Received: 30 May 2023 | Revised: 7 August 2023 | Accepted: 12 August 2023

DOI: 10.1111/dom.15260

ORIGINAL ARTICLE

WILEY

Diabetes foot complications and standardized mortality rate in type 2 diabetes

Mike Stedman MSc[1] | Adam Robinson MD[2] | George Dunn MA[3] | Bernado Meza-Torres PhD[4] | J. Martin Gibson PhD[2,5] | Neil D. Reeves PhD[6] | Edward B. Jude MD[5] | Michael Feher PhD[7] | Gerry Rayman MD[8] | Martin B. Whyte PhD[9,10] | Michael Edmonds PhD[9] | Adrian H. Heald DM[2,5]

[1]RES Consortium, UK

[2]Department of Diabetes and Endocrinology, Salford Royal Foundation Trust, Salford, UK

[3]East Cheshire Trust, Macclesfield, UK

[4]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

[5]Department of Medicine, University of Manchester, Manchester, UK

[6]Department of Life Sciences, Faculty of Science and Engineering, Manchester Metropolitan University, Manchester, UK

[7]Chelsea and Westminster Hospital, London, UK

[8]The Ipswich Diabetes Centre and Research Unit, Ipswich Hospital NHS Trust, Ipswich, UK

[9]Diabetic Foot Clinic, King's College Hospital Foundation Trust, London, UK

[10]Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK

Correspondence
Adrian H. Heald, Department of Diabetes and Endocrinology, Salford Royal Hospital, Salford, M6 8HD, UK.
Email: adrian.heald@manchester.ac.uk

Abstract

Aim: To quantify the impact of foot complications on mortality outcomes in people with type 2 diabetes (T2D), and how routinely measured factors might modulate that risk.

Materials and Methods: Data for individuals with T2D for 2010-2020, from the Salford Integrated Care Record (Salford, UK), were extracted for laboratory and clinical data, and deaths. Annual expected deaths were taken from Office of National Statistics mortality data. An index of multiple deprivation (IMD) adjusted the standardized mortality ratio (SMR_IMD). Life years lost per death (LYLD) was estimated from the difference between expected and actual deaths.

Results: A total of 11 806 T2D patients were included, with 5583 new diagnoses and 3921 deaths during 2010-2020. The number of expected deaths was 2135; after IMD adjustment, there were 2595 expected deaths. Therefore, excess deaths numbered 1326 (SMR_IMD 1.51). No foot complications were evident in $n = 9857$. This group had an SMR_IMD of 1.13 and 2.74 LYLD. In total, 2979 patients had any foot complication recorded. In this group, the SMD_IMR was 2.29; of these, 2555 (75%) had only one foot complication. Patients with a foot complication showed little difference in percentage HbA1c more than 58 mmol/mol. In multivariate analysis, for those with a foot complication and an albumin-to-creatinine ratio of more than 3 mg/mmol, the odds ratio (OR) for death was 1.93, and for an estimated glomerular filtration rate of less than 60 mL/min/1.73m^2, the OR for death was 1.92.

Conclusions: Patients with T2D but without a foot complication have an SMR_IMD that is only slightly higher than that of the general population. Those diagnosed with a foot complication have a mortality risk that is double that of those without T2D.

KEYWORDS
at risk, foot, mortality, treatment, type 2 diabetes

1 | INTRODUCTION

Diabetic foot disease is a commonly encountered condition that includes foot ulcers, infections and peripheral arterial disease. The lifetime incidence rate of diabetic foot ulceration is 19%-34%, with a yearly incidence rate of 2%.[1] The presence of diabetic foot disease is strongly correlated with a higher likelihood of cardiovascular complications, such as coronary artery disease and stroke, which significantly contribute to the overall mortality rate among people with diabetes.[2–4] The 5-year survival rate following presentation with a new diabetic foot ulcer (DFU) is 50%-60%,[3] and data derived from a Veterans Health Administration population reported that 1-, 2- and 5-year survival was only 81%, 69% and 29%, respectively.[3] The same underlying factors that contribute to diabetic foot disease, such as poor glycaemic control and hypertension,[5] compounded by socioeconomic disadvantage,[6–8] can also lead to the development and progression of renal disease, ultimately necessitating renal dialysis.[9]

Thus, the burden of diabetic foot disease extends beyond the foot itself, encompassing profound implications for cardiovascular health and renal function in individuals with diabetes.

While the demographic, metabolic, lifestyle, vascular and socioeconomic factors relating to the development of diabetic foot complications and to mortality in diabetes are known, the relative contributions of these components are not known. Furthermore, how does the mortality rate in people with diabetes but no foot complication differ from that of the wider population?

We report here our latest findings regarding risk factors for death in relation to those with 'at risk foot status' in a cohort of people who had a confirmed diagnosis of type 2 diabetes (T2D) from January 2010 to January 2020.

We hypothesized that it would be possible to estimate the relative contributions to the development of foot complications and then risk of death in those people with foot complications, from different antecedent risk factors based on those measured routinely as part of usual care.[10]

2 | MATERIALS AND METHODS

People living in Salford (Manchester, UK) with T2D are offered annual heath reviews by their primary care service. Clinical and laboratory data are automatically entered into the Salford Integrated Record (SIR).[11] Data were then extracted from the SIR for all patients with previously diagnosed, or new-onset, T2D, from 1 January 2010 to 31 December 2020 (or deceased). The data extract was approved by the local research governance panel (Reference SIR022 2020).

