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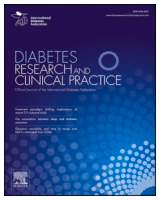

Type 2 diabetes mellitus in people with intellectual disabilities: Examining incidence, risk factors, quality of care and related complications. A population-based matched cohort study

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ABSTRACT

Aims: People with intellectual disabilities are at higher risk of type 2 diabetes mellitus (T2DM) but there are currently gaps in our understanding related to risk of new onset, care of T2DM and complications.
Methods: We examined electronic health-record data from Jan 2010 to May 2022 in 189,172 people with intellectual disabilities and 306,697 age, sex and family practice matched controls. We estimated incidence rates per 1,000-person-years, incidence rate ratios (IRRs), risk factors for T2DM (odds ratio, OR), indicators of quality of care and complications (hazard ratio, HR).
Results: Incidence of T2DM in people with intellectual disabilities was 3.74 compared to 2.21 per 1,000 person-years in controls. After allowing for the younger age of T2DM onset in intellectual disabilities, the adjusted IRR was 6.91 (95 % CI 5.81–8.22). Impaired mobility was associated with T2DM incidence in people with intellectual disabilities (OR = 7.72, 5.87–10.15). People with intellectual disabilities received blood tests for HbA1c and cholesterol, and eye and foot examinations less often; and had a 12 % higher risk of developing macrovascular complications.
Conclusions: People with intellectual disabilities are at increased risk of T2DM at younger ages, have specific risk factors, experience inequities in care and are at risk for macrovascular complications.

1. Introduction

Intellectual disabilities are characterised by lifelong intellectual, adaptive and functional impairments [1]. People with intellectual disabilities often experience complex health problems and show high rates of physical morbidities including endocrine conditions [2]. Previous work has found that the odds of having a diagnosis of diabetes mellitus (DM) is 2.46 times higher in people with intellectual disabilities compared to matched controls [3].

While research suggests that people with intellectual disabilities are at an increased risk of DM [3,4], there is currently limited work examining type 2 diabetes mellitus (T2DM) in intellectual disabilities. For instance, although a *meta*-analysis showed a pooled T2DM prevalence of 7.6 %, this was based on only four studies [5]. Additionally, to our knowledge, research investigating the risk of new onset of T2DM in intellectual disabilities compared to the general population is scant, including the incidence of T2DM across the lifespan or disaggregated by sex or other demographic characteristics. A recent study of T2DM found an incidence rate of 4.8 per 1000 person-years in people with intellectual disabilities compared to 2.7 per 1000 person-years in age- and sex-matched controls. This study also found that the risk of developing T2DM was doubled in people with intellectual disabilities (hazard ratio:

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2.15, 95 % confidence interval (CI): 2.09–2.20) [6]. However, further work is needed to examine the robustness of these findings. Indeed, many authors have called for more research into this area to better understand the risk of T2DM in people with intellectual disabilities to improve recognition and prevention strategies [3–6].

A better understanding of T2DM is important because people with intellectual disabilities have unique risk factors which may increase the possiibility of them developing T2DM, including genetic predisposition (in intellectual disabilities caused by syndromes such as Prader Willi syndrome [7], Bardet-Biedl syndrome [8] and Down syndrome [2,9]), low levels of physical activity [10], poor diet [10], and increased use of prescribed medicines including antipsychotic and antiepileptic medications[11,12], all of which can contribute to weight gain and therefore higher risk of developing T2DM. Yet, the impact of these risk factors have rarely been examined in the context of T2DM in intellectual disabilities.

Furthermore, national DM audit data from the U.K. suggests that people with intellectual disabilities and T2DM may be less likely to receive appropriate DM care, including regular check-ups, blood glucose monitoring, and medication management [13]. This can lead to poor glycaemic control, and poorer health outcomes [14–16],with some studies suggesting greater illness burden from T2DM and its complications in people with intellectual disabilities than people in the general population [15,17]. However, similar to research examining the risk of onset in T2DM, there is also sparce work exploring indicators of quality of care and T2DM related complications in intellectual disabilities.

There have been few studies of the causes of increased illness burden from T2DM in people with intellectual disabilities compared to the general population, with limited research on the incidence of T2DM, risk factors and investigating the quality of care of T2DM post diagnosis [4]. However, such information has important clinical implications for understanding disparities in care and for the prevention and management of T2DM in people with intellectual disabilities. Therefore the aims of the present study were to 1) determine the incidence rates and risk of new onset of T2DM across the lifespan, by sex, ethnicity and Body Mass Index (BMI) categories, 2) investigate risk factors for T2DM in people with intellectual disabilities compared to controls, 3) examine the quality of care related to the management of T2DM post diagnosis and 4) explore the risk of T2DM related complications after diagnosis in people with intellectual disabilities compared to matched general population controls using nationally representative primary care data from England, U.K.

2. Method

2.1. Study design, setting and participants

A matched population-based cohort study was conducted using primary care electronic health records extracted from the U.K. Clinical Practice Research Datalink (CPRD) Aurum database, which is a longitudinal database of anonymised electronic health records for 1,345 general practices (GPs) in England. U.K. CPRD Aurum was made available for research purposes in 2018 and as of May 2022 comprised data from 41,200,722 patients with 13,300,067 currently registered. The database contains data from GPs using the EMIS clinical systems and includes diagnoses, symptoms, prescriptions, referrals and tests [18,19]. Previous studies have confirmed the quality of data from CPRD Aurum [20–22]. This study protocol was approved by the CPRD Independent Scientific Advisory Committee (ISAC protocol 20-048R).

