**Incidence trends in ischaemic and non-ischaemic heart failure in people with and without type 2 diabetes, 2000-2019: an observational study in England**

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**Abstract**

**Aim:** To investigate trends in ischaemic and non-ischaemic heart failure (HF) in adults with type 2 diabetes and without diabetes between 1st January 2000 and 31st December 2019 in England.

**Methods:** We used the Clinical Practice Research Datalink datasets, linked to the Hospital Episode Statistics and Office for National Statistics, to estimate sex-specific crude and age-standardised rates of incident ischaemic and non-ischaemic HF up to 10 years per calendar year of diabetes diagnosis and diabetes status.

**Results:** In a cohort of 735,810 individuals, 5,073 ischaemic (2,038 in people with type 2 diabetes and 3,035 in those without) and 16,501 non-ischaemic (6,358 and 10,143, respectively) HF events were recorded during a median follow-up of 10 years. From 2000-2004 to 2005-2009, the age-standardised rates of ischaemic HF marginally declined, while rates remained stable for non-ischaemic HF and were consistently higher for non-ischaemic than ischaemic HF, regardless of diabetes status or sex. Adjusted incidence rate ratios demonstrated negligible impact on trends after accounting for differences in demographics, comorbidities and medications

**Conclusions:** Improving HF prevention and management strategies remains crucial to decrease the risk of HF in the general population and reduce the persistent risk-gap associated with type 2 diabetes in England.

**Key words:** Diabetes; Trends; Heart Failure Aetiology; Epidemiology; England.

**Introduction**

Type 2 diabetes is a common chronic metabolic disorder (1), with 2021 data indicating that approximately 537 million adults are living with diabetes world-wide (2), of which 90% have type 2 diabetes (3). This figure is predicted to rise to 643 million by 2030 (2). Additionally, recent data from England indicates that 3.96 million people have been diagnosed with this type 2 diabetes between 2022-2023 (4). Notably, this number is predicted to rise, as an additional 3,615,330 million people have been considered at ‘high risk’ of developing type 2 diabetes from the National Health Service (NHS) in England (5). Given its increasing incidence and prevalence (6), approaches to lower the risk of diabetes, as well as of its subsequent complications, is of major public health importance. This is particularly relevant since it was estimated that $966 billion was spent on global diabetes-related healthcare expenses in 2021 (2). Furthermore, the NHS in England currently spends around £10 billion per year on diabetes (5), of which an estimated 80% is for diabetes-related complications alone (3). This budget is predicted to rise to 15.1 billion by 2035/2036 (7).

Since recent studies have shown heart failure (HF) as one of the most common first presentations of cardiovascular diseases in people with diabetes (8), lowering the risk of HF in people with type 2 diabetes is of major public health interest. Previous observational studies from the UK have shown that people with type 2 diabetes have a 1.5-2.2 fold increased risk of incident HF compared to those without diabetes (8–11). Nonetheless, a 2018 trend analysis reported decreasing incidence of HF between 2002-2014 in the UK (12). Similarly, a 2018 cohort study reported decreasing incidence of HF among the Scottish population between 2004-2013, with approximately 2-fold higher rates in those with type 2 diabetes vs. without diabetes (11). However, more contemporary data are necessary especially given the recent advancements in cardiovascular disease prevention in people with type 2 diabetes (13), as well as the rise in cardiovascular medication prescriptions over-time in the UK (14). More recent studies from other countries have similarly reported decreasing trends in incident HF between 2000-2022 in people with type 2 diabetes, with greater rates in older vs. younger age groups (15–18). However, the majority of studies only identified hospitalised HF cases, and thereby do not represent the whole burden of HF in the general population. Furthermore, trend studies accounting for HF aetiology (ischaemic HF and non-ischaemic HF) are also sparse (18,19), particularly when explored in relation to diabetes, age, sex, or socioeconomic status. This is important to develop more tailored HF prevention strategies to most optimally lower the risk of HF in people with type 2 diabetes.

Therefore, in this study we aimed to (1) investigate trends of incident ischaemic and non-ischaemic HF in people with type 2 diabetes and without diabetes, using UK primary care, hospital and mortality data; (2) investigate whether these trends differed across groups defined by sex, age at diabetes diagnosis, and socioeconomic status.