From the SIR, weight and body mass index (BMI), glycaemic control (HbA1c), serum lipids (total cholesterol [TC], HDL-cholesterol), blood pressure (systolic and diastolic), and renal health, represented by estimated glomerular filtration rate (eGFR) or urine albumin-to-creatinine ratio (ACR), were acquired. Read coded event data[12] were also obtained, including diagnosis with T2D, smoking status and presence of a diabetic foot complication.

A diabetic foot complication was considered as at least one of: ulceration, peripheral vascular disease (PVD), neuropathy or amputation (Table S1). The last available code, including foot complications, was applied for each patient year, that is, once a patient had a foot complication recorded that diagnosis remained on their record for the remainder of the analysis and so subsequent outcomes were allocated into that category.

The national annual mortality rate and life expectancy by age and sex for each year were taken from Annual Office of National Statistics (ONS) annual life tables for England.[13] Salford has significantly higher levels of social deprivation than the national average, as mortality rates are strongly linked to deprivation. Adjustment was therefore made to allow results to be compared with national results. ONS Local Small Area (LSOA) data for recorded deaths[14] and population numbers by age and sex were used to create a standardized mortality ratio (SMR) for each LSOA. This was then linked to the LSOA Index of Multiple Deprivation (IMD) 2019[14] by linear regression. This gave a factor to bring a SMR (for a given IMD) back to national median IMD. The patient's GP practice's LSOA provided an IMD, and the patient's expected mortality rate could be adjusted to take into consideration their local deprivation, to standardize all practices back to median IMD to generate the SMR_IMD.

A baseline dataset was assembled where each patient and year was a single record 'bucket' and calculations were consolidated by assembling patient years across classes of different cohorts. Where multiple datapoints were available in a single year the average was taken; where data were not given, that year was excluded from the average. Analyses were repeated per calendar year.

Life expectancy years lost (LEYL) was calculated by multiplying expected mortality rate and actual deaths by the life expectancy for patient's age and sex to give expected LEYL as well as actual LEYL. The difference could then be divided by the number of deaths to give how many additional years of life might have been lost by those patients who have died.

2.1 | Statistics

Simple univariant analysis compared the cohorts with and without foot complications. The percentage at higher risk was identified by applying clinically accepted reference values; these included:

1. Smoking status (including ex-smoker).
2. BMI (high % > 30 kg/m^2).
3. HbA1c (high % > 58 mmol/mol).
4. Hypertension (high % > 140/90 mmHg).
5. Lipid TC/HDL ratio (high % > 5).
6. Renal eGFR (low % < 60 mL/min/1.73m^2).
7. Renal ACR (high % > 3 mg/mmol).

As these factors are not independent of each other and develop over time, a stepwise multivariate logistic regression was carried out using Analyse It software, linking the last recorded status of each risk

factor plus sex and age older than 65 years in each year to the recording of any sort of foot complication. Applying the binary variables for each risk factor allowed the resulting odds ratio (OR) to be compared with those of the other risk factors. A further multivariate logistic regression was applied to link the presence of foot complications plus presence of metabolic high-risk factors to death within any given year; again, the OR allowed comparison across risk factors. It is worth noting that as these are not independent, the effect of one risk factor might contain within it impacts from other factors, that is, foot complication will include aspects such as BMI.

3 | RESULTS

There were 11 806 patients, of whom 25% had a foot complication at some point. These patients included those with diabetes at the start of the observation period (2010) plus, in the years 2010-2020, an additional 5502 people were diagnosed with T2D. In total there were 78 930 patient years, of which 20% were patients with a foot complication. There were 3921 deaths, in whom 50% had a foot complication at the time of death. The number of individuals in each of the clinically relevant categories used in the analysis are shown (Table 1).

TABLE 1 Chosen demographic and metabolic factors, cut-off points applied and numbers in each group.

	Category split point	*n* = number in category (% *N* total cohort) Patients	*N* = total datapoints
Sex	Males	6622 (56%)	11 806
Age at T2D diagnosis	> 65 years	3858 (34%)	11 335
		Patient years	
Years since T2D diagnosis	> 10 years	28 109 (37%)	76 283
Smokers	Current and ex-smoker (0.25)	Current 15 601 (20%) ex 34 090 (44%)	77 644
BMI	Obese ≥ 30 kg/m^2	30 099 (54%)	55 985
HbA1c	At risk > 58 mmol/mol	21 441 (34%)	63 185
Blood pressure	Systolic > 140 mmHg and/or diastolic > 90 mmHg	18 497 (24%)	77 218
Lipid	TC > 5 mmol/L and/or TC/HDL > 5	17 157 (25%)	69 215
Renal	eGFR < 60 mL/min/1.73m^2	15 470 (25%)	62 807
Renal	ACR > 3 mg/mmol	10 380 (25%)	42 143

Abbreviations: ACR, albumin-to-creatinine ratio; BMI, body mass index; eGFR, estimated glomerular filtration rate; TC, total cholesterol; T2D, type 2 diabetes.

TABLE 2 Description of cohort in relation to foot problem status.