Patients ever diagnosed with intellectual disabilities were identified from the 09 May 2022 release of CPRD Aurum using SNOMED-CT codes for intellectual disabilities. National Health Service (NHS) recommended codes were used and these were supplemented with additional searchers using the CPRD code dictionary (see supplementary materials for code list). Up to two control participants without intellectual disabilities were sampled with replacement from the list of all patients registered in CPRD Aurum. Controls were matched for year of birth, sex and GP and if their start of record was no more than 365 days after that of the matched participant with intellectual disabilities.

2.2. Variables and identification of T2DM

Participants were classified as having T2DM if a diabetes diagnosis was recorded in the CPRD Aurum observation file and did not meet criteria for type 1 DM (T1DM).Participants were classified as having T1DM if they were first prescribed insulin within 91 days of the DM diagnosis and were aged less than 35 years [23], these individuals were removed from further analysis.

2.3. Measures and morbidities

We classified BMI records for adults aged 18 years or over according to the World Health Organization categories of underweight (<18.5 kg/m2), healthy weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), or obese (>30 kg/m^2). Children and young people aged 2–17 years were grouped into the same categories by international BMI standards [24,25] using the zanthro package [26] in Stata statistical software [27]. The mean of BMI values recorded in each year of age was used for each person. Since BMI was not recorded in every year, BMI categories were imputed using the method of last observation carried forward or backward, allowing patients to remain in the same category for up to 5 years following a measurement.

The management of T2DM was examined using a combination of qualityofcare measures from the NHS Quality and Outcomes Framework (QOF) Indicators, the Organisation for Economic Co-operation and Development (OECD) quality of care indicators and the National Institute for Health and Care Excellence, U.K. (NICE) guideline for T2DM (see supplementary file). These included a record of blood pressure measurements (systolic and diastolic), HbA1c measurement, cholesterol measurement, retinal screening, BMI recording, foot examination, weight management/intervention recording, lifestyle advice, flu vaccination, smoking status and COVID-19 vaccination (for 2020–21 and 2022–21).

We extracted morbidities and other long-term conditions using SNOMED-CT codes for known risk factors [28] associated with T2DM and those of interest in people with intellectual disabilities to account for as potential confounders in our analyses: hypertension, obesity, ischemic heart disease, kidney disease, hypothyroidism, other endocrine disorders, sleep problems (disturbed sleep), family history of diabetes, advice on alcohol consumption, mobility impairment (including codes such as ‘dependence on wheelchair’, ‘impaired walking’ and ‘uses zimmer frame’), steroid medication, antipsychotic medication and antidepressant medication. Complications associated with T2DM including macrovascular, renal, neurological and ophthalmic complications were also extracted.

2.4. Data source, bias and study size

Data were extracted from the Aurum dataset, and the study size was determined by the total number of people with intellectual disabilities within the CPRD Aurum dataset. The sample size of general population controls was determined by matching up to two controls to those with intellectual disabilities. As the study used all available people with intellectual disabilities within CPRD Aurum at the time of data extraction, potential sampling bias was minimised. Missing data were kept as missing, with the exception of BMI records, which was handled as described above.

2.5. Statistical analysis

The incidence of new T2DM diagnoses per 1000 person-years was analysed for person time between 2011 and 2022. The date of the first

T2DM diagnosis that was more than 365 days after the start of the person's registration was considered as the DM incidence date. Incident diagnoses of diabetes were compared between people with intellectual disabilities and controls by aggregating over age-group, sex, ethnicity and BMI category. Age was divided into the categories 0 to 4 years, 5 to 14 years and then 10-year age groups up to 85+ years. Incidence rates were estimated per 1000 person-years with 95 % confidence intervals (95 % CI) derived from the Poisson distribution. To examine the risk of new onset of T2DM in people with intellectual disabilities compared to controls, a Poisson regression model was fitted to calculate an adjusted incidence rate ratio (IRR) with 95 % CI. Within the model, the following confounding variables which could impact the estimates were adjusted for: age was fitted as a continuous predictor, with a quadratic term to allow for non-linearity. We also fitted financial year (fiscal year in the U. K. from April to March each year, referred to as year hereafter) and year-squared in the models. Sex, ethnicity and intellectual disabilities status were fitted as factors. An interaction term between age and intellectual disabilities was included and we also examined the association of BMI categories on the risk of new onset of T2DM in separate models. Predicted rates were plotted.

Indicators of quality of care were evaluated for people with prevalent T2DM for each year from 2011–12 to 2021–22. A count was documented for each indicator as to whether it had been recorded in a participant's electronic clinical record within each year. The frequencies for each indicator were expressed as a percentage of the total number of prevalent cases within the year. Measurements were presented for each year for quality of care indicators where appropriate. This was completed separately for people with intellectual disabilities and general population controls.

To examine the risk factors for T2DM in people with intellectual disabilities compared to controls a logistic regression model was fitted to examine whether a history of known risk factors for T2DM were associated with increased odds of developing T2DM, adjusting for age at diagnosis, sex and ethnicity. Risk factors for T2DM were coded as present or absent before the date of T2DM diagnosis. Odds ratio (OR) with 95 % CI were reported.

