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Social Deprivation and incident Diabetes-related Foot Disease in Patients with Type 2 Diabetes - A population-based Cohort Study

Short title: Deprivation and Diabetic Foot

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Abstract

Objective: To investigate the relationship between social deprivation and ~~development~~ incident ~~of~~ diabetes-related foot disease (DFD), in newly-diagnosed patients with type 2 diabetes ~~mellitus~~.

Research design and methods: A population-based, open retrospective cohort study, using The Health Improvement Network ~~(THIN)~~, ~~between~~ (01/01/2005 ~~and~~ 31/12/2019). Patients with type 2 diabetes, free of DFD at baseline, were stratified by the Townsend deprivation index and the risk of developing DFD was calculated. DFD was defined as a composite of foot ulcer (FU), Charcot arthropathy, lower limb amputation (LLA), peripheral neuropathy (PN), peripheral vascular disease (PVD) and~~or~~ gangrene.

Results: ~~179,870~~ 176,359 patients were eligible (5~~65.9~~% men; aged 62.9±13.1years~~-~~). After excluding 26,09~~444~~ patients with DFD before/within 15 months of type 2 diabetes diagnosis, DFD was incidentally developed in 12.~~08141~~% of study population during ~~a median follow-up of~~ 3.21years (IQR:1.37-5.88) ~~years~~. Patients in the most deprived Townsend quintile had increased risk of DFD compared to those in the~~e~~ least deprived (aHR:1.22~~1~~, 95%CI:~~-~~1.16~~5~~-1.29~~7~~) after adjusting for sex, age at type 2 diabetes diagnosis, ethnicity, smoking, BMI, HbA1c, cardiovascular disease, hypertension, retinopathy, eGFR, insulin ~~treatment~~, glucose~~-lowering//~~lipid-lowering medications and baseline foot risk. Patients ~~at~~ in the most deprived Townsend quintile had higher risk of ~~peripheral neuropathy~~ PN (aHR:~~-~~1.18~~7~~, 95%~~-~~CI:~~-~~1.11~~0~~-1.25~~4~~), FU~~foot ulceration~~ (aHR:1.44~~28~~, 95%CI:~~-~~1.17~~1~~-1.77~~48~~), PVD (aHR:1.40~~39~~, 95%CI: 1.28~~7~~-1.53~~2~~) ~~and~~ LLA (aHR:1.75, 95%CI:~~-~~1.08-2.83~~4~~) and gangrene (aHR:~~-~~8.49, 95%~~-~~CI: 1.01-71.58) compared to those in the~~e~~ least ~~deprived~~.

Conclusion: Social deprivation is an independent risk factor for the development of DFD, PN, FU~~foot ulceration~~, PVD, ~~and~~ LLA and gangrene in ~~newly diagnosed~~newly-diagnosed patients with type 2 diabetes. Considering the high individual and economic burden of DFD,

strategies targeting patients in socially deprived areas are needed to ~~and will~~ reduce health inequalities.

Key words: Type 2 diabetes mellitus, diabetic foot disease, deprivation, Townsend index, foot ulcer, peripheral vascular disease, amputation

Abbreviations:

DFD: Diabetic Foot Disease, **DFU:** Diabetes-related Foot Ulceration, **DPN:** Diabetes Peripheral Neuropathy, **LLA:** Lower Limb Amputation, **PVD:** Peripheral Vascular Disease, **CV:** Cardiovascular**, THIN:** The Health Improvement Network, **BMI:** Body Mass Index, **eGFR**: estimated Glomerular Filtration Rate, **HA1c:** Haemoglobin A1c, **SD:** Standard Deviation, **IQR:** Interquartile Range, a**HR:** adjusted Hazard Ratio, **OR:** Odds Ratio

~~1.~~ Introduction

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Diabetes mellitus is a major public health challenge, affecting more than 400 million people worldwide. (1) In the UK, an estimated £14 billion is spent a year on treating diabetes, driven by the cost of treating ~~the~~ diabetes-related complications. (2)

The global prevalence of diabetes-related foot diseases (DFD) is estimated to be 6.3% and it is one of the most expensive complications of diabetes mellitus. (3; 4) The lifetime incidence of diabetes-related foot ulceration (DFU) is 19-34%, while Lower limb amputation (LLA) incidence rate in diabetes is 2.51 per 1,000 person-years and the prevalence of diabetes peripheral neuropathy (DPN) is 50%. (5-8) DFU and LLA are associated with significant disability (9) and increased mortality (5 year mortality risk: 70% following LLA and 50% following DFU). (10)

Diabetes peripheral neuropathy (DPN), and peripheral vascular disease (PVD) are major contributors to the development of DFD, DFU and LLA. (11) Current preventative strategies are focussed on preventing PVD and DPN by improving glycaemic control and cardiovascular (CV) risk factors and providing appropriate education and foot-wear to patients. (12) These have resulted in reduction in the risk of LLA (12) but DFD remains common and hence better understanding of the risk factors is needed.

Social deprivation is a potential contributor to the risk of DFD as it is associated with obesity and CV risk and development of type 2 diabetes. (13-19) Hence, we hypothesised that social derivation is a risk factor for DFD in patients with type 2 diabetes.

To examine our hypothesis, we conducted a large population-based cohort study, using a UK nationally representative primary care database, aimed at examining the relationship between social deprivation and the incidence of DFD.

~~2.~~ Research design and methods

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~~2.1~~ Design of the study

A population-based, open retrospective cohort study, using routinely collected data from The Health Improvement Network (THIN) database between the 1st January 2005 and the 31st December 2019.

~~2.2~~ Data source: The Health Improvement Network

THIN consists of anonymised primary care records taken from over 800 UK general practices. The database is largely representative of the UK population in terms of demographics and morbidity prevalence. (20) The dataset consists of symptoms, examinations and diagnoses which are recorded using a hierarchical coding system called Read codes. (21; 22)

~~2.3~~ Study population, inclusion and exclusion criteria in the exposed cohort

All patients were recruited from practices that have been using the vision electronic system for 1 year and had acceptable mortality reporting. Patients were eligible to join the exposed cohort if they developed type 2 diabetes (based on Read codes) during ~~the~~ follow-up (**Supplementary File 1**). Patients with a ~~coded diagnoses of type 1 diabetes~~coded diagnosis of type 1 diabetes were excluded. Furthermore, patients with age at diagnosis below the age of 30 with a record of insulin prescription and no prescription record of any of the oral diabetes medications in their medical history were excluded, as they were considered to be potentially misclassified as type 2 diabetes. Patients who already have one of the outcomes of interest at baseline or those who developed them between diagnosis date and index date (i.e. 15 months after type 2 diabetes diagnosis) were excluded from the ~~longitudinal~~ incident analysis. The latency period provides a 15th month window of opportunity for assessment of baseline foot risk and documentation of diabetes related covariates.

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The exposed cohort was subcategorised by Townsend deprivation score, which is the independent exposure variable in this study. The Townsend score is a measure of material deprivation developed in 1988, from census tables. (23) It includes unemployment, overcrowding, car ownership and home ownership for small geographies, which are z-scored to produce an overall score. This is the deprivation marker included in primary care records, derived from a patients' postcode. Townsend score is already recorded in THIN database as quintiles, with the 1st quintile to be the lowest (least deprived) and ~~the~~ 5th, the highest.

~~2.4~~ Outcomes and co-variates

The primary outcome of the study was the incident diagnosis ~~subsequent recording~~ of DFD (a composite outcome of DFU, PVD, DPN, Charcot arthropathy, LLA and gangrene).