Basic data	No foot problem	Foot problem	Total	Foot problem/total as %
Patient years	63 246	15 684	78 930	19.9%
Patients	9857	2979	11 806	25.2%
New T2D diagnosis	5205	335	5540	6.0%
Average age at T2D diagnosis (years)	56.7	62.1	57.8	107.4%
Actual deaths	1953	1968	3921	50.2%
Lost to observation	531	132	663	19.9%
Years with T2D	8.5	12.4	9.3	133.8%
Average age (years)	64.4	73.7	66.2	111.3%
Average age at death (years)	76.9	79.0	78.0	101.4%
Expected deaths	1434	702	2135	32.9%
SMR	1.36	2.80	1.84	152.7%
Expected deaths including IMD	1736	860	2596	33.1%
SMR_IMD	**1.13**	**2.29**	1.51	151.5%
Expected LYL	18 157	6816	24 973	27.3%
Actual LYL	23 502	20 460	43 962	46.5%
LELY/death	**2.74**	**6.93**	4.84	143.2%

Abbreviations: IMD, index of multiple deprivation; LELY, life expectancy years lost; LYL, life years lost; SMR, standardized mortality ratio; T2D, type 2 diabetes.

Of note, 54% of those with follow-up had a BMI of 30 kg/m^2 or higher and 34% had an HbA1c of more than 58 mmol/mol.

From the ONS published actual mortality rate by age and sex for each year, there would be 2135 expected deaths. When adjusted for local IMD, the number of expected deaths was 2596. The overall SMR_ID was 1.51 (Table 2). The SMR_IMD was higher in those with a foot complication (SMR_IMD 2.29) than in those without (SMR_IMD 1.13). The life expectancy years lost was 18 989 years. This could be expressed as 2.7 years per actual death for patients without a foot complication and 6.9 years per actual death for people with a foot complication.

The OR for having a 'high' HbA1c showed little difference between groups (Table S2). Those with a foot complication had a lower proportion with obesity, and a lower proportion with out-of-range lipids (TC and TC/HDL ratio). Conversely, smoking (OR 1.19) and high blood pressure (OR 1.12) were higher in those with a foot complication. Prescriptions of angiotensin-converting enzyme (ACE) inhibitor were higher in those with a foot complication (OR 1.39). People with a foot complication were more probable than those with no foot complication to have an eGFR of less than 60 mL/min/1.73m^2 (OR 2.95) and an ACR of more than 3 mg/mmol (OR 2.28) compared with those without a foot complication (Table S2).

Of those with a foot complication, 78% had a single complication. An increasing number of complications were associated with progressively increasing SMR_IMD and increasing life years lost, while also being associated with a younger age of diagnosis with T2D and a longer duration of T2D (Table S3). Progressively increasing diabetes foot complications were associated with a lower eGFR, higher ACR, higher proportion of people with blood pressure more than 140/90 mmHg and lower TC (Table S3).

Of those with a single foot complication, 45% had PVD, 37% had ulcers and 18% had peripheral neuropathy. Foot ulcers (SMR_IMD 2.6) had the highest risk for mortality (Table S4). In those with PVD alone, the SMR_IMD was 1.8 and in those patients with only peripheral neuropathy, SMR_IMD was 1.05. However, those with

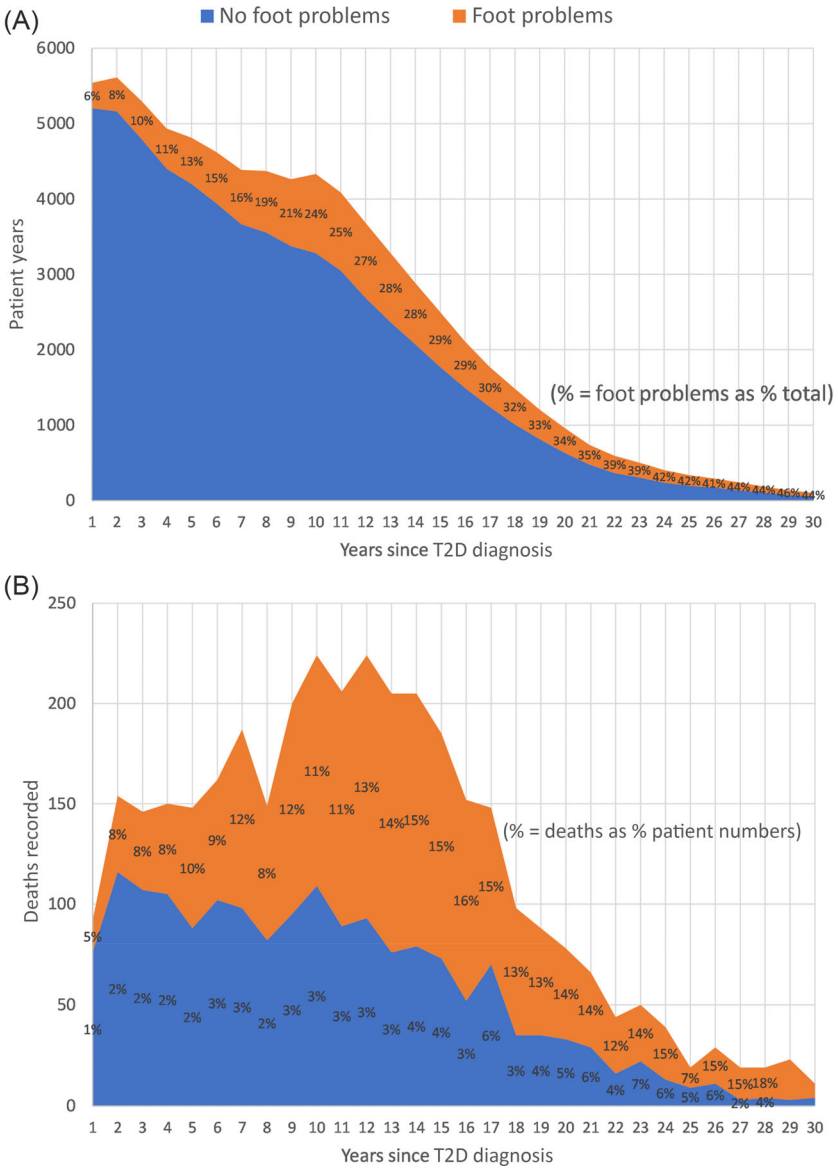

FIGURE 1 A, Impact of the duration of T2D on the numbers of people with a foot complication. B, Impact of the duration of T2D on percentage of annual deaths. T2D, type 2 diabetes.

