Running title

Developmental trajectories of control

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TITLE:

IMPACT OF DEPRIVATION, ETHNICITY AND INSULIN PUMP THERAPY ON DEVELOPMENTAL TRAJECTORIES OF DIABETES CONTROL IN TYPE 1 DIABETES

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Abstract

Background

There is marked variation in diabetes outcomes for children and adolescents across the UK. We used modelling techniques to examine the independent contributions of deprivation, ethnicity, insulin pump use and health service use on HbA_{1c} trajectories across adolescence.

Methods

Prospective data from a large UK Paediatric & Adolescent Diabetes Service on subjects with type 1 diabetes (T1D) aged 9-17 years from January 2008 to December 2013: 2560 HbA_{1c} datapoints were available on 384 patients (193 (50.4%) female).

Sequential multilevel growth models assessed the effects of sex, duration of diabetes, deprivation, ethnicity, insulin pump use and health service use on HbA_{1c}. Growth mixture models were used to identify discrete HbA_{1c} trajectories across adolescence.

Results

Mean clinic HbA_{1c} decreased from 2008 to 2013 by 0.122% (95% CI: 0.034, 0.210; p=0.007) per year. The optimal multilevel growth model showed mean HbA_{1c} increased with age (B=0.414, p<0.0001), and that mean HbA_{1c} was predicted by white/British ethnicity (B=-0.748, p=0.004), clinic visits (B=0.041, p=0.04) and pump use (B=-0.568, p<0.0001) but not deprivation.

The optimal mixture model was a 4 trajectory group solution, with 45.1% in Good Control, 39.6% with Deteriorating Control, 6.5% with Rapidly Deteriorating Control and 8.8% in Poor Control across adolescence.

Only pump use predicted trajectory group membership, being protective against membership of all other trajectories compared with Good Control.

Conclusions

Increasing uptake of insulin pumps and ensuring access to health services are likely to be the most effective means of reducing inequalities in outcomes of T1D in children and young people.

Keywords

ethnicity, developmental, child, adolescent, socioeconomic status

Introduction

The high level of geographical variation and inequality in diabetes outcomes for children and young people in the UK is an increasing public health and clinical concern.(1, 2) It is unclear whether this variation reflects sociodemographic differences in populations or reflects variation in healthcare provision, or both.

Socioeconomic deprivation has been identified as a predictor of poor glycaemic control in a number of studies,(3-8) although others do not report an association,(9, 10) including large population-based studies.(11) Ethnicity is a strong predictor of diabetes control; in the 2011-12 National Paediatric Diabetes Audit for England and Wales, young people of black ethnicity were less likely to achieve diabetes control targets (HbA_{1c} <(58mmol/mol (7.5%)) than white young people.(12) A number of other studies have suggested that black and minority ethnicity (BME) young people have poorer HbA_{1c} outcomes(4-6, 8, 10) but it remains unclear whether this largely reflects deprivation in BME groups(10) or whether non-white ethnicity confers some disadvantage over and above deprivation.(13) One postulated mechanism for deprivation or ethnicity to impact upon glycaemic control is through low access to intensive insulin therapies, with evidence that both non-white ethnicity(10) and deprivation(8) are associated with poorer initiation of insulin pump therapy. As insulin pump use remains highly variable in the UK, access to pump therapy may be a potent source of unwarranted healthcare related variation in HbA_{1c} outcomes.

Studies have thus far been cross-sectional or short-term,(4) and have not examined the independent contributions of ethnicity, deprivation and healthcare factors to variation in glycaemic control. None have used developmental trajectory analyses to examine the impacts of these factors on the development of inequalities in HbA_{1c} from childhood through adolescence.