Co-variates include age at type 2 diabetes diagnosis, sex, ethnicity, body mass index (BMI), smoking, glucose lowering treatment, lipid lowering medication, insulin treatment as a proxy for diabetes disease severity, estimated glomerular filtration rate (eGFR), haemoglobin A1c (HA1c), retinopathy, hypertension, CV disease and baseline foot risk score. Baseline foot risk coded from the relevant Read codes was categorised as 1) low risk (normal sensation, palpable pulses), 2) increased risk/moderate risk ~~increased risk~~ (neuropathy or absent pulses), 3) high risk (neuropathy or absent pulses plus deformity or skin changes in previous ulcer), 4) non-attendance of foot examination, or 5) missing foot risk data **(Supplementary File 1).** (24) Primary care practitioners insert the foot risk score as per their contractual agreement into the electronic system in the form of Read codes. ~~Primary care practitioners insert the foot risk score into the electronic system in the form of Read codes. In this study, we used these codes as they were presented in the THIN database and we have not recoded the foot score based on other information available in the database.~~

~~2.5~~ Follow up period

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The follow-up period began from the index date (15 months after type 2 diabetes diagnosis) until the patient exit date (the earliest date of either the outcome of interest, patient transferred to another practice, the final data collection date from their general practice or death).

2.6 Ethical approval

The THIN data collection scheme received multicentre research ethics committee (MREC) approval in 2003, and for this particular study, with the Scientific Review Committee approval (SRC Reference Number: 18THIN090) was obtained of this particular study in December 2018.

2.6 Statistical analysis

Continuous variables were presented as mean, ± standard deviation (SD) or median, interquartile range (IQR) depending on their distribution. Binary and categorical variables were analysed presented as frequencies and percentages.

Data cleaning and analysis was done using STATA 164.2. A Cox pProportional hHazards mModel was used to calculate crude and adjusted hazard ratio (aHR) of the composite DFD, and individual components of the composite outcome among patients in each of the Townsend deprivation quintile compared to those in the 1st quintile (least deprived), where numbers of outcomes were sufficient in each Townsend deprivation category. The proportional hazards assumption was checked using log-log plots. At cohort entry, using a logistic regression model, we calculated the odds ratio (OR) of DFD diagnosis before or within 15 months of diabetes diagnosis comparing among patients from each Townsend categorydeprivation quintile compared to those in the 1st quintile.

All effect sizes (HRs and ORs) were calculated along with 95% confidence interval. A p-value <0.05 was considered statistically significant.

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~~3.~~ Results

~~3.1~~ Study population characteristics

The baseline characteristics of patients ~~within the cohort~~ with a coded diagnosis of type 2 diabetes ~~and~~ after ~~the application of~~ exclusion ~~criteria~~ of those considered as potentially misclassified are summarized in ~~T~~t**able 1** stratified by Townsend quintiles. ~~There were~~Of the 17~~9~~6,359~~870~~ patients ~~meeting the inclusion criteria with a diagnosis of type 2 diabetes within THIN~~included in our study, there were 31,732 (18.0%), 30,655 (17.4%), 32~~1~~,021 (18.2%), 29,984 (17.0%), 22,881 (13.0%) patients from Townsend quintile 1 to 5, with 29,086 (10.8%) patients have a missing record of Townsend deprivation quintile.

56~~5~~.9~~0~~% of the total cohort were male and the mean age ~~of diagnosis~~at cohort entry was 62.~~8~~49 (SD~~+~~ 13.1~~3~~2~~1~~) years~~ old~~; Patients from the most deprived quintile were younger at study entry compared to the least deprived [~~61.83~~60.64 (SD 13.58~~30~~) vs 64.52 (SD 12.26)] ~~.~~ The majority of included patients had obesity (53.1%), and were ex (36.2%) or non-smokers (47.3~~8~~%). Patients from the most deprived quintile were more likely to have obesity at baseline and were more likely to be current smokers compared to those from the least deprived (Obesity: 58.9~~44.0~~% vs 46.7%; Current smokers: 25.7% vs 9.8%) HbA1c was recorded in 96.0% of the study participants, with a mean HbA1c value of 59.43~~57~~ (SD 22.~~437~~44) mmol/mol. Patients from the most deprived quintile were more likely to have a record of HbA1c> 69.4 mmol/mol at baseline compared to those from the least deprived (23.4% vs 20.5%). Ethnic minority patients were more likely to be from the highest deprivation quintile compared to the lowest deprivation quintile (8.9% vs 2.9%). ~~Patients from the most deprived quintile were more likely to have a record of HbA1c> 69.4 mmol/mol at baseline compared to those from the least deprived (23.4% vs 20.5%). Over a third of patients (32.6%) had HbA1c ≤47.5mmol/mol (≤6.5%), while~~ N~~n~~early half of the participants

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had hypertension (54.64%), and a quarter had CV disease (23.32%) at baseline. ~~Patients were approximately equally distributed across the first four Townsend quintiles, though there were less in the most deprived quintile.~~

Patients in the most deprived quintile had the highestr percentages of ~~smoking, obesity, moderate and~~ high foot risk score ~~at baseline~~(2.0% vs 1.2%), ~~lipid drugs and~~ insulin treatment (2.9% vs 2.0%)~~, poorer glycaemic control~~ and end stage kidney disease (0.9% vs 0.7%) at baseline compared to those from the least deprived quintile.

~~3.2 Odds ratio of having DFD at baseline amongst the five deprivation scores~~

Social deprivation and the baseline odds of DFD

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A total number of 26,094~~100~~ (14.8%) ~~440~~ patients had a recording of DFD before the index date (either before diabetes diagnosis, or during the 15-month latency between diagnosis date and the index date). The greatest percentage of patients with pre-existing DFD were those in the lowest deprivation quintile: 1st q~~Q~~uintile (14.0%~~; 4,437/31,752~~), 2nd q~~Q~~uintile (14.9%~~; 4,554/30,672~~), 3rd q~~Q~~uintile (15.3%~~; 4,911/32,041~~), 4th q~~Q~~uintile (15.7%~~; 4,721/30,022~~), 5th q~~Q~~uintile (16.7%~~; 3,832/22,921~~) and missing Townsend data (12.5%~~; 3,645/29,117~~).

~~These patients were excluded from the longitudinal analysis. However, a separate analysis for the association of social deprivation and early onset of DFD was done.~~ ~~After adjustment for all the covariates~~Following adjustment of variables highlighted in the methods section ~~mentioned~~ (except baseline foot risk score ~~(~~due to potential collinearity with baseline foot disease), all Townsend ~~deprivations~~ quintiles ~~scores~~ were associated with a higher adjusted odds ratio of having DFD at index date, ~~having as reference~~when compared to ~~the~~those in least deprived quintile~~score~~ (i.e. Townsend deprivation quintile 1) The results show increasing odds of DFD at baseline with increased deprivation score: q~~Q~~uintile 2; ~~(~~aOR

1.04; 95% CI 1.00-1.09, qQuintile 3; aOR 1.143; 95% CI 1.098-1.19, qQuintile 4; aOR 1.18; 95% CI 1.13-1.24 and qQuintile 5; aOR 1.345; 95% CI 1.28-1.41 for quintiles 2,3,4 and 5 respectively, p<0.05 for all,. Further details can be found in sSupplementary File 2). The results show a social gradient with theincreasing odds of DFD at baseline to be increased with each increase in quintilewith increased deprivation score. There was a slightly lower adjusted odds of baseline foot diseaseDFD recorded at baseline among those with a missing recording of Townsend (aOR: 0.95; 95% CI 0.91-1.00).

3.3 Social deprivation and the incident risk of DFD

These Ppatients with pre-existing DFD at baseline (14.8%; 26,100/176,525) were then excluded from the longitudinalincident analysis. However, a separate analysis for the association of social deprivation and early onset of DFD was done.