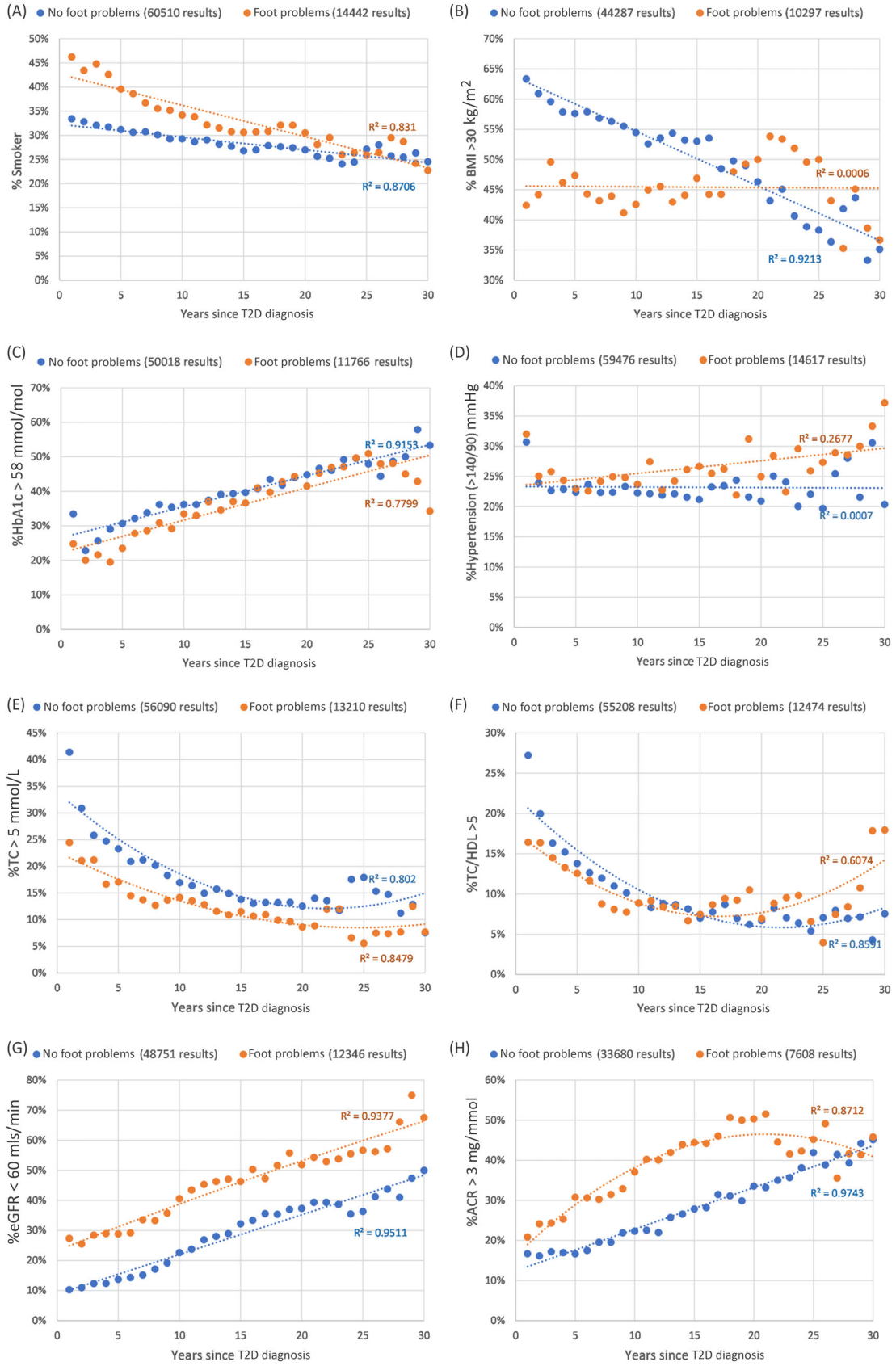

FIGURE 2 Risk factor comparison between T2D patients with a foot complication and those with no foot complication over the duration of T2D, with A, Smoking; B, BMI; C, HbA1c; D, Blood pressure; E and F, Lipids; and G and H, Renal function. ACR, albumin-to-creatinine ratio; BMI, body mass index; eGFR, estimated glomerular filtration rate; TC, total cholesterol; T2D, type 2 diabetes.

combinations of risk factors had significantly elevated SMR_IMD. Notably, amputation in the presence of other diabetes foot complications was associated with the highest SMR_IMD and the greatest number of life years lost.

The proportion of individuals with a foot complication increased with duration of diabetes (Figure 1A). However, even after 30 years, more than 50% of individuals did not have a foot complication. The prevalence of a diabetes foot complication (by total numbers) was greatest at between 9 and 13 years after diagnosis. The percentage of people with T2D and a foot complication that died for any given year was three to four times higher than those without a foot complication (Figure 1B).