Time-to-event analysis using Cox proportional-hazards models were used to examine the risk of developing T2DM complications (macrovascular, renal, neurological and ophthalmic complications) using prevalent T2DM in people with intellectual disabilities compared to general population controls, adjusting for age of diagnosis, sex, ethnicity and duration of T2DM. In these analyses, each complication associated with T2DM was examined separately. Data were depicted using Kaplan-Meier curves and hazard ratios (HR) with 95 % CI were reported.

3. Results

There were 198,263 people with intellectual disabilities (79,323 females) and 328,187 (129,710 females) general population controls as comparators who were registered in CPRD Aurum in May 2022. There were 8797 cases of prevalent T2DM in people with intellectual disabilities and 7631 in general population controls at cohort entry which were excluded from further analyses. In addition, 13,693 controls that were matched with people with intellectual disabilities with prevalent T2DM were removed. There were 294 people with intellectual disabilities and 166 general population controls with T1DM who were excluded.

After these exclusions, there were 189,172 people with intellectual disabilities and 306,697 controls eligible for analysis (supplementary Table S1). There were more males than females in both groups and the controls were slightly younger at cohort entry and exit. The median years of follow-up for people with intellectual disabilities was 4 years compared to 8 years for controls. There were a total of 3684 new diagnoses of T2DM in people with intellectual disabilities and 4676 in controls with 984,979 person-years of follow-up for people with intellectual disabilities and 2,119,351 person-years for controls (Table 1). The overall incidence rate for new diagnosis of T2DM for people with

Table 1
Incidence of type 2 diabetes by sex, ethnicity, age–group and BMI categories for people with intellectual disabilities and general population controls.

		Intellectual disability			General population controls		
		Type 2 diabetes diagnoses	Person years at risk	Incidence per 1,000 person years (95 % confidence interval; 95 %CI)	Type 2 diabetes diagnoses	Person years at risk	Incidence per 1,000 person years (95 % CI)
Total		3684	984,979.7	3.74 (3.62–3.86)	4676	2,119,351.7	2.21 (2.14–2.27)
Sex	Male	2089	608,450.4	3.43 (3.29–3.58)	2738	1,305,488.6	2.10 (2.02–2.18)
	Female	1595	376,529.2	4.24 (4.03–4.45)	1938	813,863.1	2.38 (2.28–2.49)
Ethnicity	White	2870	693,033.4	4.14 (3.99–4.30)	3275	1,293,007.1	2.53 (2.45–2.62)
	Black, Black British, Caribbean or African	91	34,064.7	2.67 (2.15–3.28)	162	64,807.2	2.50 (2.13–2.92)
	South Asian or Asian British	314	61,988.1	5.07 (4.52–5.66)	563	129,392.1	4.35 (4.00–4.73)
	Mixed or multiple ethnic groups	91	29,450.6	3.09 (2.49–3.79)	125	47,540.0	2.63 (2.19–3.13)
	Other ethnic groups	61	21,988.6	2.77 (2.12–3.56)	170	63,602.8	2.67 (2.29–3.11)
	Unknown ethnicity	257	144,454.2	1.78 (1.57–2.01)	381	521,002.6	0.73 (0.66–0.81)
Age–group	0–4	2	57,512.5	0.03 (0.00–0.13)	1	13,6934.9	0.01 (0.00–0.04)
	5–14	29	19,7308.5	0.15 (0.10–0.21)	2	414,133.0	0.00 (0.00–0.02)
	15–24	159	21,3247.2	0.75 (0.63–0.87)	66	484,887.8	0.14 (0.11–0.17)
	25–34	405	160,077.2	2.53 (2.29–2.79)	159	314,415.7	0.51 (0.43–0.59)
	35–44	691	107,470.7	6.43 (5.96–6.93)	548	212,232.6	2.58 (2.37–2.81)
	45–54	945	111,172.4	8.50 (7.97–9.06)	1263	241,987.9	5.22 (4.94–5.52)
	55–64	825	78,487.7	10.51 (9.81–11.25)	1379	175,551.2	7.86 (7.45–8.28)
	65–74	411	39,796.6	10.33 (9.35–11.38)	836	93,287.6	8.96 (8.36–9.59)
	75–84	170	15,217.6	11.17 (9.56–12.98)	358	36,458.0	9.82 (8.83–10.89)
	85+	47	4689.4	10.02 (7.36–13.33)	64	9462.9	6.76 (5.21–8.64)
BMI category	Underweight	27	37,214.6	0.73 (0.48–1.06)	12	27,377.2	0.44 (0.23–0.77)
	Healthy weight	308	202,445.2	1.52 (1.36–1.70)	368	288,906.4	1.27 (1.15–1.41)
	Overweight	720	160,739.1	4.48 (4.16–4.82)	1129	239,175.0	4.72 (4.45–5.00)
	Obese	2396	193,469.8	12.38 (11.89–12.89)	2823	206,252.3	13.69 (13.19–14.20)
	Unknown BMI	233	391,110.9	0.60 (0.52–0.68)	344	135,7640.8	0.25 (0.23–0.28)

Ethnicity was classified using 2021 Census Ethnic groups https://www.ethnicity–facts–figures.service.gov.uk/style–guide/ethnic–groups with the exception of Chinese, which is included in the "other ethnic groups" category, because of the known risk for T2DM in people of south Asian ethnicity [52].

intellectual disabilities was 3.74 per 1000 person-years, compared to 2.21 per 1000 person-years in controls. Incidence rates for T2DM were highest in people of South Asian or Asian British ethnicity in both groups (5.07 and 4.35 per 1000 person-years respectively). There was an age-related increase in incidence rates but the incidence of T2DM was higher for people with intellectual disabilities than controls in each age group. Incidence rates were highest in people in the obese BMI category in both groups, but higher in controls compared to people with intellectual disabilities (13.69 versus 12.38 per 1000 person years).