From the eligible patients of the studyOut of the 150,265 patients followed up, 18,153 (12.081 14%) developed DFD during a median follow-up of 3.273 21years (IQR 1.41-5.96) yearsfollow up. The incidence rate (per 1,000 person years; 95% CI) of developing DFD was highest in patients in the lowest Townsend quintile; increased with increasing deprivation; quintile 1; 29.8 (28.8-30.8), quintile 2; 31.21 (30.1-32.3), quintile 3; 30.45 (29.4-31.5), quintile 4; 31.7 (30.6-32.8), quintile 5; 3324.89 (33.5-36.2). Following adjustment this translated into a statistically significant increased risk of developing DFD in Quintiles 4 (aHR 1.10 (95% CI 1.04-1.15)) and 5 (aHR 1.22 (95% CI 1.16-1.29)). There was a stepwise increase in the risk of DFD with worsening deprivation between quintiles 2 and 5 compared to quintile 1Further details can be seen in (tTable 2).

Of the types of DFD, the most common outcome during the follow up was DPN (8.9%). The incidence of the individual components of the composite DFD outcomes (DPN, DFU, PVD, LLA, Charcot arthropathy and gangrene) in the different quiantiles of Townsend score is summarised in table 31 and fFigure 1.

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Most notably, ~~-~~p~~P~~atients ~~living~~ in the most deprived Townsend qu~~i~~antile (5) ~~have~~ went on to have a statistically significant ~~higher~~ increased risk of developing DPN (aHR: 1.1~~8~~7, 95% CI 1.1~~0~~-1.2~~5~~4), DFU (aHR 1.~~44~~28, 95% CI: 1.1~~7~~1-1.~~77~~48), PVD (aHR 1.~~40~~39, 95% CI: 1.2~~8~~7-1.5~~3~~2) ~~and~~ LLA (aHR 1.75,95% CI: 1.08-2.8~~3~~4) and gangrene (aHR: 8.49, 95% CI: 1.01-71.58) compared to patients ~~living~~ in the least deprived ~~(1)~~. The incidence of ~~C~~charcot arthropathy ~~(aHR 1.78, 95% CI: 0.83- 3.86) and gangrene (aHR 5.62, 95% CI: 0.60- 52.87), although seems to be more increased in~~higher among those in the most deprived Townsend quantile, but the ~~result~~ increase in risk~~is~~ was not statistically significant (aHR 1.65, 95% CI: 0.78- 3.49). ~~Details are provided in **Table 3.**~~

~~3.4~~ Risk factors of DFD from the fully adjusted model~~The relationship of other covariates and incident DFD~~

Details about the adjusted hazard ratios of the exposure Townsend deprivation quintile and the included covariates in~~of~~ the fully adjusted cox regression model are presented in **S~~s~~upplementary File 3.** In the final adjusted model for incident risk of DFD, the following covariates emerged as risk factors in addition to social deprivation: higher age [aHR (1.03; 95% C 1.03-1.04)], male sex [aHR (0.86, 95% CI: 0.84-0.89) for women compared to men], ~~e~~Caucasian ethnicity [compared to C~~e~~aucasian ethnicity, aHR (0.78, 95% CI: 0.62-0.97) for mixed race, (0.84, 95% CI: 0.59-1.19) for Chin~~e~~se/M~~m~~iddle E~~e~~astern/others, (0.63, 95% CI: 0.53-0.74) for ~~b~~Black ~~a~~Afro-Caribbean, and (0.71, 95% CI: 0.64-0.79) for South Asian], obesity [aHR (1.17, 95% CI: 1.11-1.22)], ex and current-smoking status [compared to non-smokers, aHR (1.10, 95% CI: 1.06-1.14) and (1.33, 95% CI: 1.27-1.39) respectively]~~-~~, poor glycaemic control [compared to those with HbA1c <47.5 mmol/mol, aHR (1.10, 95% CI: 1.04-1.16) and (1.19, 95% CI 1.14-1.25) among those with HbA1c between 58.5 and 69.4

mmol/mol and HbA1c > 69.4mmol/mol respectively], lower glomerular filtration rate [compared to those with eGFR > 60 ml/min/1.73m^2, aHR (1.14, 95% CI: 1.09-1.19) among those with eGFR between 30 and 60 ml/min/1.73m^2], higher foot risk score or non-recording or decline of foot risk exam [compared to those with low foot risk, aHR (1.61, 95% CI: 1.51-1.73) among patients with moderate~~edium~~ foot risk score, (2.73, 95% CI: 2.34-3.19) among patients with high foot risk score, (1.51, 95% CI: 1.23-1.85) among those who declined foot examination and (2.00, 95% CI: 1.93-2.07) among those with missing foot risk score], concurrent diagnosis of CVD [aHR (1.23, 95% CI: 1.19-1.28)], hypertension [aHR (1.03, 95% CI: 1.00-1.07)], sight threatening retinopathy [aHR (1.14, 95% CI: 1.08-1.19] and prescription of glucose lowering medication [aHR (1.13, 95% CI: 1.09-1.16)] and insulin treatment [aHR (1.36, 95% CI: 1.24-1.50)].

~~including all covariates, for every year increase in the age of type 2 diabetes diagnosis, the risk of DFD increases by 3%. The risk of DFD was lower in females, and non white ethnicity.~~

~~Obesity was found not to be a significant predictor (aHR 1.07; 95% CI 0.87 1.31). Current or ex smoking (aHR: 1.31; 95% CI 1.26 1.37 and 1.10; 95% CI 1.06 1.13, poor glycaemic control (aHR: 1.20; 95% CI: 0.15 1.25), hypertension (aHR 1.04; 95% CI 1.01 1.08), retinopathy (aHR 1.14; 95% CI 1.08 1.19), CV disease (aHR 1.23; 95% CI 1.19 1.28), and the use of insulin (aHR 1.37; 95% CI 1.25 1.50) were independent predictors of incident DFD.~~

~~Baseline foot risk classification showed the largest effect among the covariates. Unsurprisingly, patients with the highest baseline foot risk had over two and a half time higher the risk of DFD at any time during follow up (aHR 2.64; 95% CI 2.27 3.08). Details about the covariates of the full cox regression model are presented in **Supplementary File 3.**~~

4. Discussion

We found that social deprivation was a risk factor for the development of DFD, DPN, DFU, PVD, and LLA and gangrene in patients newly diagnosed with type 2 diabetes. The findings remained significant despite adjustment for many important covariates including sex, age at diagnosis type 2 diabetes, ethnicity, smoking status, BMI, HbA1c, CV disease, hypertension, retinopathy, eGFR, insulin or other prescribed diabetes medications, lipid lowering medications, and foot risk score at baseline.

Other studies examined the relationship between DFD and social deprivation. (25-28) Our results are consistent with other studies from the UK, and add to their findings. Two UK studies included more than 10,000 participants each, found that deprivation was associated with either increased risk of DFU or mortality after DFU. (26; 29) However, these studies were either cross-sectional (25); included patients with both type 1 and 2 diabetes (25; 26), focused on foot ulcer (27) or were based on regional data. (27) (28) Our study specifically looked at patients with newly diagnosed type 2 diabetes, used a database that covers multiple regions in England, was retrospective cohort by design and examined a wide range of DFD outcomes. ThusThus, our study adds novel insights to previously published literature.

Many of the studies that examined the relationship between social deprivation and DFD did not adjust for ethnicity. Adjusting for ethnicity is important considering the South Asians have been shown previously to show lower risk of DFU, LLA and DPN compared to White Europeans with type 2 diabetes. (30-32) Our findings are consistent with these studies that non White ethnicity had lower DFD risk; but we expand that as the relationship between social deprivation and DFD was independent of ethnicity in our analysis.

Not all previous studies showed a relationship between DFD and social deprivations. One study, from North-West England, did not show an association between socioeconomic status and new foot ulcers in adults with type 1 and type 2 diabetes, (27) but in this study the

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follow-up duration was shorter than our study (2 years) and did not exclude patients with DFU at baseline. Three other studies from outside the UK found no association between socioeconomic factors and infection, amputation or DFD, but these studies were small and potentially under powered (n=572, n=112, n=102). (33-35)

Our results are important as they identify a population at an increased risk of developing DPN, DFD, DFU, ~~and~~ LLA and gangrene. Hence, by focussing on screening as a preventative strategy on high risk population we could reduce the health and economic burden of DFD, type 2 diabetes and reduce health inequalities.