Overall, there was little difference in the attainment of cardiovascular risk thresholds between those with a foot complication and those without (Figure 2A–F). The exceptions to this were: (i) eGFR and ACR, where levels for those who develop a foot complication were approximately 10 years in advance of those without; and (ii) for lipid profile, where patients with a foot complication had lower cholesterol than those without. A heat map relating age at diagnosis, years of living with T2D and outcomes (proportion with foot complications, mortality with foot complication and LEYL) is provided in Table S5.

3.1 | Multivariate logistic regression analysis

Demographic and metabolic factors are not independent of each other, so the multivariate linear regression results show which factors predominate. Figure 3 links these to having history of a foot complication and then to actual deaths.

For developing foot complications, the duration with diabetes and age of T2D diagnosis are the major risk factors (both with OR > 2); although with ORs more than 1.6, renal deterioration and smoking were also significant risk factors.

Having a diagnosed foot complication (OR 3.59) is the largest risk for mortality. Renal compromise remains the next largest effect with an OR of 1.93 for elevated ACR, and for an eGFR of less than 60 mL/min/1.73m^2, the OR was 1.92. Lower blood pressure and a lower BMI in people with a defined foot complication was associated here with a negative effect. There was no association observed for HbA1c.

4 | DISCUSSION

In this study, we show that people with T2D and with a foot complication have a significantly elevated SMR_IMD. We confirm that

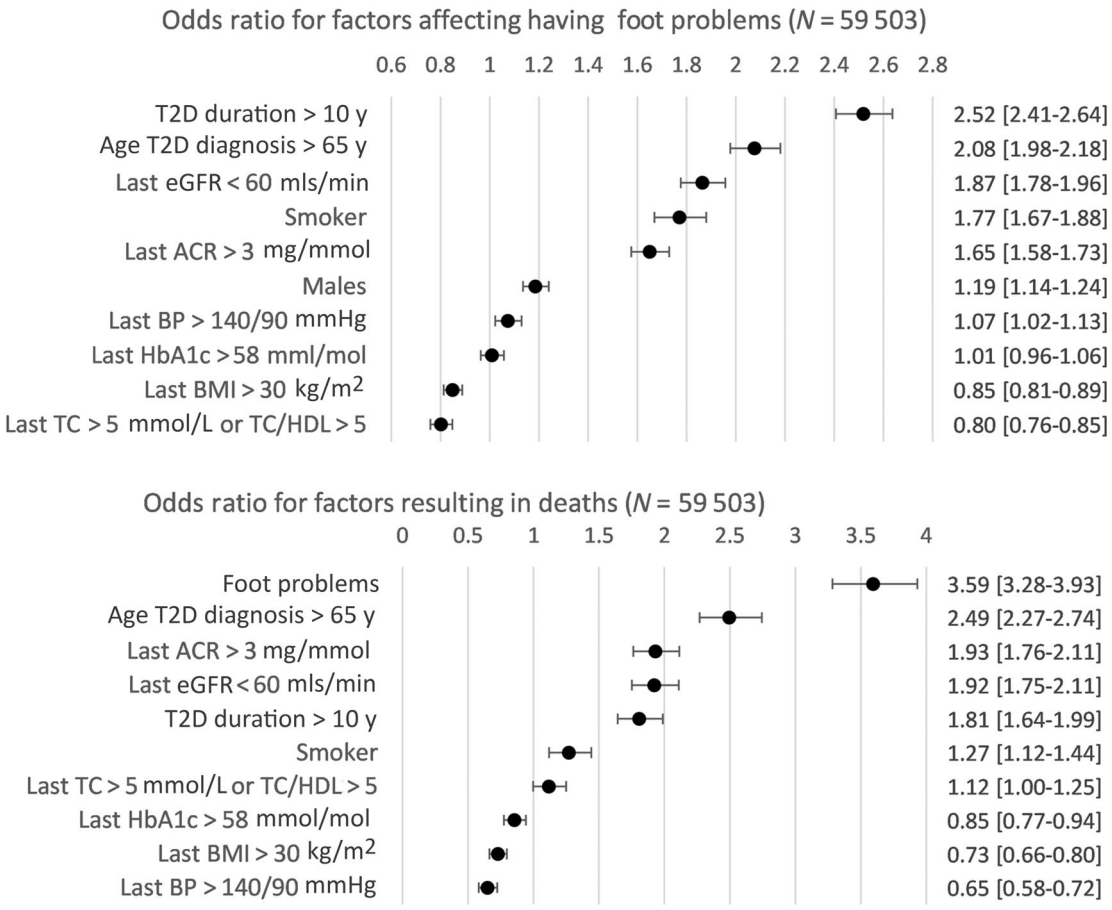

FIGURE 3 Odds ratio from logistic regression linking demographic and metabolic measures to A, History of foot complications, and then B, Recorded deaths. ACR, albumin-to-creatinine ratio; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; *N*, patient years; TC, total cholesterol; T2D, type 2 diabetes.

elevated ACR and low eGFR acted as independent risk factors for mortality. The other key finding was that people without a foot complication had an SMR_IMD that was only 13% greater than that of the general population.