Supplementary Table S3 shows risk of new onset of T2DM in people with intellectual disabilities without considering an interaction between age and intellectual disabilities. In this model the IRR for people with intellectual disabilities was 1.69 (95 % CI 1.61–1.76) times as high as the rate among controls.

The demographic characteristics of T2DM within people with intellectual disabilities, and controls are given in supplementary Table S2. In summary, more males were diagnosed with T2DM in both groups and the median age of diagnosis for T2DM was lower in intellectual disabilities compared to the general population (median age 51 years compared to 57 years). Results showed that females were at lower risk of developing T2DM compared to males (IRR 0.88, 95 % CI 0.84–0.92, Table 2) and there was a non-linear relationship between risk of T2DM and year of diagnosis. There was a significant non-linear relationship with age and risk of T2DM suggesting that as people get older, the observed age effect on risk of T2DM onset is lessoned. The interaction between age and intellectual disabilities was significant (IRR 0.97, 95 % CI 0.97–0.98, Fig. 1). At 0 years old the IRR for T2DM in people with intellectual disabilities was 6.91 times (95 % CI 5.81–8.22) as high as the rate among controls.

This age interaction was explored further by fitting additional Poisson regression models (supplementary Table S4). Between the ages of 15–24 years the IRR for people with intellectual disabilities was nearly 5 times (95 % CI 3.63–6.49) as high as the rate for controls. This decreased to 4.45 (95 % CI 3.70–5.36) between 25–34 years old. By the age group 55–64 years old, IRR for T2DM decreased further to 1.33 (95 % CI 1.22–1.45) in people with intellectual disabilities compared to controls and 1.16 (95 % CI 1.03–1.31) between the ages of 65–74 years old. From the age group 75–84 years old there was no significant difference in the IRR for T2DM between the groups.

Compared to people of white ethnicity, people of all other ethnicities were at elevated risk of developing T2DM, with the highest risk being among people of South Asian or Asian British ethnicity (IRR 2.78, 95 % CI 2.59–2.98).

Adjusting for BMI categories (supplementary Table S5), intellectual disabilities-age interaction was reduced and the risk of new onset of T2DM was 2.88 (95 % CI 2.42–3.43) as high in people with intellectual disabilities compared to controls. Compared to people with a healthy BMI , new onset of T2DM in people classified as overweight was 2.30 times (95 % CI 2.10–2.51) and 6.84 times (95 % CI 6.31–7.41) as high in people who were classified as obese. People who were classified as underweight had an IRR of 0.60 (95 % CI 0.44–0.83) compared to those with a healthy BMI.

When adjusting for age at diagnosis, sex, ethnicity and history of known risk factors for T2DM, the largest risk factor for developing T2DM in people with intellectual disabilities was a history of mobility issues prior to their T2DM diagnosis compared to controls (OR = 7.72, 95 % CI 5.87–10.15; supplementary Table S6). This was followed by a history of sleep problems (OR = 1.55, 95 % CI 1.23–1.95) and hypothyroidism (OR = 1.36, 95 % CI 1.01–1.82). A previous history of antidepressant medication, hypertension, ischemic heart disease and steroid medication prescription were less strongly associated with T2DM in people with intellectual disabilities than in the general population.

There were similar trends across time for quality of care indicators and targets, with a decline in the proportion of people being offered monitoring and interventions during the COVID-19 pandemic years (2020/21 and 2021/22; supplementary Table S7). Examining the median recording of indicators of quality of care, Table 3 shows that HbA1c, cholesterol, retinal and foot examinations were less well recorded in people with intellectual disabilities, while blood pressure recording was comparable between people with intellectual disabilities and controls, as was smoking status and BMI. Rates of people with T2DM being offered lifestyle advice to better manage their DM was less than 50 % in both groups and only a minority of people with T2DM (less than 10 %) were offered weight management (codes such as 'refer to weight management program', 'refer to dietician' and 'referral for exercise therapy'). Further details relating to the indicators of quality of care measurements divided by year can be found in supplementary Tables S7 and S8.

People with intellectual disabilities had a 12 % higher risk of developing macrovascular complications (HR = 1.12, 95 % CI 1.02–1.24; Table 4, supplementary Fig. S2) following their T2DM diagnosis compared to controls. However, people with intellectual disabilities had a lower risk of being diagnosed with both neurological (HR = 0.82, 95 % CI 0.70–0.97) and ophthalmic complications (HR = 0.82, 95 % CI 0.70–0.86) compared to controls. There was no significant difference in the risk of developing renal complications in people with intellectual disabilities compared to controls ($p > 0.05$).