The effect sizes reported in this study for the association between social deprivation and DFD are modest. This reflects the multifactorial nature of the development of DFD, where multiple other DFD risk factors were also identified in our study with similar modest effect sizes such as obesity, CVD, smoking and poor glycaemic control. In addition, identifying social deprivation as a ~~high risk~~high-risk population for DFD is likely to be beneficial for a wider range of DFD risk factors considering the established links between DFD and obesity and CVD ~~(ref).~~" (36)

Our findings showed that having a high foot risk score (which is defined based on multiple clinical parameters) had the largest effect size in terms of predicting DFD. This is consistent with previous study that showed using a combined risk score/tests had better sensitivity that~~n~~ using individual tests in predicting the development of DFD. (37)

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The results of the present study should be interpreted within the context of the study limitations and strengths. One possible limitation is that the use of routinely collected primary care data may lack ~~of~~ accuracy and completeness of recording. However, THIN has been shown to be representative to the UK population in terms of mortality and major chronic diseases. (20; 38; 39) Another possible limitation is the possibility of delayed type 2 diabetes

diagnosis in the deprived quintile, thereby a more severe diabetes cohort among the deprived subgroups. However, a latency period of 15 months provides sufficient time to record for proxy covariates that indicate diabetes severity such as insulin prescription, HbA1c measurement, concurrent macrovascular complications such as retinopathy and nephropathy. These covariates are adjusted for in our analysis. Another limitation is the large proportion of missing ethnicity ~~missing~~ data. However, we have used a missing ethnicity category in the multivariable analysis to minimise the impact of missing data in this variable. Reassuringly, our analysis showed that South Asians and Black Afro-Caribbeans had lower risk of incident DFD compared to White Caucasians, which is consistent with previous studies ~~(Ref)"~~(30; 32; 40) This is the largest, population-based study, representative of the UK population, study to-date that has examined the impact of deprivation on DFD, and reported outcomes other than DFU and LLA. The large sample size also allowed us to adjust for many biologically important covariates.

In conclusion, deprivation is a risk factor of DFD, DPN, DFU, PVD, LLA, and gangrene in patients newly diagnosed with type 2 diabetes. Screening and preventative strategies targeting this ~~high risk~~high-risk population could reduce the economic and health burden of type 2 diabetes and reduce inequalities.

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Author contributions:

JR: Organise and conduct the study.

CA: Interpretation of the results, proposed the structure of the paper, formulated the paper.

PK, AS, JSC: Interpretation of the results, statistical analysis.

KG, NT, CS: Critically appraised the paper, make the final suggestions.

AAT, KN: Proposed the idea, critically appraised the paper, make the final suggestions.

All authors reviewed and revised the manuscript and agreed to submission of the final manuscript.

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Transparency declaration:

The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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~~characteristics of the study population.~~

Table 1: Baseline characteristics in the total population and according to Townsend deprivation quintiles.

~~Townsend Quintile~~	~~1st Quintile~~	~~2nd Quintile~~	~~3rd Quintile~~	~~4th Quintile~~	~~5th Quintile~~	~~Missing~~	~~All~~
~~Participants, n (%)~~	~~32,305 (18.0)~~	~~31,247 (17.4)~~	~~32,689 (18.2)~~	~~30,644 (17.0)~~	~~23,380 (13.0)~~	~~29,605 (16.5)~~	~~179,870~~
~~Age, mean(SD)~~	~~64.48 (12.33)~~	~~64.55 (12.69)~~	~~62.96 (13.17)~~	~~62.06 (13.68)~~	~~60.55 (13.69)~~	~~61.76 (13.38)~~	~~62.84 (13.21)~~
~~Age category, n(%)~~							
~~<30 years~~	~~129 (0.4)~~	~~171 (0.55)~~	~~226 (0.69)~~	~~305 (1)~~	~~277 (1.18)~~	~~235 (0.79)~~	~~1343 (0.75)~~
~~30-40 years~~	~~670 (2.07)~~	~~776 (2.48)~~	~~1176 (3.6)~~	~~1,438 (4.69)~~	~~1,325 (5.67)~~	~~1337 (4.52)~~	~~6,722 (3.74)~~
~~40-50 years~~	~~3,313 (10.26)~~	~~3,262 (10.44)~~	~~4,232 (12.95)~~	~~4,435 (14.47)~~	~~3,793 (16.22)~~	~~4,249 (14.35)~~	~~23,284 (12.94)~~
~~50-60 years~~	~~7,353 (22.76)~~	~~6,804 (21.77)~~	~~7,649 (23.4)~~	~~7,150 (23.33)~~	~~5,937 (25.39)~~	~~7,453 (25.17)~~	~~42,346 (23.54)~~
~~60-70 years~~	~~9,749 (30.18)~~	~~9,132 (29.23)~~	~~9,159 (28.02)~~	~~8,097 (26.42)~~	~~5,965 (25.51)~~	~~7,890 (26.65)~~	~~49,992 (27.79)~~
~~>70 years~~	~~11,091 (34.33)~~	~~11,102 (35.53)~~	~~10,247 (31.35)~~	~~9,219 (30.08)~~	~~6,083 (26.02)~~	~~8,441 (28.51)~~	~~56,183 (31.24)~~
~~Male, n (%)~~	~~19,107 (59.1)~~	~~17,844 (57.1)~~	~~18,173 (55.6)~~	~~16,446 (53.7)~~	~~12,267 (52.5)~~	~~16,776 (56.7)~~	~~100,613 (55.9)~~
~~Ethnicity, n (%)~~							
~~Caucasian~~	~~13,725 (42.49)~~	~~14,207 (45.47)~~	~~14,965 (45.78)~~	~~14,267 (46.56)~~	~~11,720 (50.13)~~	~~13,640 (46.07)~~	~~82,524 (45.88)~~
~~Afro Caribbean~~	~~160 (0.5)~~	~~171 (0.55)~~	~~371 (1.13)~~	~~525 (1.71)~~	~~715 (3.06)~~	~~667 (2.25)~~	~~2,609 (1.45)~~
~~South Asian~~	~~595 (1.84)~~	~~596 (1.91)~~	~~1,061 (3.25)~~	~~1,288 (4.2)~~	~~1,061 (4.54)~~	~~1,463 (4.94)~~	~~6,064 (3.37)~~
~~Mixed Race~~	~~148 (0.46)~~	~~130 (0.42)~~	~~202 (0.62)~~	~~207 (0.68)~~	~~244 (1.04)~~	~~380 (1.28)~~	~~1,311 (0.73)~~
~~Chinese/Middle eastern/Others~~	~~48 (0.15)~~	~~53 (0.17)~~	~~63 (0.19)~~	~~92 (0.3)~~	~~82 (0.35)~~	~~113 (0.38)~~	~~451 (0.25)~~
~~Missing data~~	~~17,629 (54.57)~~	~~16,090 (51.49)~~	~~16,027 (49.03)~~	~~14,265 (46.55)~~	~~9,558 (40.88)~~	~~13,342 (45.07)~~	~~86,911 (48.32)~~
~~Smoking Status, n(%)~~							
~~Non-smoker~~	~~17,221 (53.31)~~	~~15,710 (50.28)~~	~~15,243 (46.63)~~	~~13,204 (43.09)~~	~~9,343 (39.96)~~	~~14,305 (48.32)~~	~~85,026 (47.27)~~
~~Smoking discontinued~~	~~11,843 (36.66)~~	~~11,725 (37.52)~~	~~12,134 (37.12)~~	~~11,252 (36.72)~~	~~7,976 (34.11)~~	~~10,166 (34.34)~~	~~65,096 (36.19)~~
~~Smoker~~	~~3,185 (9.86)~~	~~3,779 (12.09)~~	~~5,264 (16.1)~~	~~6,156 (20.09)~~	~~6,031 (25.8)~~	~~5,111 (17.26)~~	~~29,526 (16.42)~~
~~Missing data~~	~~56 (0.17)~~	~~33 (0.11)~~	~~48 (0.15)~~	~~32 (0.1)~~	~~30 (0.13)~~	~~23 (0.08)~~	~~222 (0.12)~~
~~BMI, median (IQR)~~	~~29.7 (26.5-33.7)~~	~~30.2 (26.8-34.4)~~	~~30.8 (27.2-35.3)~~	~~31.2 (27.5-35.8)~~	~~31.6 (27.6-36.5)~~	~~30.8 (27.1-35.4)~~	~~30.6 (27.1-35.1)~~