The relationship between renal dysfunction and the risk of diabetes foot complications is well described.[9,15,16] We confirm that the main differentiating clinical factors between those with and without foot complications were eGFR and ACR. While a low eGFR is difficult to reverse, an elevated ACR can be decreased with targeted treatment.[17,18] If achieved, this can reduce progression to end stage renal disease and to reduced mortality.[19,20] Our finding that an elevated urine ACR is associated with a higher rate of death is in keeping with previous reports.[21,22] This highlights the importance of monitoring ACR as a relevant marker of vascular risk.[5] It is apparent from UK data that the ACR testing rate at the diabetes annual review is substantially below other routinely measured variables at around 75% in any year.[8,23,24] There is therefore an opportunity to target individuals with an elevated ACR with a sodium-glucose co-transporter-2 inhibitor, in addition to treatment with an ACE inhibitor or angiotensin receptor blocker.[25]

We found that the mortality rate was significantly higher in younger versus older people with a foot complication. This contrasts with the findings of Costa et al. in a clinic study in France,[26] where the study also showed that the presence of a DFU carries high amputation and mortality rates, particularly in the presence of advancing age. Our findings support the premise that those diagnosed with T2D at a younger age are at the greatest risk of having a shortened life expectancy.

The European Association for the Study of Diabetes and American Diabetes Association guidelines, released in 2022, emphasized the importance of exercise for glycaemic and cardiovascular risk management, in addition to the prescribing of targeted pharmacotherapy, to reduce the rate of progression of renal damage and reduce overall cardiovascular risk.[27] An 8-year prospective study in patients with T2D and neuropathy has shown that sedentary time was the strongest predictor of DFU development, even after adjustment for HbA1c, neuropathy, pedal pulses, motor nerve amplitude and physical activity.[28] Typically, patients who spent more than 12 hours per day being sedentary developed a foot ulcer, whereas those who were sedentary for less than 9 hours did not develop a foot ulcer. Being less mobile may contribute to the elevated SMR_IMD seen with diabetes foot ulceration, as greater recumbency has been shown to have adverse consequences for cardiovascular health.[29] This research is consistent with the tissue stress theory,[30] that prolonged levels of low physical stress through a sedentary lifestyle reduce the skin tissue tolerance to loading. This would then predispose patients to high susceptibility to skin injuries to the feet when weight-bearing physical activity occurs.

Cardio autonomic neuropathy (CAN) is an under-recognized complication of diabetes and is more common is those at greater age, with greater duration of diabetes, worse metabolic control and the presence of other microvascular complications, hence, shared risk factors for the presence of the at-risk foot. CAN is a significant risk for cardiovascular mortality[31,32] and may be a mediator of some of the greater mortality in the at-risk foot population that we observed. Work is needed to evaluate the incorporation of cardiovascular reflex tests in routine practice in the foot clinic. Of interest, the foot complications group was not significantly different in terms of blood pressure control or HbA1c. This might represent a tightening of control after the development of foot complications, but possibly too late to regress cardiovascular risk (the 'metabolic memory' effect).[33] BMI was lower in the T2D at-risk foot group. This 'obesity paradox' for diabetes may relate to co-morbidities such as smoking, or cachexia in co-existent chronic kidney disease.[34] We did not find an association between blood pressure and mortality. This has been seen in other studies looking at mortality in individuals with T2D.[35–37] Blood pressure has a U-shaped relationship with mortality in T2D, particularly in those with established cardiovascular disease (CVD), or in patients with a high-risk profile (such as patients with foot complications). Given that coronary perfusion occurs mainly during diastole, hypotension may directly contribute to coronary insufficiency.[38]

Regarding the association between a lower BMI and elevated mortality rate, we and others have found that a lower BMI in individuals with diabetes is a marker of poor health and therefore of elevated cardiovascular risk, in both a meta-analysis and a retrospective mortality analysis of individuals with diabetes.[39,40]

In people with T2D, foot ulceration must be seen as a harbinger of more adverse outcomes,[2,5] with an even greater SMR for those undergoing an amputation. Tight control of blood glucose and focused management of cardiovascular and renal parameters remains a priority, in addition to regular specialist podiatry review and intervention as appropriate. We have provided further evidence here for the importance of targeting renal health.[25,41]

4.1 | Strengths and limitations

This is a retrospective real-world study with inherent bias thereof. The number of reviews in 2020 was reduced by social restrictions implemented during the COVID-19 pandemic. Nevertheless, the dataset is comprehensive in relation to the sampling frame of people diagnosed with T2D on or before 1 January 2010 and living in Salford, UK. The coding of death reflects the recording of death in general practice. Coding issues in other areas may be imperfect, such as recoding when patients with T2D are started on insulin to 'type 1 diabetes'.[41,42] The diabetes population of Salford (UK) did not include many people of non-Caucasian ethnicity. There may be disparities of care in people from ethnic minority backgrounds, which would influence the development of diabetes complications.[8] Furthermore, we accept that the population of Salford is not necessarily representative of the UK as a whole.

In conclusion, people with T2D plus a foot complication have a higher mortality risk compared with those with T2D and no reported foot complication, who themselves have a mortality risk that is only 13% higher than that of the general population. That the group

without foot complications had such a small incremental cardiovascular risk highlights the significant effect of foot complications on the T2D cohort as a whole.

Traditional cardiovascular risk factor control had comparatively little impact on the OR for death. This suggests that once foot complications and renal complications develop, the paradigm changes. We urgently need prospective studies to determine how best to reduce the high residual risk of CVD in patients with diabetes foot complications and/or renal disease.

AUTHOR CONTRIBUTIONS

MS: conceived the study and led on analysis. AR: clinical perspective. GD: expert podiatry input. BNT: statistical validation and methodology review. JMG: epidemiological perspective and clinical input. NDR: expert perspective on foot health. EBJ: expert clinical perspective on foot health. MF: expert academic perspective. GR: epidemiological perspective and clinical input. MBW: epidemiological perspective and clinical input and led on paper revisions. ME: expert academic and clinical perspective. AHH: conceived the study (with MS) and led on paper writing.

ACKNOWLEDGEMENTS

None.

CONFLICT OF INTEREST STATEMENT

No author has any conflict of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.15260.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Martin B. Whyte https://orcid.org/0000-0002-2897-2026
Adrian H. Heald https://orcid.org/0000-0002-9537-4050

REFERENCES

1. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. *N Engl J Med*. 2017;376(24):2367-2375. doi:10.1056/NEJMra1615439
2. Boulton AJM, Whitehouse RW. The diabetic foot. In: Feingold KR, Anawalt B, Blackman MR, et al., eds. *Endotext*. South Dartmouth (MA); 2000.
3. Jeffcoate WJ, Vileikyte L, Boyko EJ, Armstrong DG, Boulton AJM. Current challenges and opportunities in the prevention and management of diabetic foot ulcers. *Diabetes Care*. 2018;41(4):645-652. doi:10.2337/dc17-1836
4. Saluja S, Anderson SG, Hambleton I, et al. Foot ulceration and its association with mortality in diabetes mellitus: a meta-analysis. *Diabet Med*. 2020;37(2):211-218. doi:10.1111/dme.14151
5. Young MJ, McCardle JE, Randall LE, Barclay JI. Improved survival of diabetic foot ulcer patients 1995–2008: possible impact of aggressive cardiovascular risk management. *Diabetes Care*. 2008;31(11):2143-2147. doi:10.2337/dc08-1242
6. Anderson SG, Shoo H, Saluja S, et al. Social deprivation modifies the association between incident foot ulceration and mortality in type 1 and type 2 diabetes: a longitudinal study of a primary-care cohort. *Diabetologia*. 2018;61(4):959-967. doi:10.1007/s00125-017-4522-x
7. Chaturvedi N, Jarrett J, Shipley MJ, Fuller JH. Socioeconomic gradient in morbidity and mortality in people with diabetes: cohort study findings from the Whitehall study and the WHO multinational study of vascular disease in diabetes. *BMJ*. 1998;316(7125):100-105. doi:10.1136/bmj.316.7125.100
8. Whyte MB, Hinton W, McGovern A, et al. Disparities in glycaemic control, monitoring, and treatment of type 2 diabetes in England: a retrospective cohort analysis. *PLoS Med*. 2019;16(10):e1002942. doi:10.1371/journal.pmed.1002942
9. Bonnet JB, Sultan A. Narrative review of the relationship between CKD and diabetic foot ulcer. *Kidney Int Rep*. 2022;7(3):381-388. doi:10.1016/j.ekir.2021.12.018
10. NHS Digital. Quality and Outcomes Framework. [Accessed 30 June 2022]. Available from: https://qof.digital.nhs.uk/.
11. Salford Integrated Record. Available from. https://www.graphnethealth.com/knowledge-hub/case-studies/salford-integrated-record-improving-care-for-salford-patients-and-powering-the-pioneering-salford-lung-study/#:~:text=The%20Salford%20Integrated%20Record%20(SIR,which%20benefits%20the%20local%20population.
12. Read Codes. [Accessed 30 July 2022]. Available from: https://digital.nhs.uk/services/terminology-and-classifications/read-codes.
13. Office for National Statistics. [Accessed 31 July 2022]. Available from: https://www.ons.gov.uk/.
14. English Indices of Deprivation. Available from. https://www.gov.uk/government/collections/english-indices-of-deprivation.
15. Aragon-Sanchez J, Lazaro-Martinez JL, Garcia-Alvarez Y, Morales EG, Hernandez-Herrero MJ. Albuminuria is a predictive factor of in-hospital mortality in patients with diabetes admitted for foot disease. *Diabetes Res Clin Pract*. 2014;104(1):e23-e25. doi:10.1016/j.diabres.2014.01.006
16. Wolf G, Muller N, Busch M, et al. Diabetic foot syndrome and renal function in type 1 and 2 diabetes mellitus show close association. *Nephrol Dial Transplant*. 2009;24(6):1896-1901. doi:10.1093/ndt/gfn724
17. Bailey CJ, Day C, Bellary S. Renal protection with SGLT2 inhibitors: effects in acute and chronic kidney disease. *Curr Diab Rep*. 2022;22(1):39-52. doi:10.1007/s11892-021-01442-z
18. Wang K, Hu J, Luo T, et al. Effects of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers on all-cause mortality and renal outcomes in patients with diabetes and albuminuria: a systematic review and meta-analysis. *Kidney Blood Press Res*. 2018;43(3):768-779. doi:10.1159/000489913
19. Palmer SC, Mavridis D, Navarese E, et al. Comparative efficacy and safety of blood pressure-lowering agents in adults with diabetes and kidney disease: a network meta-analysis. *Lancet*. 2015;385(9982):2047-2056. doi:10.1016/S0140-6736(14)62459-4
20. Qiu M, Ding LL, Zhou HR. Comparative efficacy of five SGLT2i on cardiorenal events: a network meta-analysis based on ten CVOTs. *Am J Cardiovasc Drugs*. 2022;22(1):69-81. doi:10.1007/s40256-021-00484-8
21. Liu S, Niu J, Wu S, et al. Urinary albumin-to-creatinine ratio levels are associated with subclinical atherosclerosis and predict CVD events and all-cause deaths: a prospective analysis. *BMJ Open*. 2021;11(3):e040890. doi:10.1136/bmjopen-2020-040890
22. Yang J, Huang J, Wei S, et al. Urine albumin-creatinine ratio is associated with prognosis in patients with diabetic foot osteomyelitis.

Diabetes Res Clin Pract. 2021;180:109043. doi:10.1016/j.diabres.2021.109043
23. National Diabetes Audit Programme. [Accessed 13 May 2023]. Available from: https://digital.nhs.uk/data-and-information/clinical-audits-and-registries/national-diabetes-audit
24. Willison A, Tully V, Davey P. All patients with diabetes should have annual UACR tests. Why is that so hard. *BMJ Qual Improv Rep*. 2016;5(1):u209185.w3747. doi:10.1136/bmjquality.u209185.w3747
25. ElSayed NA, Aleppo G, Aroda VR, et al. 11. Chronic kidney disease and risk management: standards of care in diabetes-2023. *Diabetes Care*. 2023;46(Suppl 1):S191-S202. doi:10.2337/dc23-S011
26. Costa RHR, Cardoso NA, Procopio RJ, Navarro TP, Dardik A, de Loiola Cisneros L. Diabetic foot ulcer carries high amputation and mortality rates, particularly in the presence of advanced age, peripheral artery disease and anemia. *Diabetes Metab Syndr*. 2017;11(Suppl 2):S583-S587. doi:10.1016/j.dsx.2017.04.008
27. Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of diabetes (EASD). *Diabetes Care*. 2022;45(11):2753-2786. doi:10.2337/dci22-0034
28. Orlando G, Reeves ND, Boulton AJM, et al. Sedentary behaviour is an independent predictor of diabetic foot ulcer development: an 8-year prospective study. *Diabetes Res Clin Pract*. 2021;177:108877. doi:10.1016/j.diabres.2021.108877
29. Lavie CJ, Ozemek C, Carbone S, Katzmarzyk PT, Blair SN. Sedentary behavior, exercise, and cardiovascular health. *Circ Res*. 2019;124(5):799-815. doi:10.1161/CIRCRESAHA.118.312669
30. Mueller MJ, Maluf KS. Tissue adaptation to physical stress: a proposed "physical stress theory" to guide physical therapist practice, education, and research. *Phys Ther*. 2002;82(4):383-403.
31. Fisher VL, Tahrani AA. Cardiac autonomic neuropathy in patients with diabetes mellitus: current perspectives. *Diabetes Metab Syndr Obes*. 2017;10:419-434. doi:10.2147/DMSO.S129797
32. Serhiyenko VA, Serhiyenko AA. Cardiac autonomic neuropathy: risk factors, diagnosis and treatment. *World J Diabetes*. 2018;9(1):1-24. doi:10.4239/wjd.v9.i1.1
33. Miller RG, Orchard TJ. Understanding metabolic memory: a tale of two studies. *Diabetes*. 2020;69(3):291-299. doi:10.2337/db19-0514
34. Kwon Y, Kim HJ, Park S, Park YG, Cho KH. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. *PLoS One*. 2017;12(1):e0168247. doi:10.1371/journal.pone.0168247
35. Bergmark BA, Scirica BM, Steg PG, et al. Blood pressure and cardiovascular outcomes in patients with diabetes and high cardiovascular risk. *Eur Heart J*. 2018;39(24):2255-2262. doi:10.1093/eurheartj/ehx809
36. Bohm M, Schumacher H, Teo KK, et al. Cardiovascular outcomes and achieved blood pressure in patients with and without diabetes at high cardiovascular risk. *Eur Heart J*. 2019;40(25):2032-2043. doi:10.1093/eurheartj/ehz149
37. Cooper-DeHoff RM, Gong Y, Handberg EM, et al. Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary artery disease. *JAMA*. 2010;304(1):61-68. doi:10.1001/jama.2010.884
38. Peri-Okonny PA, Patel KK, Jones PG, et al. Low diastolic blood pressure is associated with angina in patients with chronic coronary artery disease. *J Am Coll Cardiol*. 2018;72(11):1227-1232. doi:10.1016/j.jacc.2018.05.075
39. Gao F, Wang ZJ, Shen H, Yang SW, Nie B, Zhou YJ. Impact of obesity on mortality in patients with diabetes: meta-analysis of 20 studies including 250,016 patients. *J Diabetes Investig*. 2018;9:44-54.
40. Heald AH, Jenkins DA, Williams R, et al. Mortality in people with type 2 diabetes following SARS-CoV-2 infection: a population level analysis of potential risk factors. *Diabetes Ther*. 2022;13:1037-1051.
41. Stedman M, Rea R, Duff CJ, et al. The experience of blood glucose monitoring in people with type 2 diabetes mellitus (T2DM). *Endocrinol Diabetes Metab*. 2022;5(2):e00302. doi:10.1002/edm2.302
42. de Lusignan S, Sadek N, Mulnier H, Tahir A, Russell-Jones D, Khunti K. Miscoding, misclassification and misdiagnosis of diabetes in primary care. *Diabet Med*. 2012;29(2):181-189. doi:10.1111/j.1464-5491.2011.03419.x

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Stedman M, Robinson A, Dunn G, et al. Diabetes foot complications and standardized mortality rate in type 2 diabetes. *Diabetes Obes Metab*. 2023;1-9. doi:10.1111/dom.15260