**Methods**

**Data sources**

This cohort study used data from the Clinical Practice Research Datalink (CPRD) GOLD and Aurum datasets, linked to the Hospital Episode Statistics Admitted Patient Care (HES APC) and the Office for National Statistics (ONS) death registration data. The CPRD is a large, routinely collected primary care database, representative of the UK population in terms of age and sex (20,21). It includes information on patient demographics, clinical, laboratory, and medical records, comprising ~11.3 million people from 674 general practices (CPRD GOLD) and ~23.1 million patients from 993 general practices (CPRD Aurum). The HES database details all patient admissions to NHS hospitals while ONS collects information on death (i.e., date and cause): both datasets were linked to CPRD only for individuals in England. This study has been conducted in line with the RECORD guidelines (**Supplement**) and a pre-registered protocol approved by an Independent Scientific Advisory Committee (protocol: 21\_000355). The electronic record codes used to define the population and outcomes are available on GitHub (link: <https://github.com/KajalPanchalProjects/Codelists-and-Statacode2>).

**Study population**

We identified all adults (≥18 years) in CPRD GOLD and Aurum with a first recorded date of type 2 diabetes diagnosis (index date of main exposure) between 1st January 2000 and 31st December 2009. People were excluded if they did not have available linkage with HES APC and ONS datasets or did not have a least 12-months of prior registration to an ‘up to standard’ practice since their index date. In case of overlapping practices from CPRD GOLD and AURUM, practices from CPRD Aurum were removed to avoid duplication of data. Patients with prevalent cardiovascular disease (heart failure, peripheral vascular disease, stroke, and ischaemic heart disease [defined as having either coronary heart disease, angina, myocardial infarction, coronary artery bypass graft or percutaneous coronary intervention]) prior to or at the index date were excluded. We also excluded people with missing information on age, sex, ethnicity, deprivation, systolic blood pressure, smoking, and body mass index (BMI). Further details of the cohort inclusion and exclusion criteria are reported in **Supplementary Figure S1** and **S2**.

**Diabetes and covariates**

We defined people with type 2 diabetes based on the first ever recorded Read (CPRD GOLD) and SNOMED-CT (CPRD Aurum) codes. All people with type 2 diabetes were matched up to 1:4 to people without diabetes with the same sex, year of birth, and practice; the index date for the nonexposed population (i.e., those without diabetes) was the same as that of the matched individual with diabetes. For each individual, we extracted the following information: age (years) at index date, sex, ethnicity (extracted in HES: White, Black, South Asian, Mixed/Other, Unknown), smoking status (ever-smoker, never-smoker), alcohol consumption (current, ex, never) and deprivation (measured in Index of Multiple Deprivation (IMD) as fifths: 1, least deprived; 5, most deprived)). IMD combines data from seven domain indices: income, employment, education, skills and training, health and disability, crime, barriers to housing and services, and living environment to produce a singular, summative relative measure of deprivation at small local area level in England (22). We also extracted information on comorbidities (anaemia, asthma, atrial fibrillation, cancer, chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease (COPD), dementia, depression, hypertension, osteoarthritis, rheumatoid arthritis, and thyroid disorders; this information was defined as the latest documented diagnosis code any time prior to or at index date using CPRD or HES databases. In CPRD, we also captured information on prescriptions (including antihypertensives, antiplatelets, digoxin, and lipid-lowering medications), BMI, systolic blood pressure, and total cholesterol any time prior to or at index date.

**Outcomes**

We identified incident HF events using the first date of diagnosis of HF in either CPRD GOLD, CPRD Aurum, HES APC (primary diagnosis), or ONS mortality data (primary cause) after the index date. We defined HF as ischaemic if it followed a diagnosis of IHD (defined as having either coronary heart disease, angina, myocardial infarction, coronary artery bypass graft or percutaneous coronary intervention) since the index date; and non-ischaemic otherwise. Follow-up was from index date until the occurrence of incident ischaemic or non-ischaemic HF, study exit (transfer out date or last collection date), death, or 10 years.