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BMI categories, n(%)							
Underweight (<18.5 kg/m2)	149 (0.46)	170 (0.54)	164 (0.5)	124 (0.4)	133 (0.57)	151 (0.51)	891 (0.5)
Normal weight (18.5-25 kg/m2)	4,867 (15.07)	4,206 (13.46)	3,934 (12.03)	3,552 (11.59)	2,693 (11.52)	3,742 (12.64)	22,994 (12.78)
Overweight (25-30 kg/m2)	11,666 (36.11)	10,669 (34.14)	10,315 (31.55)	9,054 (29.55)	6,362 (27.21)	9,229 (31.17)	57,295 (31.85)
Obese (>30 kg/m2)	15,063 (46.63)	15,643 (50.06)	17,691 (54.12)	17,365 (56.67)	13,772 (58.91)	15,976 (53.96)	95,510 (53.1)
Missing data	560 (1.73)	559 (1.79)	585 (1.79)	549 (1.79)	420 (1.8)	507 (1.71)	3,180 (1.77)
HbA1c, mean(SD)	28.48 (21.72)	59.01 (22.18)	59.39 (22.27)	59.85 (22.66)	60.41 (23.17)	59.56 (22.46)	59.40 (22.38)
HbA1c recorded n(%)	30,985 (95.91)	30,035 (96.12)	31,422 (96.12)	29,233 (95.39)	22,373 (95.69)	28,401 (95.93)	17,2449 (95.87)
HbA1c categories[#], n(%)							
≤47.5 mmol/mol	11,032 (34.15)	10,395 (33.27)	10,589 (32.39)	9,579 (31.26)	7,320 (31.31)	9,685 (32.71)	58,600 (32.58)
47.5-58.5 mmol/mol	10,300 (31.88)	10,113 (32.36)	10,486 (32.08)	9,742 (31.79)	7,174 (30.68)	9,295 (31.4)	57,110 (31.75)
58.5-69.4 mmol/mol	3,062 (9.48)	2,987 (9.56)	3,298 (10.09)	3,178 (10.37)	2,425 (10.37)	2,979 (10.06)	17,929 (9.97)
>69.4 mmol/mol	6,591 (20.4)	6,540 (20.93)	7,049 (21.56)	6,734 (21.97)	5,454 (23.33)	6,442 (21.76)	38,810 (21.58)
Missing data	1,320 (4.09)	1,212 (3.88)	1,267 (3.88)	1,411 (4.6)	1,007 (4.31)	1,204 (4.07)	7,421 (4.13)
eGFR, mean(SD)	78.57 (18.79)	78.67 (19.51)	80.23 (19.94)	80.89 (20.41)	82.82 (20.92)	82.03 (20.12)	80.41 (19.95)
eGFR recorded, n(%)	31,563 (97.70)	30,286 (96.92)	31,863 (97.47)	29,871 (97.48)	22,976 (98.27)	29,181 (98.57)	175,740 (97.70)
eGFR categories, n(%)							
≥60 mL/min/1.73m2)	26,668 (82.55)	25,363 (81.17)	27,083 (82.85)	25,312 (82.6)	19,838 (84.85)	25,291 (85.43)	149,555 (83.15)
30-59 mL/min/1.73m2)	4,659 (14.42)	4,656 (14.9)	4,504 (13.78)	4,303 (14.04)	2,931 (12.54)	3,684 (12.44)	24,737 (13.75)
<30 mL/min/1.73m2)	236 (0.73)	267 (0.85)	276 (0.84)	256 (0.84)	207 (0.89)	206 (0.7)	1,448 (0.81)
Missing data	742 (2.3)	961 (3.08)	826 (2.53)	773 (2.52)	404 (1.73)	424 (1.43)	4,130 (2.3)
CVD, n (%)	7,184 (22.24)	7,339 (23.49)	7,653 (23.41)	7,467 (24.37)	5,817 (24.88)	6,348 (21.44)	41,808 (23.24)
Hypertension, n (%)	18,013 (55.76)	17,530 (56.1)	17,988 (55.03)	16,436 (53.64)	12,198 (52.17)	15,706 (53.05)	97,871 (54.41)
Retinopathy, n (%)	3,035 (9.39)	3,080 (9.86)	3,077 (9.41)	2,944 (9.61)	2,279 (9.75)	2,916 (9.85)	17,331 (9.64)
Treatment, n (%)							
Insulin	687 (2.13)	716 (2.29)	828 (2.53)	843 (2.75)	744 (3.18)	819 (2.77)	4637 (2.58)

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~~Lipid Drugs~~	~~23,621 (73.12)~~	~~22,764 (72.85)~~	~~23,865 (73.01)~~	~~22,322 (72.84)~~	~~17,205 (73.59)~~	~~20,389 (68.87)~~	~~130,166 (72.37)~~
~~Other DM Drugs~~	~~17,135 (53.04)~~	~~16,620 (53.19)~~	~~18,630 (56.99)~~	~~18,147 (59.22)~~	~~14,489 (61.97)~~	~~17,620 (59.52)~~	~~10,2641 (57.06)~~
~~Foot Risk, n (%)~~							
~~High~~	~~400 (1.24)~~	~~493 (1.58)~~	~~502 (1.54)~~	~~525 (1.71)~~	~~471 (2.01)~~	~~379 (1.28)~~	~~2,770 (1.54)~~
~~Moderate~~	~~2,407 (7.45)~~	~~2,392 (7.66)~~	~~2,756 (8.43)~~	~~2,660 (8.68)~~	~~2,241 (9.6)~~	~~2,440 (8.24)~~	~~14,899 (8.28)~~
~~Low~~	~~13,270 (41.08)~~	~~13,367 (42.78)~~	~~13,948 (42.67)~~	~~13,046 (42.57)~~	~~9,568 (40.92)~~	~~14,913 (50.37)~~	~~78,112 (43.43)~~
~~Declined~~	~~133 (0.41)~~	~~131 (0.42)~~	~~174 (0.53)~~	~~182 (0.59)~~	~~212 (0.91)~~	~~216 (0.73)~~	~~1048 (0.58)~~
~~Missing data~~	~~16,095 (49.82)~~	~~14,864 (47.57)~~	~~15,309 (46.83)~~	~~14,231 (46.44)~~	~~10,885 (46.56)~~	~~11,657 (39.38)~~	~~83,041 (46.17)~~
~~DFD, n (%) *~~	~~4,496 (13.92)~~	~~4,616 (14.77)~~	~~4,964 (15.19)~~	~~4,787 (15.62)~~	~~3,895 (16.66)~~	~~3,686 (12.45)~~	~~26,444 (14.7)~~

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Townsend Quintile	1st Quintile	2nd Quintile	3rd Quintile	4th Quintile	5th Quintile	Missing	All
Participants, n (%)	(n=31,732)	(n=30,655)	(n=32,021)	(n=29,984)	(n=22,881)	(n=29,086)	(n=176,359)
Age, mean(SD)	64.52 (12.26)	64.59 (12.62)	63.02 (13.12)	62.15 (13.60)	60.64 (13.58)	61.83 (13.30)	62.91 (13.13)
Age category, n(%)							
<30 years	105 (0.33)	145 (0.47)	195 (0.61)	262 (0.87)	232 (1.01)	199 (0.68)	1,138 (0.65)
30-40 years	646 (2.04)	747 (2.44)	1,136 (3.55)	1,380 (4.60)	1,277 (5.58)	1,290 (4.44)	6,476 (3.67)
40-50 years	3,242 (10.22)	3,197 (10.43)	4,143 (12.94)	4,336 (14.46)	3,712 (16.22)	4,174 (14.35)	22,804 (12.93)

50-60 years	7,241 (22.82)	6,670 (21.76)	7,494 (23.40)	7,002 (23.35)	5,829 (25.48)	7,337 (25.23)	41,573 (23.57)
60-70 years	9,611 (30.29)	8,988 (29.32)	8,993 (28.08)	7,950 (26.51)	5,863 (25.62)	7,770 (26.71)	49,175 (27.88)
>70 years	10,887 (34.31)	10,908 (35.58)	10,060 (31.42)	9,054 (30.20)	5,968 (26.08)	8,316 (28.59)	55,193 (31.30)
Male, n (%)	18,779 (59.18)	17,518 (57.15)	17828 (55.68)	16,114 (53.74)	12,041 (52.62)	16,497 (56.72)	98,777 (56.01)
Ethnicity, n (%)							
Caucasian	13,452 (42.39)	13,911 (45.38)	14,626 (45.68)	13,938 (46.48)	11,467 (50.12)	13,394 (46.05)	80,788 (45.81)
Afro Caribbean	583 (1.84)	573 (1.87)	1,010 (3.15)	1,244 (4.15)	1,038 (4.54)	1,426 (4.90)	5,874 (3.33)
South Asian	159 (0.50)	168 (0.55)	357 (1.11)	499 (1.66)	687 (3.00)	653 (2.25)	2,523 (1.43)
Mixed Race	143 (0.45)	126 (0.41)	196 (0.61)	200 (0.67)	234 (1.02)	372 (1.28)	1,271 (0.72)
Chinese/Middle Eastern/Others	45 (0.14)	51 (0.17)	62 (0.19)	87 (0.29)	78 (0.34)	112 (0.39)	435 (0.25)
Missing data	17,350 (54.68)	15,826 (51.63)	15,770 (49.25)	14,016 (46.74)	9,377 (40.98)	13,129 (45.14)	85,468 (48.46)
Smoking Status, n(%)							
Non-smoker	16,917 (53.31)	15,410 (50.27)	14,909 (46.56)	12,920 (43.09)	9,153 (40.00)	14,052 (48.31)	83,361 (47.27)
Smoking discontinued	11,638 (36.68)	11,503 (37.52)	11,921 (37.23)	11,029 (36.78)	7,810 (34.13)	10,010 (34.42)	63,911 (36.24)
Smoker	3,122 (9.84)	3,710 (12.10)	5,146 (16.07)	6,005 (20.03)	5,888 (25.73)	5,006 (17.21)	28,877 (16.37)
Missing data	55 (0.17)	32 (0.10)	45 (0.14)	30 (0.10)	30 (0.13)	18 (0.06)	210 (0.12)
BMI, median (IQR)	29.00 (26.00-33.00)	30.00 (26.00-34.00)	30.00 (27.00-35.00)	31.00 (27.00-35.00)	31.00 (27.00-36.00)	30.00 (27.00-35.00)	30.00 (27.00-35.00)
BMI categories, n(%)							
Underweight (<18.5 kg/m2)	145 (0.46)	164 (0.53)	159 (0.50)	116 (0.39)	128 (0.56)	142 (0.49)	854 (0.48)
Normal weight (18.5-25 kg/m2)	4,762 (15.01)	4,106 (13.39)	3,844 (12.00)	3,455 (11.52)	2,629 (11.49)	3,656 (12.57)	22,452 (12.73)
Overweight (25-30 kg/m2)	11,482 (36.18)	10,479 (34.18)	10,137 (31.66)	8,890 (29.65)	6,233 (27.24)	9,079 (31.21)	56,300 (31.92)
Obese (>30 kg/m2)	14,810 (46.67)	15,374 (50.15)	17,320 (54.09)	17,000 (56.70)	13,485 (58.94)	15,720 (54.05)	93,709 (53.14)
Missing data	533 (1.68)	532 (1.74)	561 (1.75)	523 (1.74)	406 (1.77)	489 (1.68)	3,044 (1.73)
HbA1c, mean(SD)	58.54 (21.73)	59.04 (22.17)	59.40 (22.28)	59.87 (22.61)	60.45 (23.16)	59.57 (22.44)	59.43 (22.37)
HbA1c recorded n(%)	30,459 (95.99)	29,502 (96.24)	30,800 (96.19)	28,621 (95.45)	21,913 (95.77)	27,930 (96.03)	169,225 (95.95)
HbA1c categories[#], n(%)							

≤47.5 mmol/mol	10,781 (33.98)	10,191 (33.24)	10,365 (32.37)	9,352 (31.19)	7,138 (31.20)	9,498 (32.65)	57,325 (32.50)
47.5-58.5 mmol/mol	10,168 (32.04)	9,937 (32.42)	10,294 (32.15)	9,538 (31.81)	7,038 (30.76)	9,166 (31.51)	56,141 (31.83)
58.5-69.4 mmol/mol	3,014 (9.50)	2,943 (9.60)	3,232 (10.09)	3,131 (10.44)	2,383 (10.41)	2,936 (10.09)	17,639 (10.00)
>69.4 mmol/mol	6,496 (20.47)	6,431 (20.98)	6,909 (21.58)	6,600 (22.01)	5,354 (23.40)	6,330 (21.76)	38,120 (21.62)
Missing data	1,273 (4.01)	1,153 (3.76)	1,221 (3.81)	1,363 (4.55)	968 (4.23)	1,156 (3.97)	7,134 (4.05)
eGFR, mean(SD)	78.55 (18.74)	78.62 (19.46)	80.17 (19.90)	80.78 (20.36)	82.71 (20.83)	81.94 (19.98)	80.34 (19.90)
eGFR recorded, n(%)	31,001 (97.70)	29,704 (96.90)	31,210 (97.47)	29,230 (97.49)	22,486 (98.27)	28,674 (98.58)	172,305 (97.70)
eGFR categories, n(%)							
≥60 mL/min/1.73m2)	26,200 (82.57)	24,866 (81.12)	26,515 (82.81)	24,748 (82.54)	19,410 (84.83)	24,835 (85.38)	146,574 (83.11)
30-59 mL/min/1.73m2)	4,571 (14.41)	4,575 (14.92)	4,424 (13.82)	4,230 (14.11)	2,876 (12.57)	3,636 (12.50)	24,312 (13.79)
<30 mL/min/1.73m2)	230 (0.72)	263 (0.86)	271 (0.85)	252 (0.84)	200 (0.87)	203 (0.70)	1,419 (0.80)
Missing data	731 (2.30)	951 (3.10)	811 (2.53)	754 (2.51)	395 (1.73)	412 (1.42)	4,054 (2.30)
CVD, n (%)	7,052 (22.22)	7,222 (23.56)	7,522 (23.49)	7,331 (24.45)	5,702 (24.92)	6,255 (21.51)	41,084 (23.30)
Hypertension, n (%)	17,731 (55.88)	17,250 (56.27)	17,675 (55.20)	16,148 (53.86)	11,988 (52.39)	15,495 (53.27)	96,287 (54.60)
Retinopathy, n (%)	905 (2.85)	949 (3.10)	1,038 (3.24)	995 (3.32)	773 (3.38)	942 (3.24)	5,602 (3.18)
Treatment, n (%)							
Insulin	629 (1.98)	641 (2.09)	768 (2.40)	752 (2.51)	665 (2.91)	738 (2.54)	4,193 (2.38)
Lipid Drugs	23,254 (73.28)	22,415 (73.12)	23,450 (73.23)	21,918 (73.10)	16,926 (73.97)	20,084 (69.05)	128,047 (72.61)
Other DM Drugs	16,826 (53.03)	16,280 (53.11)	18,244 (56.98)	17,761 (59.23)	14,209 (62.10)	17,294 (59.46)	100,614 (57.05)
Foot Risk, n (%)							
High	391 (1.23)	485 (1.58)	495 (1.55)	513 (1.71)	454 (1.98)	369 (1.27)	2,707 (1.53)
Moderate	2,346 (7.39)	2,344 (7.65)	2,696 (8.42)	2,599 (8.67)	2,193 (9.58)	2,394 (8.23)	14,572 (8.26)
Low	12,985 (40.92)	13,044 (42.55)	13,568 (42.37)	12,699 (42.35)	9,322 (40.74)	14,605 (50.21)	76,223 (43.22)
Declined	126 (0.40)	128 (0.42)	171 (0.53)	176 (0.59)	208 (0.91)	213 (0.73)	1,022 (0.58)
Missing data	15,884 (50.06)	14,654 (47.80)	15,091 (47.13)	13,997 (46.68)	10,704 (46.78)	11,505 (39.56)	81,835 (46.40)
DFD, n (%) *	4,437 (13.98)	4,554 (14.86)	4,910 (15.33)	4,720 (15.74)	3,830 (16.74)	3,643 (12.52)	26,094 (14.80)

N: Number of patients, **SD**: Standard Deviation, **BMI**: Body Mass Index, **HbA1c**: Haemoglobin A1c, **eGFR**: estimated Glomerular Filtration Rate, **CVD**: Cardiovascular Disease, **DFD**: Diabetic Foot Disease

[#] ≤47.5 mmol/mol = ≤6.5%, 47.5-58.5 mmol/mol = 6.5-7.5%, 58.5-69.4 mmol/mol = 7.5-8.5%, >69.4 mmol/mol = >8.5%

*DFD refers to baseline, these patients are excluded from our study

Table 2. ~~The relationship between~~ Townsend deprivation quiantiles and the incidence~~t~~ of diabetic foot disease as a composite outcome.

~~(Townsend quantile)~~	~~Composite DFD* n (%)~~	~~Median Follow up [years(IQR)]~~	~~Incidence rate per 1,000 person years(95% CI)~~	~~aHR (95% CI)*~~
~~1~~	~~3,429 (12.33)~~	~~3.28 (1.38-5.96)~~	~~31.03 (30.01-32.08)~~	~~Ref~~
~~2~~	~~3,385 (12.71)~~	~~3.23 (1.38-5.89)~~	~~32.33 (31.26-33.44)~~	~~1.03 (0.99-1.08)~~
~~3~~	~~3,440 (12.41)~~	~~3.19 (1.38-5.86)~~	~~31.69 (30.64-32.76)~~	~~1.04 (0.99-1.09)~~
~~4~~	~~3,293 (12.74)~~	~~3.11 (1.35-5.74)~~	~~32.98 (31.87-34.12)~~	~~1.09 (1.04-1.15)~~
~~5~~	~~2,662 (13.66)~~	~~3.08 (1.30-5.63)~~	~~35.98 (34.64-37.38)~~	~~1.21 (1.15-1.27)~~
~~Missing data~~	~~2,828 (10.91)~~	~~3.33 (1.41-6.13)~~	~~26.54 (25.58-27.53)~~	~~0.95 (0.90-0.99)~~

(Townsend quiantile)	Composite DFD*n (%)	Median Follow up [years (IQR)]	Incidence rate per 1,000 person years (95% CI)	aHR (95% CI)*
1	3,267 (11.97)	3.33 (1.42-6.03)	29.77 (28.77-30.81)	Ref
2	3,238 (12.41)	3.29 (1.42-5.96)	31.17 (30.11-32.26)	1.04 (0.99-1.09) p=0.110
3	3,278 (12.09)	3.25 (1.43-5.95)	30.45 (29.42-31.51)	1.04 (0.99-1.09) p=0.092
4	3,133 (12.40)	3.17 (1.38-5.81)	31.69 (30.60-32.82)	1.10 (1.04-1.15) p<0.001
5	2,557 (13.42)	3.15 (1.34-5.72)	34.86 (33.54-36.24)	1.22 (1.16-1.29) p<0.001
Missing data	2,680 (10.53)	3.38 (1.45-6.21)	25.32 (24.38-26.30)	0.94 (0.90-0.99) p=0.028

N: number of patients, **IQR**: Interquartile Range, **DFD**: Diabetic Foot Disease, **aHR**: adjusted Hazard Ratio.

*The adjustment model includes sex, age at type 2 diabetes diagnosis, ethnicity, smoking, BMI, HbA1c, cardiovascular disease, retinopathy, renal function analysed as eGFR, insulin treatment, glucose-lowering medications and baseline foot risk.

#In case of multiple DFD events at follow-up, censoring at the first event.

Table 3. The relationship between Townsend deprivation quiantiles and the iIncidence of peripheral neuropathy, foot ulcer, peripheral vascular disease, lower limbp amputation, Charcot arthropathy and gangrene. the different types of diabetic foot neuropathy.

Outcome	n (%)	Median Follow up [years(IQR)]	Incidence rate per 1,000 person years(95% CI)	aHR (95% CI)*
Peripheral neuropathy	-	-	-	-
1	2,475 (8.9)	3.43 (1.48 6.15)	21.67 (20.83 22.54)	Ref
2	2,459 (9.23)	3.38 (1.48 6.11)	22.71 (21.83 23.63)	1.05 (0.99 1.11)
3	2,401 (8.66)	3.35 (1.48 6.08)	21.32 (20.48 22.19)	1.01 (0.96 1.07)
4	2,334 (9.03)	3.27 (1.43 5.96)	22.55 (21.65 23.49)	1.09 (1.03 1.16)
5	1,828 (9.38)	3.26 (1.39 5.94)	23.63 (22.57 24.74)	1.17 (1.10 1.24)
Missing data	1,962 (7.57)	3.47 (1.51 6.34)	17.84 (17.07 18.65)	0.93 (0.87 0.98)
Ulcer	-	-	-	-
1	410 (1.47)	3.85 (1.73 6.59)	3.33 (3.02 3.67)	Ref
2	410 (1.54)	3.80 (1.74 6.56)	3.51 (3.18 3.87)	1.03 (0.90 1.18)
3	430 (1.55)	3.72 (1.70 6.55)	3.55 (3.23 3.91)	1.06 (0.93 1.22)
4	409 (1.58)	3.65 (1.66 6.45)	3.66 (3.32 4.03)	1.10 (0.96 1.26)
5	353 (1.81)	3.65 (1.64 6.38)	4.22 (3.8 4.68)	1.28 (1.11 1.48)
Missing data	405 (1.56)	3.87 (1.70 6.86)	3.43 (3.12 3.79)	1.04 (0.91 1.20)
Peripheral vascular disease	-	-	-	-
1	1,052 (3.78)	3.68 (1.63 6.42)	8.78 (8.27 9.33)	Ref
2	1,075 (4.04)	3.65 (1.63 6.41)	9.46 (8.91 10.05)	1.06 (0.97 1.15)
3	1,148 (4.14)	3.56 (1.61 6.36)	9.78 (9.23 10.36)	1.11 (1.02 1.20)
4	1,102 (4.26)	3.48 (1.57 6.26)	10.17 (9.59 10.79)	1.14 (1.05 1.25)
5	998 (5.12)	3.46 (1.55 6.18)	12.39 (11.64 13.18)	1.39 (1.27 1.52)
Missing data	850 (3.28)	3.73 (1.64 6.69)	7.36 (6.88 7.87)	0.92 (0.84 1.01)
Lower limp amputation	-	-	-	-
1	32 (0.12)	3.90 (1.76 6.64)	0.26 (0.18 0.36)	Ref