The increase in HbA_{1c} from childhood to adolescence in type 1 diabetes (T1D) is well described,(14, 15) and reflects the insulin insensitivity of puberty together with the psychosocial transitions of adolescence. However, there may in fact be a number of different developmental trajectories for HbA_{1c} from childhood through adolescence, potentially influenced by biological, social and psychological characteristics and potentially amenable to different intervention strategies. The last 20 years has seen the rapid development of statistical methods to study developmental trajectories.(16) The first is multilevel growth models which identify average trends over time and capture individual departures from the average trend, something that standard regression models cannot. However, like standard regression models, growth models assume that individuals are drawn from the same population and that development over time can be mapped using one set of parameters. In contrast, group-based trajectory models or growth mixture models allow for the possibility that there may be different sub-populations following different developmental trajectories.(16) In diabetes, for example, clinicians might observe that some adolescents keep good control throughout the teenage years while in others control deteriorates markedly. However this issue has previously been difficult to study. A very small number of studies have begun to apply these methods to study the effects of psychosocial characteristics on developmental trajectories in HbA_{1c}.(17-19) The effects of ethnicity,

deprivation, initiation of insulin pump and health service use on HbA_{1c} trajectories have not been studied.

We used a large longitudinal dataset from a high-performing regional specialist child and adolescent diabetes clinic which draws patients from across much of south-east England. We first used multi-level models for change to examine the influence of deprivation, ethnicity, initiation of insulin pump use and health service use on the average HbA_{1c} trajectory from childhood through adolescence. We then used growth mixture models to assess whether there were identifiable discrete trajectories of HbA_{1c} change in the sample, and examine whether deprivation, ethnicity, insulin pump use and health service use influenced trajectory membership.

Methods

Data were obtained from the clinical database of the University College Hospital Paediatric & Adolescent Diabetes Service. Data were routinely collected prospectively at each clinic visit from January 2008 to December 2013 as part of routine ongoing service evaluation and for participation in national audits. At each clinic visit, the treating clinician recorded HbA_{1c} and insulin treatment regimen (number of daily insulin injections or insulin pump use). Routinely collected hospital administrative data on age, sex, ethnicity and area of residence (used to calculate small area deprivation measures) were obtained from the hospital data systems. These analyses are restricted to participants who had had HbA_{1c} measured within our clinic between the ages of 9.0 to 17.99 years in 2008 to 2013 inclusive.

Measures

HbA_{1c} was measured at each visit using the point of care Siemens/Bayer DCA 2000+ Analyzer. Values reported as being above the upper end of the instrument's range (i.e. >130 mmol/mol(14%)) were assigned a value of 130mmol/mol (14.0%) in these analyses. Note that all clinic patients are routinely tested for abnormal haemoglobins, and HbA_{1c} is not measured in this group.

Ethnicity was obtained from parental self-report at time of registration with the clinic using a non-standardised National Health Service typology. Parents could identify their child as white, "British", black British, Asian British, multiple categories of mixed ethnicity or as belonging to a particular ethnic group. Due to a lack of precision (e.g. the "British" group likely included small numbers of non white young people identifying as British separately to those identifying as black British or Asian British), we dichotomised the sample into those identifying as white or 'British' (white or British group (85.9%)) and those identifying with non-white ethnic groups (non-white (n=53; 14.1%)). The latter group included 29 identifying as black or African, 14 from south Asian ethnic groups, with the remainder of mixed or other ethnicity.

Socioeconomic status measured using the UK Index of Multiple Deprivation (IMD) 2010, which provides a relative measure of deprivation across seven domains for small areas in England. IMD rank scores were assigned to quintiles using national thresholds, with 5 being the least deprived and 1 being the most deprived.(20) For the growth mixture models, a binary measure was used taking deprivation to be the most deprived (1^{st}) quintile.

Treatment type (number of insulin injections or CSII use) was recorded at each time point. For analysis, treatment was classified as CSII or injection regimens due to very low numbers in our clinic using <4 injections per day. For each individual using CSII, the date of initiation of CSII was the first point at which the patient was coded as being on a CSII regimen.

We used the annual number of clinic visits where an HbA_{1c} was recorded (i.e. total visits between 2008 & 2013 divided by time in follow-up for each patient) as a proxy for health service use for each patient.

