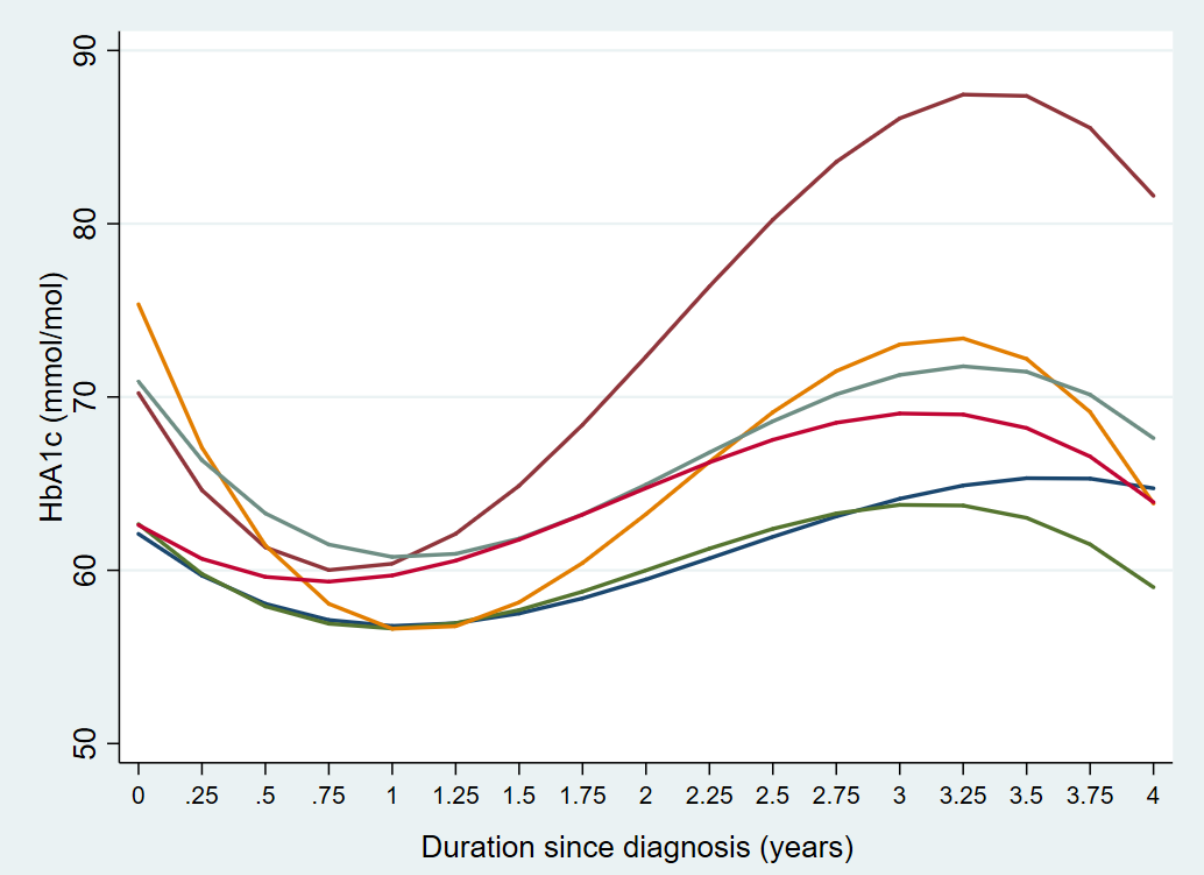

Figure 1B. Legend: