Socioeconomic Deprivation and the Risk of Sight-Threatening Diabetic Retinopathy (STDR)

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Title:
Socioeconomic deprivation and the risk of sight-threatening diabetic retinopathy (STDR): a population-based cohort study in the UK

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Twitter summary

A UK study reveals an elevated risk of sight-threatening diabetic retinopathy in socioeconomically deprived individuals with diabetes, underscoring health equity issues.

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Objective

To evaluate the associations between socioeconomic deprivation and the risk of sight-threatening diabetic retinopathy (STDR) in individuals with type 1 and type 2 diabetes.

Research design and methods

Using data derived from 175,628 individuals with diabetes in the Health Improvement Network, we assessed the risk of STDR across Townsend Deprivation Index quantiles using Cox proportional hazard regression models.

Results

Compared to the least deprived individuals, those in the most deprived quintile with type 1 diabetes had a 2.85 times higher risk of developing STDR (95% CI 1.05-7.73), and those with type 2 diabetes had a 25% higher risk (1.13-1.40).

Conclusions

Increasing socioeconomic deprivation is associated with a higher risk of developing STDR in people with diabetes. This underscores persistent health disparities linked to poverty, even within a country offering free universal healthcare. Further research is needed to address health equity concerns in socioeconomically deprived regions.

Article highlights

- **Why did we undertake this study?**

  Deprivation has been associated with various diabetes-related health issues, including morbidity, mortality, and blood glucose levels; however, its specific relationship with sight-threatening diabetic retinopathy (STDR) in people with diabetes remains relatively unclear.

- **What is the specific question(s) we wanted to answer?**

  Whether deprivation played a significant role in the development of STDR in both people with type 1 and type 2 diabetes.

- **What did we find?**

  A higher risk of developing STDR was observed in people with diabetes in more deprived areas.

- **What are the implications of our findings?**

  Within the context of the UK's free universal healthcare system, addressing health equity in deprived areas has the potential to prevent STDR in people with diabetes.

Introduction

Diabetic retinopathy (DR), affecting over one-third of the 537 million adults with diabetes in 2021, is a leading cause of preventable blindness (1). Sight-threatening diabetic retinopathy (STDR) is an advanced stage of DR affecting one in ten individuals with diabetes, which presents a significant health burden globally (2). While past studies linked low socioeconomic status with STDR in type 1 diabetes (T1DM), these studies often with small and nonrepresentative populations, lacked dedicated designs and were performed in countries without universal healthcare access (3, 4). In a country with universal healthcare, we aim to rigorously investigate the associations between socioeconomic deprivation and the risk of STDR in individuals with T1DM and type 2 diabetes (T2DM), respectively.

Research Design and Methods

Two open cohorts were performed in the Health Improvement Network (THIN), a large primary care-based electronic medical records database generalizable to the UK population for demographics, major condition prevalence, and death rates (5). We included individuals newly diagnosed with T1DM (aged below 40 and with insulin prescription) or those with newly diagnosed T2DM (aged over 16) between 1st January 2005 and 21st February 2020. To ensure only incident diabetes individuals were captured, the study entry began 12 months after registration. Townsend deprivation index quantile was used to measure socioeconomic deprivation, incorporating four components: unemployment, car ownership, homeownership, and household overcrowding (6). As the outcome was incident STDR, individuals with STDR at baseline were excluded. All conditions were identified using Read codes (7).

All participants were followed up from 15 months after the initial diagnosis date of diabetes (a latency period to minimize reverse causation bias) until the earliest occurrence of first diagnosis

of STDR, individuals left practice, practice ceased contributing to the database, death, or study end (21st February 2020).

The incidence rates (IR) of STDR (per 1,000 person-years) across Townsend quintiles were estimated by Poisson regression. Cox proportional hazard regression models estimated the crude and adjusted hazard ratios (aHR) for STDR, adjusting for key confounding factors: age, sex, ethnicity (grouped and classified based on UK census) (8), weight and height (T1DM cohort), body mass index categories (T2DM cohort), HbA_{1c} categories, smoking status, hypertension, peripheral vascular disease, ischemic heart disease, heart failure, chronic kidney disease, diabetic foot disease, antidiabetic drugs and lipid-lowering drugs. Missing data for ethnicity and smoking status were included in analyses as a missing category. A trend test was conducted using the multivariable-adjusted model. The risk of STDR across age groups and Townsend index missingness status were compared. All statistical tests were two-tailed and a $P < 0.05$ was considered statistically significant. Analyses were conducted using Stata 16.

Results

The T1DM cohort and the T2DM cohort comprised 4,406 participants and 171,222 participants, respectively (Figure 1 and Table 1).

Type 1 Diabetes (T1DM) Cohort

With a median follow-up of 3.7 years (interquartile range [IQR] 1.6-6.5), 89 of 4,406 individuals in the T1DM Cohort developed STDR, reflecting a crude IR of 4.6 per 1,000 person-years. Compared to individuals in the lowest two deprivation quintiles, the risk of STDR increased with deprivation levels (trend test: $P < 0.001$) and reached its highest level in the highest deprivation quintile (aHR 2.85, 95%CI 1.05-7.73) (Table 2).

Type 2 Diabetes (T2DM) Cohort

During a median follow-up of 3.8 years (IQR 1.7-6.6), 5, 363 out of 171,222 individuals with T2DM developed STDR, representing a crude IR of 7.1 per 1,000 person-years. The risk of developing STDR was associated with escalating deprivation levels (trend test: P = 0.001) and reached its highest level in the highest deprivation quintile (aHR 1.25, 95%CI 1.13-1.40) compared to the lowest deprivation quintile (Table 2).

The results of age subgroup analyses were consistent with the main findings (Table 2). Unlike the unchanged STDR risk in the T1DM cohort, individuals without Townsend index exhibited a slightly higher STDR risk (aHR 1.20, 95%CI 1.12-1.28) compared to those with Townsend index in the T2DM cohort.

Conclusions

We found that the risk of developing STDR increases with elevated levels of deprivation in individuals with T1DM and those with T2DM. Compared with the least deprived group, individuals with T1DM and T2DM in the most deprived group had nearly three times and 25% higher risk of STDR, respectively. In a country with free universal healthcare, the observed difference in the risk of STDR among different socioeconomic deprivation levels could be largely attributed to underlying factors beyond healthcare access. Our findings highlight the importance of implementing comprehensive health equity strategies that engage diverse stakeholders and prioritize proactive management and care in socioeconomically disadvantaged areas.

Similar to our results, a recent US study using data derived from 1,116,361 adults with diabetes reported that the risk of hypoglycemic and hyperglycemic crises increases with the elevated level of socioeconomic deprivation (9). The results of a Scottish primary care-based study were partly similar to our findings. After adjusting for age and gender, a higher prevalence of DR in individuals with T1DM (n = 1861) was observed only in the most deprived quintile (aHR 2.40, 95% CI 1.36-4.27), compared to the least deprived quintile. No association was observed between deprivation and the prevalence of DR in individuals with T2DM (n = 18,197) (10). Conversely, another large UK primary care-based study with 7.7 million participants reported an association of deprivation with the incidence of DR/severe retinopathy in individuals with T2DM (no trend was observed), but not in individuals with T1DM (11). While these studies provide valuable insights, their capacity to furnish precise estimates is hindered by flaws within their designs (e.g. failure to exclude individuals with the outcome of interests at baseline and to adjust for essential confounders [e.g. smoking, HbA_{1c} levels, and comorbidities]) (10, 11).

The evident association of deprivation with the risk of STDR in individuals living with diabetes observed in a country with a universal healthcare system are possibly attributed to underlying factors beyond healthcare access. Firstly, the built environment plays a pivotal role, where inadequate housing conditions, deficient community infrastructure, and limited access to green spaces intertwine, impacting overall well-being and health conditions (12). Secondly, restricted educational opportunities and lower health literacy in these areas may lead to limited engagement in health awareness programs and social support networks, impacting preventive health behaviors, such as diabetes self-management and actively attending eye screening and treatment programs (13, 14). Thirdly, the racial composition and its related language barriers, even with free interpreter service and proactive investigations on race inequality, may still pose significant hurdles, impeding effective communication with healthcare providers and access to

healthcare services and essential health information (15, 16). Lastly, fragmented social structures and weakened community connections exacerbate the impact of the aforementioned factors, limiting resource access, hindering community engagement, and elevating stress levels within deprived areas, thus perpetuating health disparities (17-19). Addressing these multifaceted issues requires comprehensive interventions spanning socioeconomic, environmental, and educational domains to improve the overall well-being of deprived communities.

Given that the National Health Service (NHS) offers universal free healthcare services and medications to all individuals in the UK, the observed variations in the risk of STDR among different socioeconomic deprivation groups suggested that health equity becomes crucial in socioeconomically disadvantaged regions. Individuals with lower incomes were more likely to have greater healthcare requirements (20), suggesting that prioritized healthcare services, rather than equitable provision, should be addressed in deprived communities. When providing healthcare services, socioeconomic disadvantage and health requirements should be considered as critical determinants, since increased NHS resources invested in the most impoverished areas might generate a bigger absolute increase in health outcomes compared to the wealthier regions (21). Given that individuals with high levels of deprivation are less likely to utilize planned and preventative healthcare services (22), it is essential to implement targeted healthcare interventions, such as promoting participation in DR screening programs and providing educational activities to enhance self-glucose control skills.

The large sample size, longitudinal population-based study design, and long follow-up period have ensured that the data in this study are nationally generalizable. The adjustment of important potential confounders has improved the power of the associations between

socioeconomic deprivation and STDR. However, a limitation arises from the approximately 16% missing data in Townsend deprivation indices. To address this, we conducted a sensitivity analysis comparing the risk of STDR between individuals with and without Townsend index to offer a comprehensive picture to readers. While ethnicity has been fully controlled in our analyses, if we hold a sufficient number of participants from minority groups, performing subgroup analyses in different ethnic groups would surely strengthen our conclusion. Lastly, our study had constraints in examining associations between individual components of the Townsend index and STDR due to data unavailability. Nonetheless, the Townsend index, a widely recognized composite measure, affords a more holistic assessment of deprivation than its individual elements.

In conclusion, we found socioeconomic deprivation was associated with the increased risk of STDR in people with T1DM and T2DM. This study highlights the importance of addressing health equity concerns and its relevance to the prevention of STDR.

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Author Contributions. L.T. developed the idea, designed the study, analyzed the data, and led the writing of the manuscript under the supervision of J.W and K.N. J.W checked the analysis code parallelly and revised the paper. J.W and K.N. proposed the idea, critically appraised the paper, and made final suggestions. J.H., K.T., F.C., C.S., M.Y., M.K., and A.D. provided specialist input. All authors reviewed the manuscript and agreed to submit the final manuscript. L.T. and J.W. are the guarantors of this work. There is no funding support and no potential conflicts of interest in this study.

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Table 1. Baseline characteristics of individuals with type 1 and type 2 diabetes across Townsend Deprivation Index quintiles

Type 1 diabetes	Townsend Deprivation Index				
	1 (*n* = 811) (lowest deprivation)	**2 (*n* = 752)**	**3 (*n* = 778)**	**4 (*n* = 687)**	**5 (*n* = 573) (highest deprivation)**
Age (years), mean ± SD	15.3 ± 8.5	17.1 ± 9.6	17.5 ± 9.5	18.0 ± 10.0	18.2 ± 10.5
Male, *n (%)*	479 (59.1)	431(57.3)	455 (58.5)	403 (58.7)	348 (60.7)
Ethnicity, *n (%)*					
White	347 (42.8)	323 (43.0)	361 (46.4)	321(46.7)	267 (46.6)
Mixed or Multiples	1 (0.1)	2 (0.3)	1 (0.1)	3 (0.4)	6 (1.1)
Other ethnic groups	4 (0.5)	1 (0.1)	2 (0.3)	5 (0.7)	3 (0.5)
Black, Black British, Black Welsh, Caribbean or African	0 (0.0)	5 (0.7)	4 (0.5)	4 (0.6)	9 (1.6)
Asian, Asian British, Asian Welsh	7 (0.9)	6 (0.8)	11 (1.4)	6 (0.9)	7 (1.2)
Missing	452(55.7)	415 (55.2)	399 (51.3)	348 (50.7)	281 (49.0)
Smoking Status, *n (%)*					
Smoker	43 (5.3)	70 (9.3)	86 (11.1)	93 (13.5)	125 (21.8)
Ex-smoker	34 (4.2)	40 (5.3)	59 (7.6)	46 (6.7)	31 (5.4)
Non-smoker	301 (37.1)	280 (37.2)	295 (37.9)	262 (38.1)	192 (33.5)
Missing	433 (53.4)	362 (48.1)	338 (43.4)	286 (41.6)	225 (39.3)
HbA_{1c} level, *n (%)*					
<6.5%	113 (13.9)	118 (15.7)	100 (12.9)	102 (14.9)	73 (12.7)
6.5-7.5%	179 (22.1)	191 (25.4)	168 (21.6)	131 (19.1)	106 (18.5)
7.5-8.5%	177 (21.8)	152 (20.2)	160 (20.6)	143 (20.8)	120 (20.9)
≥8.5%	179 (22.1)	172 (22.9)	217 (27.9)	187 (27.2)	176 (30.7)
Missing	163 (20.1)	119 (15.8)	133 (17.1)	124 (18.1)	98 (17.1)
Hypertension, *n (%)*	1 (0.1)	7 (0.9)	4 (0.5)	10 (1.5)	10 (1.8)
Chronic kidney disease, *n (%)*	5 (0.6)	9 (1.2)	7 (0.9)	10 (1.5)	12 (2.1)
Diabetic Foot Disease, *n (%)*	10 (1.2)	16 (2.1)	5 (0.6)	11 (1.6)	7 (1.2)
Metformin, *n (%)*	23 (2.8)	28 (3.7)	33 (4.2)	30 (4.4)	39 (6.8)

Lipid-lowering drugs, *n (%)*	14 (1.7)	14 (1.9)	19 (2.4)	21 (3.1)	21 (3.7)

Type 2 diabetes	**Townsend Deprivation Index**				
	1 (*n* = 30,909) (lowest deprivation)	**2 (*n* = 29,765)**	**3 (*n* = 31,049)**	**4 (*n* = 29,087)**	**5 (*n* = 22,181) (highest deprivation)**
Age (years), mean ± SD	64.3 ± 12.3	64.4 ± 12.6	62.8 ± 13.1	61.9 ± 13.6	60.3 ± 13.6
Male, *n (%)*	18,314 (59.3)	17,044 (57.3)	17,326 (55.8)	15,647 (53.8)	11,679 (56.7)
Ethnicity, *n (%)*					
White	13,102 (42.4)	13,492 (45.3)	14,183 (45.7)	13,510 (46.5)	11,117 (50.1)
Mixed or Multiples	140 (0.5)	119 (0.4)	189 (0.6)	200 (0.7)	227 (1.0)
Other ethnic groups	45 (0.2)	49 (0.2)	61 (0.2)	85 (0.3)	78 (0.4)
Black, Black British, Black Welsh, Caribbean or African	157 (0.5)	167 (0.6)	352 (1.1)	484 (1.7)	681 (3.1)
Asian, Asian British, Asian Welsh	572 (1.9)	563 (1.9)	984 (3.2)	1,227 (4.2)	1,017 (4.6)
Missing	16,893 (54.7)	15,375 (51.7)	15,280 (49.2)	13,581 (46.7)	9,061 (40.9)
Smoking Status, *n (%)*					
Smoker	3,056 (9.9)	3,640 (12.2)	5,016 (16.2)	5,850 (20.1)	5,740 (25.9)
Ex-smoker	11,324 (36.6)	11,139 (37.4)	11,545 (37.2)	10,675 (36.7)	7,546 (34.0)
Non-smoker	16,474 (53.3)	14,954 (50.2)	14,443 (46.5)	12,533 (43.1)	8,865 (40.0)
Missing	55(0.2)	32 (0.1)	45 (0.1)	29 (0.1)	30 (0.1)
BMI (kg/m^2), mean ± SD	30.6 ± 6.0	31.2 ± 6.3	31.8 ± 6.7	32.3 ± 6.9	32.6 ± 7.2
HbA_{1c} level, *n (%)*					

≤6.5%	13,711 (44.4)	12,714 (42.7)	12,822 (41.3)	11,516 (39.6)	8,485 (38.3)
6.5-7.5%	11,975 (38.7)	11,637 (39.1)	11,918 (38.4)	11,233 (38.6)	8,531 (38.5)
7.5-8.5%	2,719 (8.8)	2,885 (9.7)	3,204 (10.3)	3,027 (10.4)	2,396 (10.8)
≥8.5%	1,844 (6.0)	1,989 (6.7)	2,446 (7.9)	2,624 (9.0)	2,269 (10.2)
Missing	660 (2.1)	540 (1.8)	659 (2.1)	687 (2.4)	500 (2.3)
Hypertension, *n (%)*	17,162(55.5)	16,668 (56.0)	17,060 (55.0)	15,535 (53.4)	11,546 (52.1)
Peripheral vascular disease, *n (%)*	730 (2.4)	832 (2.8)	947 (3.1)	1,025 (3.5)	928 (4.2)
Stroke, *n (%)*	2,088 (6.8)	2,227 (7.5)	2,233 (7.2)	2,137 (7.4)	1,714 (7.7)
Ischemic heart disease, *n (%)*	4,996 (16.2)	5,074 (17.1)	5,280 (17.0)	5,226 (18.0)	4,043 (18.2)
Heart Failure, *n (%)*	923 (3.0)	1,013 (3.4)	1,101 (3.6)	1,168 (4.0)	924 (4.2)
Chronic kidney diseases, *n (%)*	5,428 (17.6)	5,396 (18.1)	5,238 (16.9)	4,963 (17.1)	3,404 (15.4)
Diabetic Foot Disease, *n (%)*	4,226 (13.7)	4,309 (14.5)	46,97 (15.1)	4,462 (15.3)	3,635 (16.4)
Metformin, *n (%)*	15,560 (50.3)	14,995 (50.4)	16,831 (54.2)	16,467 (56.6)	13,125 (59.2)
Insulin, *n (%)*	1,756 (5.7)	1,775 (6.0)	2,154 (6.9)	2,213 (7.6)	1,873 (8.4)
Other glucose-lowering medications, *n (%)*	4,370 (15.9)	4,380 (16.0)	5,012 (18.3)	4,997 (18.2)	4,141 (15.1)
Lipid-lowering drugs, *n (%)*	22,600 (73.1)	21,720 (73.0)	22,716 (73.2)	21,220 (73.0)	16,347 (73.7)

SD, standard deviation; HbA_{1c}, hemoglobin A1c.

Table 2. The risk of developing sight-threatening diabetic retinopathy (STDR) across Townsend deprivation index quintiles in individuals with type 1 and type 2 diabetes

Type 1 Diabetes	Townsend Deprivation Index				
	1 (lowest deprivation)	2	3	4	5 (highest deprivation)
N	811	752	778	687	573
STDR, *n (%)*	6 (0.7)	9 (1.2)	17 (2.2)	25 (3.6)	16 (2.8)
Person-years	3,582.1	3,377.7	3,454.1	2,913.9	2,568.2
Incidence rate (per 1,000 person-years)	1.7	2.7	4.9	8.6	6.2
Crude HR (95% CI)	Ref	1.69 (0.59-4.89)	2.67 (1.01-7.03)	5.08 (2.05-12.60)	4.15 (1.61-10.72)
Adjusted HR (95% CI) [*]	Ref	0.98 (0.32-3.08)	1.42 (0.50-4.03)	2.05 (0.76-5.55)	2.85 (1.05-7.73)
			Trend test: P <0.001		
By age					
<18 years (Adjusted HR, 95% CI)	Ref	0.38 (0.04-3.80)	1.03 (0.20-5.27)	2.56 (0.60-11.08)	2.88 (0.65-12.80)
≥18 years (Adjusted HR, 95% CI)	Ref	1.10 (0.29-5.32)	1.47 (0.36-6.01)	1.64 (0.43-6.35)	2.42 (0.61-9.59)

Type 2 Diabetes	Townsend Deprivation Index				
	1 (lowest deprivation)	2	3	4	5 (highest deprivation)
N	30,909	29,765	31,049	29,087	22,181
STDR, *n (%)*	881 (2.9)	858 (2.9)	942 (3.0)	930 (3.2)	701 (3.2)
Person-years	137,627.6	130,988.2	136,477.3	125,716.4	95,856.6
Incidence rate (per 1,000 person-years)	6.4	6.6	6.9	7.4	7.3
Crude HR (95% CI)	Ref	1.04 (0.94-1.15)	1.06 (0.96-1.17)	1.13 (1.02-1.24)	1.17 (1.05-1.30)
Adjusted HR (95% CI) [†]	Ref	1.06 (0.95-1.17)	1.08 (0.98-1.20)	1.18 (1.07-1.31)	1.25 (1.13-1.40)
			Trend test: P = 0.001		

By age					
<65 years (Adjusted HR, 95% CI)	Ref	1.02 (0.89-1.17)	1.12 (0.98-1.29)	1.20 (1.05-1.38)	1.21 (1.04-1.42)
≥65 years (Adjusted HR, 95% CI)	Ref	1.08 (0.93- 1.27)	1.01 (0.87-1.18)	1.11 (0.96-1.30)	1.24 (1.07-1.45)

STDR, sight-threatening diabetic retinopathy; HR, hazard ratio; Ref, reference group; CI, confidence interval.
*Adjusted for age, sex, ethnicity, weight, height, HbA_{1c}, smoking status, hypertension, chronic kidney disease (stage 3 to 5), diabetic foot disease, glucose-lowering medicine, and lipid-lowering medicine.
[†]Adjusted for age, sex, ethnicity, body mass index, HbA_{1c}, smoking status, hypertension, chronic kidney disease (stage 3 to 5), diabetic foot disease, glucose-lowering medicine, lipid-lowering medicine, peripheral vascular disease, ischemic heart disease stroke, and heart failure.