Analyses

To assess average growth trajectories across the sample, following Singer & Willetts(21) we constructed a series of multi-level models for change using the *xtmixed* commands in Stata 13. We began with unadjusted growth models using age as the temporal metric. Age was centred on age 9 for analyses. We then tested the association of demographic factors such as sex and duration of diabetes in the models. We then sequentially added our hypothesized predictors using the Aikake information criterion (AIC) and sample-adjusted Bayesian information criterion (BIC) at each step to judge model performance compared with previous models. In this we first added time invariant predictors i.e. deprivation (by quintile), ethnicity (white or British versus non-white) and number of clinic visits (continuous). We then added CSII use as a time-varying predictor. At each step, quadratic terms and interactions were examined and included in models only where significant and where they improved model fit. Terms were tested for significance in subsequent models if p value <0.1 in the previous model iteration.

Growth mixture modeling was undertaken using the *mixture* commands in MPlus 7.1 (www.statmodel.com). Models used maximum likelihood estimation with robust standard errors to account for missing data, with 500 random starts used in each model for maxiumum likelihood optimization; this was sufficient in all models to replicate the best log-likelihood ratio. We began with a single trajectory model and sequentially increased trajectory number, assessing model fit at each step using the AIC, sample adjusted BIC, entropy and the Vuong-Lo-Mendell-Rubin test. The latter was used to test fit with k classes compared to a model with k-1 classes; a p-value <0.05 rejects the k − 1 class model in favour of the k class model.(22) As suggested by the literature, we judged the best model on the basis of clinical plausibility and model fit criteria.(16) Having identified the best mixture model, we then examined the effects of our hypothesized predictors on an individual's likelihood of belonging to one of the trajectory classes using the *mixture* commands in MPlus.

Results

2560 HbA_{1c} datapoints were available on 384 patients with T1D (193 (50.4%) female) from January 2008 to December 2013. The average number of HbA_{1c} clinic datapoints per patient was 6.7 (range 1 to 21), with mean time spent in the clinic being 4.0 (SD 1.65) years (range 0.05 to 6.0 years). Median number of annual visits was 3.1 (IQR: 2.5, 3.8). Demographic characteristics of the sample are shown in Table 1, together with last-recorded treatment regimen (as this changed across the study period).

The sample was well distributed across deprivation quintiles in both sexes, with minor under-representation of the most deprived quintile. At entry to the cohort, 40.5% were using CSII, with 68.0% using CSII as their last recorded regimen. The remainder were all on multiple daily injection (MDI) regimens. Year of diagnosis was available in 358 participants, with median year of diagnosis being 2005 (range 1994 to 2013; IQR 2002-2008).

There were no differences between sexes in ethnicity, treatment regimen or deprivation. Deprivation and ethnicity were strongly associated with regimen. 92% (n=11) of those using twice daily insulin and 52.2% (82) of those using MDI were in the most deprived population quintile compared with 18.4 (38) of those using CSII ($p<0.0001$). 23.7% (40) of those using injection regimens were non 'white/British' compared with 6.3% (13) of those using CSII ($p<0.0001$).

Multi-level growth models

An unadjusted growth model for time showed that mean HbA_{1c} for the clinic decreased over time from 2008 to 2013 by 0.122% (95% CI: 0.034, 0.210; $p=0.007$) per year. As age and time are the same metric and thus collinear in any model, subsequent models used age as the metric, centred on age 9.

Sequential multi-level models for change in HbA_{1c} with increasing age from 9 to 18 years are shown in Table 2. Model A, the unadjusted growth model, shows that mean HbA_{1c} increased significantly with age; due to the larger linear coefficient and smaller quadratic coefficient, within the age-range of the model the increase tapered and ceased at age 18 years. Sex was not associated with mean HbA_{1c}. Duration of diabetes was also not significantly associated with mean HbA_{1c} ($p=0.1$) and sex and duration were not included in further models. The best model (lowest model fit criteria) was Model E. There was a significant main effect for CSII but no significant interaction of CSII and age. This meant that, for each individual, transition from injection to CSII treatment was associated with a mean decrease in HbA_{1c} of 0.6% at the time of initiation, however subsequently remaining on CSII was not associated with greater or lesser change in HbA_{1c} than for those on injections i.e. greater duration of CSII did not influence HbA1c. In this model, linear and quadratic age terms, ethnicity, visits and the interaction of visits and age each remained significant however the effect of deprivation was entirely attenuated. We identified no significant interactions of ethnicity with insulin regimen, visits or deprivation. Time in follow-up was not a significant predictor of HbA1c when added to the model including CSII, and was thus not included in the final model.

Growth mixture models

Table 3 shows sequential growth mixture models for change in HbA_{1c} from age 9 to 17 years, commencing with specification of a single class through to specification of 4 classes. The table shows the entropy and change in AIC, BIC for each model together with the proportions of the sample in each trajectory class and the values and significance of the intercepts, linear slope and quadratic slope for each class.

Improvements in AIC and BIC suggested that the 4 class model was the best fit with the data and we deemed it the most clinically plausible. The 4 class model is shown graphically in Figure 1. The largest group are those who maintain good control throughout adolescence, showing a slight but temporary deterioration in early adolescence (Good Control group, 45.1%). The second largest group are those in whom control deterioriates in a linear fashion across adolescence (Deterioriating Control group, 39.6%). In a much smaller group, control deteriorated rapidly across early adolescence before improving in later adolescence, reflecting the significant quadratic term in the model (Rapidly Deteriorating Control group, 6.5%). The final group were those who maintained poor control across adolescence (Poor Control, 8.8%)

We then examined which factors predicted an individual's membership of the HbA_{1c} trajectory classes in the final 4 class mixture (Table 4). Sex and duration did not predict trajectory membership. The best model included deprivation, ethnicity, visits and CSII use, however regimen became the only significant predictor in the model with the effects of deprivation, ethnicity and visits all attenuated. CSII use was associated with protection against being in all other trajectory groups compared with being in the Good Control group.

Discussion

We found that ethnicity, frequency of health service use and insulin pump use influenced the average trajectory of HbA_{1c} across adolescence and that insulin regimen influenced an individual's pattern of HbA_{1c} change across adolescence.

The average trajectory for HbA_{1c} was to increase across early adolescence to a peak in late adolescence and decrease thereafter. We found that deprivation had no effect on HbA_{1c} when insulin regimen was introduced into the model, suggesting that the mechanism by which deprivation influences glycaemic control in our sample is through poor access to intensive insulin therapies. In contrast, non-white ethnicity exerted an effect on HbA_{1c} independently of insulin regimen, health service use or deprivation. Whilst minority ethnicity young people had much lower CSII use in our sample, we identified no significant interactions of ethnicity with insulin regimen, visits or deprivation. Our findings suggest that whilst young people from minority groups do have poorer access to CSII, ethnicity also impacts upon diabetes control through cultural and behavioural factors unrelated to deprivation, frequency of health service use or access to pump therapy.

These findings relate to the average growth trajectory of our sample across adolescence. However, we found that a 4 class mixture model best fitted our data, suggesting that young people fit into 4 clinically plausible patterns of HbA_{1c} change across adolescence. Around half our sample maintained an excellent HbA_{1c} (≤58mmol/mol (7.5%)) with minimal change across adolescence (Good control trajectory). The second largest group showed gradual deterioration of control across adolescence (Deteriorating control trajectory). The smallest group experienced a dramatic deterioration in early adolescence with later improvement ((Rapidly deteriorating control trajectory), whilst around 10% maintained poor control across adolescence (Poor control trajectory). Insulin regimen was the only significant predictor of trajectory group membership. The apparent protective effect of CSII against being in the Poor Control trajectory may relate to reverse causality, as those in poor control in early adolescence are rarely considered clinically good candidates for offer of CSII. However this is unlikely to be the case with either of the deteriorating control trajectories.

Taken together these growth and mixture models suggest that access to CSII is the strongest predictor of HbA_{1c} across adolescence. CSII initiation was associated with a fall in HbA_{1c} that was maintained across adolescence, and CSII was protective against being in trajectories of deteriorating HbA_{1c} across adolescence.

Comparison with the literature

Our study is unique in studying longitudinal predictors of glycaemic trajectories in UK children and adolescents and in modeling the independent effects of deprivation, ethnicity, insulin regimen and health service use.

Studies from the USA, New Zealand and Denmark each reported an association between minority ethnicity and poorer HbA_{1c} over time,(4, 13, 23) although associations with deprivation were inconsistent. Little data is available on the impact of insulin regimen intensification on the association of ethnicity and diabetes control. In an observational study

of insulin intensification in one London clinic, intensification appeared to benefit white young people the most, with little benefit for ethnic minority groups.(24)

The few previous studies of trajectories of diabetes control across adolescence have all been small US studies drawn from largely white high socioeconomic status research samples and focused on psychosocial predictors of diabetes control across adolescence.(17-19, 25) None have modeled the combined impact of structural factors including ethnicity, health service use or deprivation on trajectory membership. We identified 4 discrete trajectories of control across adolescence, in comparison to previous studies which identified 2(19, 25) or 3(17, 18) trajectory groups. Our findings were similar to that of Rohan et al., who found the majority in stable good control, with a large group beginning in moderate control that gradually deteriorated across adolescence and a small group with persistent poor control across adolescence.(17) However we also identified a fourth group i.e. those with rapidly deteriorating control. The impact of insulin regimen on trajectory was only examined by one study, who also found that CSII use was protective against deteriorating control trajectories.(25)

Strengths and limitations

We used two advanced statistical techniques to provide different perspectives on change in HbA_{1c} over time in individuals using all available data. Mixture modelling techniques used and criteria for determining model fit and trajectory class number were taken from mixture modelling best practice(22) and are similar to those used in other trajectory analyses in adolescent diabetes.(18, 19) Whilst our sample was from a single high performing large clinic, it is similar to the UK population in terms of socioeconomic status, ethnically diverse and has a range of insulin regimens in use. Our sample is the largest thus far used in growth mixture modelling in diabetes.

Our data are subject to a number of limitations. We used DCA data which provide a ceiling effect for HbA_{1c}, as we assigned any with value >130mmol as being 130mmol/mol. This affected a very small number of datapoints (n=79; 2%). Ethnicity was self-assigned and our categories (white or British versus identifying as non-white ethnic group) are not directly comparable to standard ethnicity classifications. However, our categorization distinguishes those who identify with an ethnic minority group from those who identify with British culture. Whilst we used best available methods to identify trajectory groups in the mixture modelling, it is important to recognise that mixture modelling is an exploratory technique and it is possible that chance relationships in our data may influence trajectory group findings.(26) However the trajectory groups we identified were similar to those found in other studies and were clinically plausible.

Conclusions

Change in HbA_{1c} across adolescence is influenced by ethnicity, insulin regimen and health service use. Deprivation influences glycaemic control largely through poor access to intensive insulin therapies. Increasing uptake of insulin pump use and ensuring access to

health services are likely to be the most effective means of reducing inequalities in outcomes of T1D in children and young people.

Funding sources

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Conflict of interests

All authors declare they have no conflicts of interest.

Table 1. Demographic and clinical characteristics of participants

		Males	Females	Total
Mean age across all visits mean (SD)		13.4 (2.4)	13.5 (2.5)	13.3 (2.5)
Mean age first visit in this sample (SD)		12.5 (2.6)	12.5 (2.6)	12.5 (2.6)
Insulin regimen % (n)	2 injections per day	3.7 (7)	2.6 (5)	3.2 (12)
	Multiple daily injections	40.6 (76)	43.2 (82)	41.9 (158)
	CSII	55.6 (104)	54.2 (103)	54.9 (207)
Ethnicity % (n)	white or British	87.1 (163)	84.7 (160)	14.1 (53)
	Non 'white'	12.8 (24)	15.3 (20)	85.9 (323)
Socioeconomic status: IMD quintile % (n)	1 (most deprived)	14.4 (27)	15.9 (30)	15.2 (57)
	2	19.8 (37)	19.6 (37)	19.7 (74)
	3	21.4 (40)	20.1 (38)	20.7 (78)
	4	25.1 (47)	25.4 (48)	25.3 (95)
	5 (least deprived)	19.3 (36)	19.0 (36)	19.2 (72)