2	31 (0.12)	3.85 (1.76-6.62)	0.26 (0.18-0.37)	1.01 (0.62-1.66)
3	48 (0.17)	3.77 (1.73-6.61)	0.39 (0.3-0.52)	1.58 (1.01-2.47)
4	45 (0.17)	3.71 (1.69-6.52)	0.4 (0.3-0.53)	1.61 (1.02-2.55)
5	37 (0.19)	3.71 (1.67-6.46)	0.44 (0.32-0.6)	1.75 (1.08-2.84)
Missing data	34 (0.13)	3.91 (1.72-6.94)	0.29 (0.2-0.4)	1.11 (0.68-1.81)
Charcot arthropathy	-	-	-	-
1	12 (0.04)	3.90 (1.76-6.64)	0.1 (0.05-0.17)	Ref
2	8 (0.03)	3.85 (1.76-6.62)	0.07 (0.03-0.14)	0.72 (0.29-1.76)
3	8 (0.03)	3.77 (1.74-6.61)	0.07 (0.03-0.13)	0.67 (0.27-1.64)
4	12 (0.05)	3.71 (1.69-6.53)	0.11 (0.06-0.19)	1.08 (0.48-2.42)
5	16 (0.08)	3.71 (1.67-6.46)	0.19 (0.12-0.31)	1.78 (0.83-3.86)
Missing data	6 (0.02)	3.92 (1.72-6.95)	0.05 (0.02-0.11)	0.47 (0.17-1.25)
Gangrene				-
1	1 (0)	3.91 (1.76-6.64)	0.01 (0-0.06)	Ref
2	3 (0.01)	3.85 (1.76-6.62)	0.03 (0.01-0.08)	3.23 (0.33-31.62)
3	2 (0.01)	3.77 (1.73-6.61)	0.02 (0-0.07)	2.26 (0.20-25.66)
4	4 (0.02)	3.71 (1.69-6.53)	0.04 (0.01-0.09)	1.77 (0.51-44.58)
5	4 (0.02)	3.71 (1.67-6.47)	0.05 (0.02-0.13)	5.62 (0.60-52.87)
Missing data	1 (0)	3.92 (1.72-6.95)	0.01 (0-0.06)	1.11 (0.07-18.13)

Outcome	n (%)	Median Follow up [years(IQR)]	Incidence rate per 1,000 person years(95% CI)	aHR (95% CI)*
Peripheral neuropathy				
1	2,483 (9.10)	3.47 (1.51-6.18)	21.98 (21.13-22.86)	Ref
2	2,449 (9.38)	3.43 (1.51-6.15)	22.88 (21.99-23.81)	1.04 (0.98-1.10) p=0.169
3	2,394 (8.83)	3.39 (1.52-6.15)	21.53 (20.68-22.41)	1.01 (0.96-1.07) p=0.716
4	2,320 (9.18)	3.32 (1.47-6.02)	22.72 (21.82-23.67)	1.08 (1.02-1.15) p=0.006
5	1,836 (9.64)	3.31 (1.43-5.99)	24.05 (22.98-25.18)	1.18 (1.11-1.25) p<0.001
Missing data	1,963 (7.72)	3.52 (1.54-6.38)	18.05 (17.27-18.87)	0.92 (0.87-0.98) p=0.009
Ulcer				
1	192 (0.70)	3.94 (1.79-6.67)	1.57 (1.36-1.80)	Ref
2	210 (0.80)	3.90 (1.80-6.64)	1.81 (1.58-2.07)	1.13 (0.93-1.38) p=0.221

3	209 (0.77)	3.82 (1.76-6.65)	1.74 (1.52-1.99)	1.11 (0.91-1.35) p=0.288
4	220 (0.87)	3.73 (1.71-6.55)	1.98 (1.74-2.26)	1.28 (1.05-1.55) p=0.014
5	186 (0.98)	3.75 (1.70-6.49)	2.23 (1.93-2.58)	1.44 (1.17-1.77) p<0.001
Missing data	222 (0.87)	3.95 (1.74-6.96)	1.89 (1.66-2.16)	1.18 (0.97-1.43) p=0.103
Peripheral vascular disease				
1	1,045 (3.83)	3.75 (1.67-6.47)	8.81 (8.29-9.36)	Ref
2	1,067 (4.09)	3.71 (1.66-6.45)	9.49 (8.94-10.08)	1.06 (0.97-1.15) p=0.201
3	1,141 (4.21)	3.61 (1.65-6.41)	9.84 (9.28-10.42)	1.11 (1.02-1.21) p=0.015
4	1,093 (4.33)	3.55 (1.60-6.31)	10.22 (9.63-10.84)	1.15 (1.05-1.25) p=0.002
5	994 (5.22)	3.53 (1.58-6.23)	12.49 (11.74-13.29)	1.40 (1.28-1.53) p<0.001
Missing data	845 (3.32)	3.79 (1.67-6.76)	7.39 (6.91-7.91)	0.92 (0.84-1.01) p=0.083
Lower limpb amputation				
1	32 (0.12)	3.95 (1.80-6.69)	0.26 (0.18-0.37)	Ref
2	31 (0.12)	3.92 (1.80-6.67)	0.27 (0.19-0.38)	1.02 (0.62-1.67) p=0.952
3	47 (0.17)	3.84 (1.77-6.67)	0.39 (0.29-0.52)	1.54 (0.98-2.42) p=0.060
4	44 (0.17)	3.76 (1.72-6.58)	0.40 (0.29-0.53)	1.58 (1.00-2.50) p=0.052
5	37 (0.19)	3.78 (1.71-6.53)	0.44 (0.32-0.61)	1.75 (1.08-2.83) p=0.023
Missing data	34 (0.13)	3.97 (1.76-7.00)	0.29 (0.21-0.40)	1.12 (0.69-1.82) p=0.658
Charcot arthropathy				
1	13 (0.05)	3.96 (1.80-6.70)	0.11 (0.06-0.18)	Ref
2	11 (0.04)	3.92 (1.80-6.67)	0.09 (0.05-0.17)	0.90 (0.40-2.02) p=0.807
3	11 (0.04)	3.85 (1.78-6.67)	0.09 (0.05-0.16)	0.84 (0.38-1.89) p=0.679
4	12 (0.05)	3.76 (1.72-6.59)	0.11 (0.06-0.19)	0.99 (0.45-2.19) p=0.983
5	16 (0.08)	3.78 (1.72-6.54)	0.19 (0.12-0.31)	1.65 (0.78-3.49) p=0.191
Missing data	6 (0.02)	3.97 (1.76-7.01)	0.05 (0.02-0.11)	0.43 (0.16-1.14) p=0.090
Gangrene				
1	1 (0.00)	3.96 (1.80-6.70)	0.01 (0.00-0.06)	Ref
2	5 (0.02)	3.92 (1.80-6.67)	0.04 (0.02-0.10)	5.01 (0.58-42.94) p=0.142
3	4 (0.01)	3.85 (1.78-6.67)	0.03 (0.01-0.09)	3.99 (0.44-35.85) p=0.216
4	9 (0.04)	3.76 (1.72-6.59)	0.08 (0.04-0.16)	9.82 (1.23-78.17) p=0.031
5	6 (0.03)	3.78 (1.72-6.54)	0.07 (0.03-0.16)	8.49 (1.01-71.58) p=0.049
Missing data	5 (0.02)	3.97 (1.76-7.01)	0.04 (0.02-0.10)	5.35 (0.62-46.07) p=0.127

HR: Hazard Ratio**, 95% CI:** Confidence Interval, **aHR:** adjusted Hazard Ratio

*The results are adjusted for: age at type 2 diabetes diagnosis, sex, ethnicity, smoking status, BMI, eGFR, retinopathy, hypertension, cardiovascular disease, HbA1c, insulin treatment, glucose lowering medication, lipid lowering medication

Figure legends.

Figure 1. ~~The incidence of individual components of diabetic foot disease outcomes in the different quantiles of Townsend score.Social~~Townsend deprivation quintiles and the incident risk of individual components of diabetic foot disease