For macrovascular and renal complications, the risk of developing these complications increased by 4–5 % for each additional year of age at diagnosis. Risk of developing renal complications increased by 2 % for each additional year of duration of T2DM while it increased by 5 % for neurological complications. Risk of ophthalmic and macrovascular complications decreased by 1 % and 2 % for each additional year of having T2DM, respectively. Females with T2DM had a 23 % higher risk of being diagnosed with renal complications (HR = 1.23, 95 % CI 1.14–32) compared to men with T2DM but a 38 % lower risk for macrovascular complications (HR = 0.62, 95 % CI 0.56–0.68), a 20 % lower risk for neurological complications (HR = 0.80, 95 % CI 0.68–0.93) and a 9 % lower risk for ophthalmic complications (HR = 0.91, 95 % CI 0.87–0.96). Compared to people of white ethnicity with T2DM, overall people of South Asian or Asian British ethnicity had a 45 % lower risk of being diagnosed with neurological complications (HR = 0.55, 95 % CI 0.40–0.76) but a 13 % higher risk of developing ophthalmic complications (HR = 1.13, 95 % CI 1.04–1.22).

Table 2
Results of a Poisson regression model including an age-intellectual disabilities interaction term on risk of new onset of T2DM in people with intellectual disabilities compared to general population controls. Diabetes incidence rate ratios (IRR) were adjusted for each of the variables shown.

		IRR	95 % CI		p-value
			LL	UL	
Intellectual disabilities		6.91	5.81	8.22	<0.0001
Year (per year)		1.24	1.20	1.28	<0.0001
Year-squared		0.98	0.98	0.99	<0.0001
Age (per year)		1.24	1.23	1.25	<0.0001
Age-squared		0.99	0.99	0.99	<0.0001
Intellectual disabilities-age interaction		0.97	0.97	0.98	<0.0001
Sex	Male	Ref.			
	Female	0.88	0.84	0.92	<0.0001
Ethnicity	White	Ref.			
	Black, Black British, Caribbean or African	1.56	1.38	1.77	<0.0001
	South Asian or Asian British	2.78	2.59	2.98	<0.0001
	Mixed or multiple ethnic groups	1.42	1.24	1.62	<0.0001
	Other ethnic groups	1.58	1.38	1.80	<0.0001
	Unknown ethnicity	0.60	0.55	0.65	<0.0001

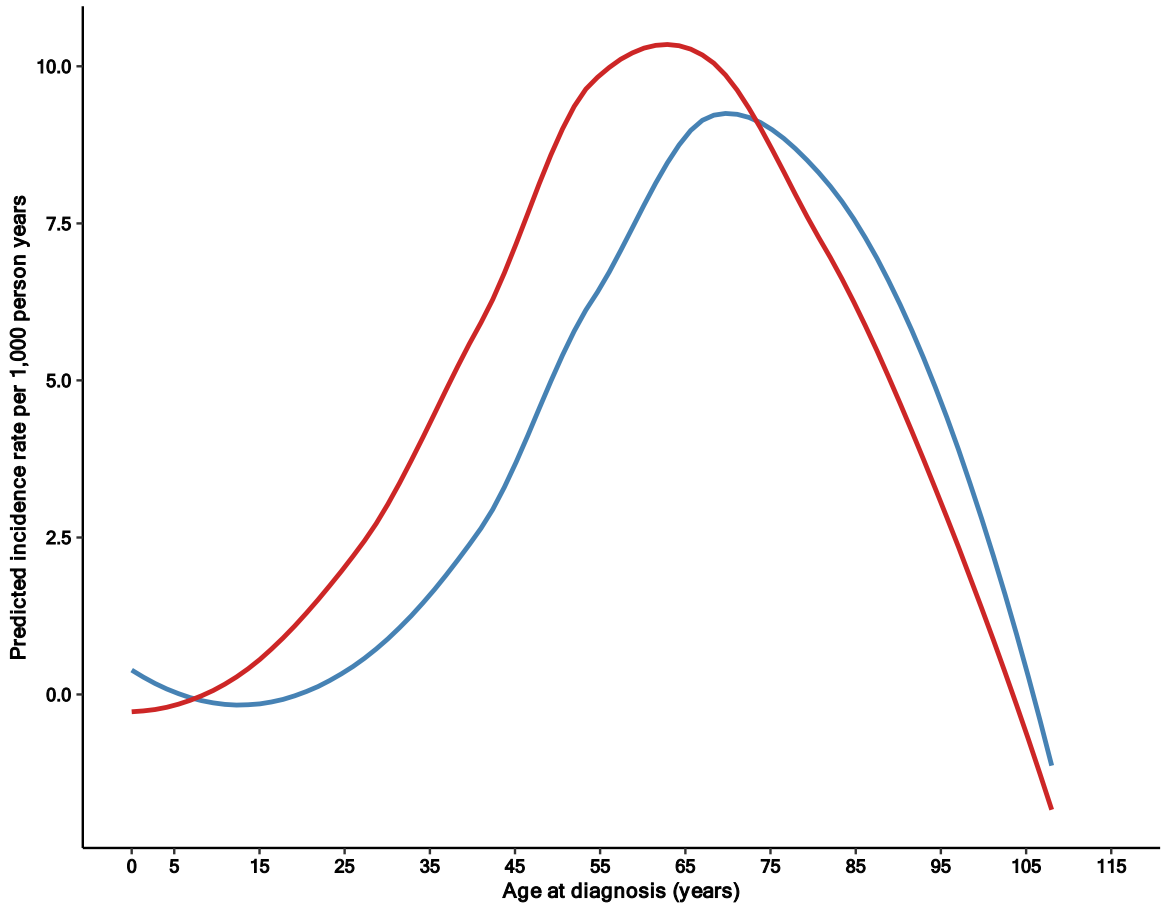

Fig. 1. Predicted incidence of T2DM by age-group with an age by intellectual disabilities interaction for people with intellectual disabilities (red) and general population controls (blue). Fig. 1 *shows the predicted incidence of T2DM by age from the Poisson regression model with an age-intellectual disabilities interaction term. As the graph illustrates, the incidence of T2DM is shifted earlier in age until older age for people with people with intellectual disabilities (red) compared to controls (blue).*

Table 3
Comparison of median percentages across years of quality-of-care measurements recorded between 2011–12 to 2019–20 (avoiding the COVID-19 pandemic).

	Median percentage recorded (IQR)		
	Intellectual disabilities	Controls	p-value of comparison
Systolic blood pressure measurement	90.92 (90.31–91.22)	91.50 (90.65–91.83)	0.27
Diastolic blood pressure measurement	90.94 (90.33–91.23)	91.50 (90.65–91.83)	0.29
HbA1c measurement	87.24 (85.27–87.43)	89.11 (88.49–89.74)	0.01
Cholesterol measurement	82.78 (80.34–82.91)	85.90 (83.40–86.22)	0.01
Retinal screening	49.18 (46.31–55.95)	57.24 (54.71–63.54)	0.02
Foot exam	70.88 (69.84–71.63)	76.42 (74.52–76.67)	0.003
Weight management/ intervention	8.56 (7.95–9.20)	6.70 (6.28–6.90)	0.001
Lifestyle advice	48.77 (47.72–49.46)	48.09 (46.62–52.38)	0.97
Influenza vaccination recorded	29.11 (26.89–32.19)	30.18 (27.23–33.18)	0.90
Smoking status recorded	80.08 (78.57–80.74)	79.08 (77.98–80.28)	0.38
BMI recording	80.11 (79.81–82.10)	80.42 (79.11–82.45)	0.90

4. Discussion

Using a large representative primary care dataset, we showed that there is a higher incidence of T2DM in people with intellectual disabilities compared to controls, particularly at a younger ages, with risk of new onset of T2DM significantly higher in people with intellectual disabilities from adolescence until the 65–74 age group. We estimated an IRR of 6.91 (95 % CI 5.81–8.22) for T2DM in people with intellectual disabilities if an interaction with age is considered. Furthermore, there was an increased risk of new onset of T2DM in some ethnic minority groups such as those from black and south Asian ethnicity backgrounds across the groups.

We demonstrated that there are differences in risk factors associated with the development of T2DM between people with intellectual disabilities and general population controls. Although obesity, endocrine disorders (other than thyroid disease) and prescription of antipsychotic medications had a similar association with T2DM in the two groups, there were stronger associations with T2DM and mobility issues, sleep disorders and thyroid disorder in people with intellectual disabilities, while a previous history of antidepressant medication, hypertension, ischemic heart disease and steroid medication prescription were less strongly associated with T2DM than in the general population. We identified evidence for proactive monitoring inequalities for people with intellectual disabilities with blood tests for HbA1c and cholesterol, and eye and foot examinations being significantly less likely to be offered. People with intellectual disabilities had higher rates of macrovascular complications but lower rates of neurological and ophthalmic complications, while rates of renal complications were similar compared to

Table 4
Complications associated with T2DM in people with intellectual disabilities compared to the general population controls.

		Complications associated with T2DM																	
		Macrovascular				Renal				Neurological				Ophthalmic					
		HR	95 % CI		p-value	HR	95 % CI		p-value	HR	95 % CI		p-value	HR	95 % CI		p-value		
			LL	UL			LL	UL			LL	UL			LL	UL			
Intellectual disabilities		1.12	1.02	1.24	0.02	1.00	0.93	1.08	0.93	0.82	0.70	0.97	0.02	0.82	0.70	0.86	<0.0001		
Age at T2DM diagnosis		1.04	1.03	1.04	<0.0001	1.05	1.05	1.05	<0.0001	1.00	1.00	1.01	0.28	1.00	0.99	1.00	0.32		
Duration of T2DM		0.98	0.97	0.99	0.002	1.02	1.01	1.03	0.0003	1.05	1.04	1.07	<0.0001	0.99	0.98	0.99	0.004		
Sex	Male	Ref.				Ref.				Ref.				Ref.					
	Female	0.62	0.56	0.68	<0.0001	1.23	1.14	1.32	<0.0001	0.80	0.68	0.93	0.005	0.91	0.87	0.96	0.0002		
Ethnicity	White	Ref.				Ref.				Ref.				Ref.					
	Black, Black British, Caribbean or African	0.73	0.51	1.04	0.08	0.87	0.68	1.11	0.25	0.93	0.59	1.48	0.77	1.11	0.96	1.27	0.15		
	South Asian or Asian British	1.06	0.89	1.27	0.49	0.92	0.80	1.05	0.21	0.55	0.40	0.76	0.0003	1.13	1.04	1.22	0.003		
	Mixed or multiple ethnic groups	0.93	0.68	1.26	0.63	1.00	0.81	1.25	0.97	0.96	0.62	1.50	0.87	1.29	1.13	1.47	0.0002		
	Other ethnic groups	0.97	0.71	1.34	0.87	0.74	0.57	0.96	0.03	0.61	0.34	1.07	0.09	1.13	0.98	1.30	0.10		
	Unknown ethnicity	1.20	1.02	1.40	0.03	0.91	0.80	1.03	0.14	0.86	0.65	1.15	0.32	0.81	0.74	0.89	<0.0001		

controls, even considering the duration of T2DM.

Previous smaller and localised studies have suggested increased rates of DM in people with intellectual disabilities [3,15,17] and showed that older age is associated with higher DM prevalence [3]. While there are only a handful of studies specifically investigating T2DM in intellectual disabilities, our findings are similar to the existing literature [5,6], including a recent Danish population-based matched cohort study which showed a significant increase in risk for T2DM in people with intellectual disabilities [6]. However, in our analysis, we demonstrate the extent of the increased risk if age is considered, with highest risk amongst young people with intellectual disabilities, from adolescence into older age. This is a novel finding and has important implications, as people with intellectual disabilities are potentially exposed to the adverse consequences of T2DM over a longer period of time, and earlier-onset diagnosis of T2DM carries an excess risk of microvascular complications, adverse cardiovascular outcomes, and earlier death [29], suggesting that to prevent complications, better prevention and monitoring are required for people with intellectual disabilities from an earlier age.

Within the sample population, we observed similar risk factors for onset of T2DM as previous work, including males being at increased risk [30,31], and an excess risk for people from certain ethnic minority backgrounds, especially those from south Asian backgrounds [32]. BMI is another major contributor to T2DM risk, and we found higher risk of onset in those recorded as being overweight or obese. In people with intellectual disabilities, there was some evidence to suggest that the effect of BMI might be sex specific, where there is an observable difference in BMI of females with intellectual disabilities compared to general population but not males (supplementary Fig. S1). Previous work has also shown that females with intellectual disabilities have higher prevalence of T2DM than females in the general population [33]. In the present study we found a higher incidence rate of T2DM in females with intellectual disabilities (4.24 per 1000 person years) compared to males with intellectual disabilities (3.43 per 1000 person years) and nearly double the rate found in matched female general population controls (2.38 per 1000 person years). Future work could examine the underlying reasons for the sex differences further.

We have identified that some co-occurring conditions may have a stronger association with T2DM in people with intellectual disabilities compared to the general population, such as a prior history of sleep problems and thyroid disorders, both of which are more common in people with intellectual disabilities [2]. Compared to controls, mobility issues prior to the T2DM diagnosis was the most important risk factor for T2DM in intellectual disabilities suggesting that inability to participate in physical exercise and a sedentary lifestyle has detrimental effects on the development of T2DM especially in intellectual disabilities [10]. Mobility issues are more prevalent in intellectual disabilities compared to the general population, potentially related to higher rates of obesity [34,35] and limited physical activity [36]. Our findings highlight the need to tackle health risks associated with mobility issues in intellectual disabilities at an early stage, including providing aids and access to appropriate forms of physical exercise [37]. These findings have implications for improved surveillance and prevention in people with intellectual disabilities presenting with these issues in the context of risk of T2DM.

Other research has identified that people with certain genetic conditions associated with intellectual disabilities such as Down Syndrome, Prader Willi Syndrome and Bardet-Biedl syndrome are at increased risk for DM [7–9]. Although this may account for some of the increased risk observed in the present study, these groups only represent a relatively small proportion of the overall population with intellectual disabilities. Most recent studies suggest that, even within the general population, early-onset T2DM carries a distinct genetic architecture [38], and it is possible that there are additional or different genetic risks for T2DM in people with intellectual disabilities who do not have a diagnosis of a recognised genetic syndrome. Therefore in-depth exploration into genetic factors that could contribute to the higher T2DM risk in people

with intellectual disabilities warrants future investigations.

With regards to management of conditions associated with DM, our analyses support the application of existing NHS guidance for the assertive management of obesity, hypertension, cardiovascular health, and reducing or monitoring the long-term impact of antipsychotic medication in people with intellectual disabilities. While we found a 12 % higher risk of macrovascular complications (e.g. diabetic foot and stroke) in people with intellectual disabilities compared to controls, risk of developing ophthalmic (e.g. retinopathy and maculopathy) and neurological complications (e.g. neuropathy and polyneuropathy) were 18 % lower in people with intellectual disabilities for both compli. Literature on T2DM related complications in intellectual disabilities is limited, however, a study using primary care data from The Netherlands found higher rates of diabetic foot in people with intellectual disabilities but lower rates of other complications, despite overall higher rates of T2DM in people with intellectual disabilities compared to the general population [39], similar to the present study. It is likely that T2DM related complications are being underdiagnosed in people with intellectual disabilities perhaps due to the presentation of ophthalmic and neurological complications requiring reliable reporting of symptoms compared to macrovascular complications, which may be easier to be observed. Another explanation may be that people with intellectual disabilities and T2DM are experiencing delays in diagnosing and treatment of specific T2DM related complications [39] compared to the general population. These findings have important implications for the long-term management of T2DM in people with intellectual disabilities and require further investigation to understand their impact on morbidity and mortality.

In terms of quality of care indicators that may require improvement, annual health checks for people with intellectual disabilities in the UK [40] may have helped to improve basic checks in primary care, such as blood pressure and BMI. However, people with intellectual disabilities and T2DM were less likely to have eye and foot checks, and our results indicate that this is an area where improvements are required. The pathways for these checks involve input from clinics or specialists outside of primary care and suggests that work may be required to improve these, for example, better communication between primary and secondary care, provision of accessible information, and implementing reasonable adjustments to improve uptake and completion of checks.

Another area for improvement is weight management and lifestyle advice. These results support similar previous work of T2DM in intellectual disabilities which found that weight management approaches such as physical activity are low in this population [36]. Barriers previously identified include poor understanding of DM in people with intellectual disabilities [41]. Structured education for people with intellectual disabilities and training for caregivers to support self-efficiency may be required to address this. There have been efforts to adapt health promotion programs for people with intellectual disabilities, including specific education programs [42–44] with some evidence to suggest people with mild and moderate intellectual disabilities may adhere to supported self-management of T2DM [45]. Further work may be required to ensure such programs are successfully implemented within the NHS. In the USA, specialist input (defined as a visit to an endocrinologist, diabetes care educationalist or other relevant specialist) were associated with better diabetes care for people with intellectual disabilities [46].

Overall, there is a need for improved DM care for people with intellectual disabilities to help prevent and manage the condition effectively. Healthcare providers and caregivers should be aware of the increased risk of T2DM in this population and take steps to ensure that appropriate screening and management strategies are in place, including offering screening at earlier ages, and proactive follow-up of those with T2DM to avoid complications.

There are several limitations to our study which should be discussed. Firstly, there was a difference in follow-up time between people with intellectual disabilities and the general population controls, perhaps due to people with intellectual disabilities being more likely to change practice more frequently than controls. We used the approach of analysing all available data from our sample and the analytical methods we employed took into account the length of follow-up time, therefore the differing amount of person time was incorporated into the analyses. For both the Poisson and Cox models, the estimated risk and hazard ratios represented an average during the period of follow-up and were assumed not to change over time. Missing data may have also impacted our results, however, multiple imputation was not appropriate in our study because electronic health record values are typically missing not at random [47,48]. Our results could also have been impacted by underdiagnosing of T2DM in people with intellectual disabilities and the general population controls, and it would be beneficial to investigate the rates of underdiagnosis in people with intellectual disabilities in future studies, particularly given the significant health inequities they experience [49]. Another limitation was that we could not adjust for socioeconomic status in our analysis. However, socioeconomic status can be difficult to use and interpret in studies of people intellectual disabilities, particularly when compared to other populations. This is because in the U.K. the majority of people with intellectual disabilities are unemployed [50] and in receipt of state benefits and are often placed in care settings [51] in neighbourhoods that do not reflect their families' socioeconomic status. Moreover, certain variables that could potentially contribute to T2DM risk such as parental BMI, being born small for gestational age and detailed data on diet are not sufficiently recorded for all individuals in their electronic health records, therefore we could not account for the impact of these variables on our results. Consequently future studies would benefit from considering the impact of socioeconomic status and other variables on the risk of new onset of T2DM in people with intellectual disabilities. As previously noted there could potentially be underdiagnosing or delays in the diagnosis of T2DM related complications in people with intellectual disabilities which could affect the accuracy of the results. Therefore these results should be interpreted with caution and future work in this area is urgently needed to provide a clearer understanding of T2DM related complications in intellectual disabilities. Moreover, due to the way in which the indicators of quality of care data were extracted and processed, we did not have data to conduct a more in-depth investigation of quality of care, such as patient reported aspects of care.

5. Conclusions

Our findings suggest that screening for T2DM should be offered at younger ages to people with intellectual disabilities. Furthermore, people with intellectual disabilities and a past history of mobility, sleep issues and hypothyroidism may require targeted screening and prevention. Due to our representative sample, these findings are generalisable to other people with intellectual disabilities, and we have also identified areas for improvement in monitoring for complications of T2DM, requiring improvement of pathways for eye and foot checks, as well as to improve uptake of blood tests.

Author contribution

R.A.B., M.C.G. and A.S. were involved in the conception, design, and conduct of the study. A.S. and R.A.B. planned the data analysis. R.A.B. conducted the data analysis with help from M.C.G. All authors wrote, reviewed and edited the manuscript. R.A.B. and M.C.G. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing

Summary data are available upon reasonable request; whilst underlying data is managed by CPRD. All proposals requesting data access need to specify planned uses with approval of the study team and from CPRD before data release.

CRediT authorship contribution statement

R.Asaad Baksh: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Sarah E. Pape:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Li F. Chan:** Writing – review & editing, Writing – original draft, Conceptualization. **Rory Sheehan:** Writing – review & editing, Writing – original draft, Funding acquisition. **Adam White:** Writing – review & editing, Writing – original draft. **Umesh Chauhan:** Writing – review & editing, Writing – original draft, Funding acquisition. **Martin C. Gulliford:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **André Strydom:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2025.112090.

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