N for IMD = 376; N for ethnicity = 376; N for insulin regimen = 377

Table 2. Multilevel model for change in HbA_{1c} with age

		Model A: growth model		Model B: add deprivation		Model C: add ethnicity		Model D: add visits		Model E: add CSII treatment	
		B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Constant / Intercept		7.754		7.989		8.524		8.453		8.692	
Age (centred on 9 years)	linear	0.315 (0.205, 0.424)	<0.0001	0.334 (0.223, 0.445)	<0.0001	0.335 (0.224, 0.447)	<0.0001	0.478 (0.353, 0.603)	<0.0001	0.388 (0.268, 0.508)	<0.0001
	quadratic	-0.019 (-0.032, -0.006)	0.003	-0.022 (-0.034, -0.009)	0.001	-0.022 (-0.034, -0.009)	0.001	-0.023 (-0.035, -0.010)	0.001	-0.016 (-0.028, -0.005)	0.006
index of multiple deprivation (IMD) quintile	1			0		0		0		0	
	2			-0.048 (-0.564, 0.468)	0.9	0.008 (-0.513, 0.528)	0.9	-0.102 (-0.582, 0.378)	0.7	-0.070 (-0.558, 0.416)	0.8
	3			-0.261 (-0.747, 0.225)	0.3	-0.118 (-0.623, 0.387)	0.6	-0.184 (-0.647, 0.289)	0.4	-0.007 (-0.481, 0.465)	0.9
	4			-0.457 (-0.907, -0.008)	0.046	-0.277 (-0.753, 0.198)	0.3	-0.288 (-0.729, 0.153)	0.2	-0.181 (-0.633, 0.265)	0.4
	5			-0.659 (-1.141, -0.176)	0.007	-0.476 (-0.998, 0.047)	0.07	-0.534 (-1.037, -0.031)	0.04	-0.323 (-0.823, 0.176)	0.2
	Effect of IMD on change with age			-							
Ethnicity	non-white					0				0	
	white or British					-0.769 (-1.318, -0.220)	0.006	-0.714 (-1.209, -0.220)	0.005	-0.737 (-1.247, -0.227)	0.005
	Effect of ethnicity on change with age					-		-		-	
Number of visits per year	Visits							0.006 (-0.001, 0.012)	0.08	0.009 (0.002, 0.080)	0.003

	Effect of visits on change with age					-0.016 (-0.022, -0.011)	<0.0001	-0.012 (-0.018, -0.006)	<0.0001
CSII treatment	Injection regimen							0	
	Pump user							-0.578 (-0.769, -0.389)	<0.0001
	Effect of CSII on change with age							-	
Model sample size (N)	2560	2559	% change	2558	% change	2558	% change	2274	% change
Aikake information criterion (AIC)	7378.827	7335.636	-0.6%	7322.352	-0.2%	7293.44	-0.4%	6080.70	-16.6%
Bayesian information criterion (BIC)	7437.304	7376.567	-0.8%	7369.127	-0.1%	7351.91	-0.3%	6143.72	-16.4%

Notes: HbA_{1c} is shown here only in NGSP units (%) as these were the units in which the models were run. BIC is sample-adjusted.

Table 3. Mixture models for HbA1c trajectories from age 9 to 17 years

		1 class model			2 class model			3 class model			4 class model		
Number of classes specified		1			2			3			4		
Sample (N)		386			386			386			386		
Indicies of model fit													
AIC		4346.975			3919.457			3735.817			3634.71		
change in AIC from previous model					-9.8%			-4.7%			-2.7%		
Sample adjusted BIC		4356.371			3931.984			3751.476			3653.501		
change in adjusted BIC from previous					-9.7%			-4.6%			-2.6%		
Entropy					0.847			0.763			0.784		
Proportions in each trajectory class		Class	N	%	Class	N	%	Class	N	%	Class	N	%
		1	386	100%	1	78	20.2%	1	45	11.7%	1	34	8.8
					2	308	79.8%	2	145	37.6%	2	153	39.6
								3	196	50.8%	3	25	6.5
											4	174	45.1
Vuong-Lo-Mendell-Rubin test			N/A			2 versus 1 class p=0.0008			3 versus 2 classes p=0.09			4 versus 3 classes p=0.17	
		Mean	*SE*	*p*	*Mean*	*SE*	*p*	*Mean*	*SE*	*p*	*Mean*	*SE*	*p*
Class 1	Intercept	7.779	0.091	<0.0001	8.762	0.312	<0.0001	9.821	0.913	<0.0001	12.173	0.692	<0.0001
	Linear slope	0.257	0.063	<0.0001	0.775	0.197	<0.0001	0.691	0.457	0.13	-0.597	0.281	0.05
	Quadratic slope	-0.012	0.009	0.17	-0.048	0.025	0.057	-0.045	0.047	0.3	0.057	0.031	0.07

Class 2	Intercept		7.586	0.101	<0.0001	8.349	0.123	<0.0001	8.409	0.116	<0.0001
	Linear slope		0.157	0.053	0.003	0.264	0.085	0.002	0.148	0.073	0.04
	Quadratic slope		-0.009	0.006	0.15	-0.018	0.012	0.146	-0.008	0.01	0.4
Class 3	Intercept					7.276	0.104	<0.0001	7.724	0.361	<0.0001
	Linear slope					0.127	0.052	0.015	1.739	0.271	<0.0001
	Quadratic slope					-0.014	0.006	0.023	-0.136	0.04	0.001
Class 4	Intercept								7.247	0.101	<0.0001
	Linear slope								0.103	0.051	0.04
	Quadratic slope								-0.012	0.006	0.04

Notes : Table shows mixture models for 1 through to 4 classes of HbA_{1c} trajectories. Model fit indices are shown together with % change from previous model with 1 fewer class, the proportions of the sample in each trajectory class in that model and class intercepts and slopes (linear and quadratic). The Vuong-Lo-Mendell-Rubin test measures the superiority of the specified model compared to that with 1 fewer class. N/A= not available.

HbA_{1c} is shown here only in NGSP units (%) as these were the units in which the models were run.

Figure 1. Graphical representation of the 4 class mixture model for HbA_{1c} trajectories from age 9 to 17 years

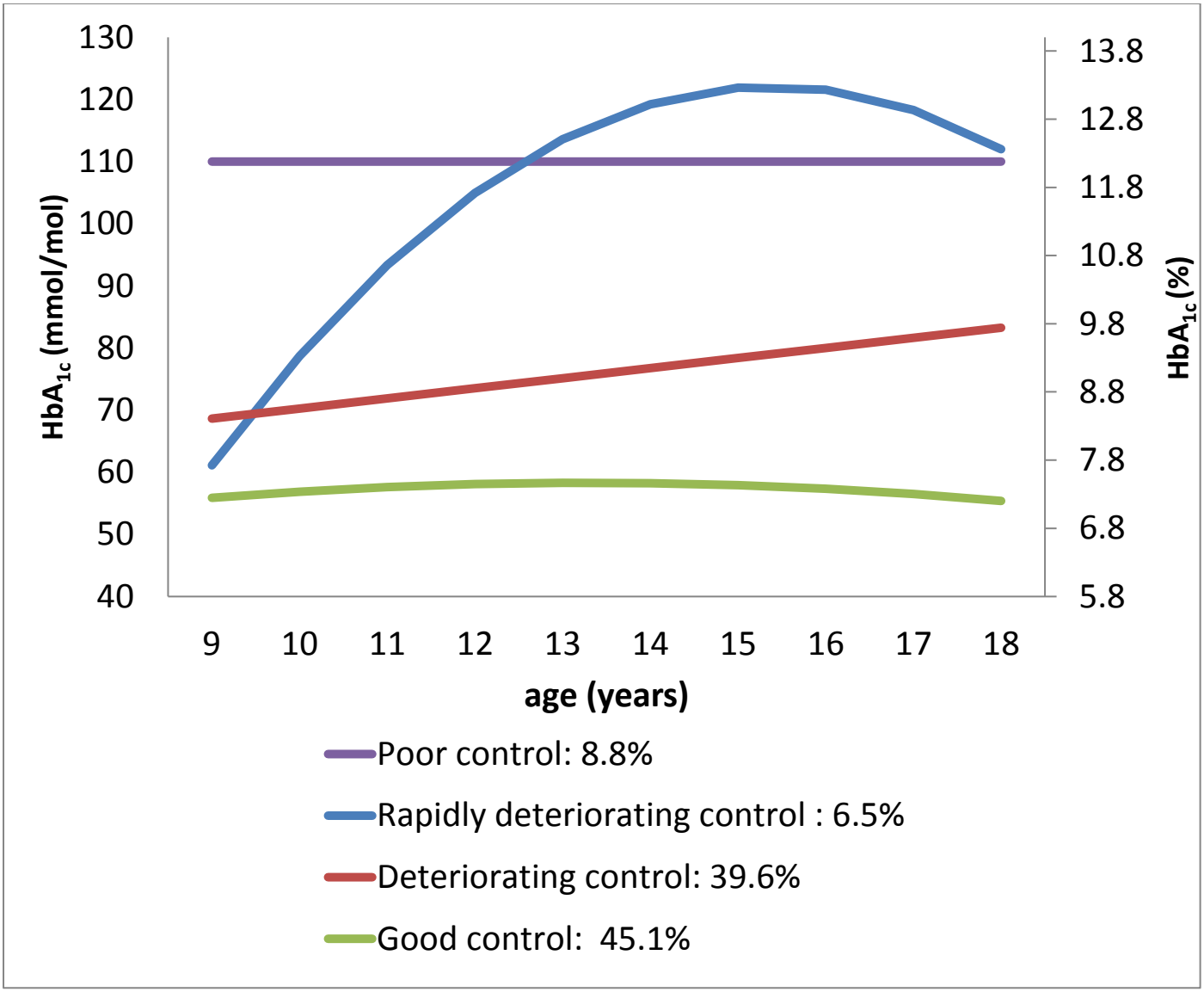

Table 4. Predictor model for membership of HbA1c trajectory class in the final 4 class mixture model

	Model including Deprivation, Ethnicity & Visits				Model including Deprivation, Ethnicity, Visits & CSII			
N			384				372	
AIC			3609.902				3458.119	
Sample adjusted BIC			3640.236				3490.952	
Deprivation: bottom quintile v others	B	SE	OR	p	B	SE	OR	p
Good control	0		1		0		1	
Poor control	0.051	0.879	1.05	0.9	0.300	0.686	1.35	0.7
Deterioriating control	0.652	0.476	1.92	0.17	0.263	0.469	1.30	0.6
Rapidly deterioriating control	1.446	0.542	4.25	0.008	0.844	0.609	2.33	0.17
Ethnicity: white or British v non-white								
Good control	0		1		0		1	
Poor control	-2.706	0.994	0.07	0.007	-0.060	0.773	0.94	0.9
Deterioriating control	0.387	0.674	1.47	0.6	0.585	0.469	1.79	0.2
Rapidly deterioriating control	-1.719	0.614	0.18	0.005	-0.926	0.609	0.40	0.13
Visits (continuous)								
Good control	0		1		0		1	
Poor control	0.129	0.111	1.14	0.2	0.054	0.066	1.06	0.4
Deterioriating control	0.019	0.04	1.02	0.6	0.067	0.04	1.07	0.10
Rapidly deterioriating control	-0.176	0.064	0.84	0.006	-0.12	0.073	0.89	0.10
Insulin Regimen: CSII v. MDI								
Good control					0		1	
Poor control					-3.244	0.96	0.04	0.001
Deterioriating control					-1.724	0.449	0.18	<0.0001
Rapidly deterioriating control					-2.331	0.652	0.10	<0.0001

Table shows coefficients (B), standard errors (SE) and p-values for regression of trajectory group membership on each predictor, with exponentiated coefficients (Odds ratios, OR). Model fit criteria (AIC and BIC) also shown.

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