**Statistical analysis**

We reported sex-stratified baseline characteristics at the index date by diabetes status, using mean (standard deviation, SD) for continuous and number (proportion) for categorical data. Missing baseline data are detailed in **Supplementary Table S1**.

We used Poisson regression models to estimate sex-stratified age-standardised rates (at the mean population age of 60 years) of ischaemic and non-ischaemic HF per calendar year of diabetes diagnosis and diabetes status. For the analysis of ischaemic HF, follow-up was censored at the occurrence of non-ischaemic HF, and vice versa. To account for the potential time-varying effect of diabetes duration on incidence rates, in all individuals the follow-up was set to a maximum of 10 years; we therefore restricted the cohort to individuals with an index date between 1st January 2000 until 31st December 2009 (and a maximum follow-up until 31st December 2019). We planned sensitivity analyses using maximum follow-up times of 3 and 5 years but, given the low incidence rates, it was possible to use only the threshold of 5 years.

We further estimated age-standardised rates stratified by deprivation (IMD) status, to investigate differences between the most vs. least deprived quintile groups; and crude rates across age groups (<60, 60-69, 70-79, and ≥80 years), to explore the effect of age at type 2 diabetes diagnosis. Due to the limited number of events in some groups, we were unable to stratify estimates across ethnicity.

We utilised Poisson regression models to also calculate age-standardised rates at index date of two time periods (2000-2004 and 2005-2009) and age-adjusted incidence rate ratios (IRR) comparing 2000-2004 to 2005-2009. In complete-case models, IRRs were further adjusted for IMD, ethnicity, smoking, alcohol intake status, comorbidities, BMI, systolic blood pressure, total cholesterol level, and medication prescriptions.

In sensitivity analyses, we estimated age-standardised rates after redefining HF outcomes as either inpatient HF using HES APC data or HF death using ONS data to assess the impact of outcome definition on rates. Secondly, we quantified incidence rates after including people with prevalent IHD at study entry, which considers ischaemic HF as an incident HF with prevalent IHD at or prior to the index date.

We conducted the data preparation and statistical analyses in Stata/BE 17, 18, and Python 3.8 and reported rates with robust 95% confidence intervals.

**Results**

**Study population characteristics**

A total of 735,810 individuals were included in the cohort (**Table 1**): 351,874 men (106,349 with type 2 and 245,525 without diabetes) and 383,936 women (108,626 and 275,310, respectively). In both men and women, compared to individuals without diabetes those with type 2 diabetes were less likely to be of White ethnicity and from the least deprived quintile. Men with type 2 diabetes had higher BMI (30.5 vs. 26.4 kg/m2) and systolic blood pressure (142 vs. 136 mmHg) compared to those without, whereby a similar finding was also observed in women (31.8 vs. 26.3 kg/m2 and 141 vs. 134 mmHg, respectively). In both men and women, total cholesterol levels were similar comparing individuals with type 2 diabetes vs. without diabetes. There was a greater prevalence of several comorbidities (i.e., chronic kidney disease, hypertension, depression) and prescription of all medications in individuals with type 2 diabetes than those without (**Table 1**).

**Trends in ischaemic heart failure**

During a median (interquartile range, IQR) follow-up of 10.0 (5.3-10.0) years, 5,073 (0.69%) individuals experienced a first incident ischaemic HF; of these, 1,215 (1.14%) and 1,818 (0.74%) occurred in men with and without type 2 diabetes, respectively, while 823 (0.76%) and 1,217 (0.44%) in women with and without type 2 diabetes, respectively (**Table 2**).

In men with type 2 diabetes, there was a progressive reduction in age-standardised rates of ischaemic HF in individuals with a diagnosis of diabetes between 2000-2004 and a plateau thereafter (**Figure 1**): rates were 1.25 (95% CI: 1.15-1.34) per 1,000 person-years for the period 2000-2004 and 1.10 (1.02-1.17) for 2005-2009 (**Table 2**). Age-standardised rates were more stable in men without type 2 diabetes: from 0.76 (0.71-0.81) per 1,000 person-years between 2000-2004 to 0.67 (0.63-0.71) between 2005-2009. These figures translated into an age-adjusted IRR of 0.81 (0.73-0.91) and 0.93 (0.84-1.01) in individuals with type 2 diabetes and without diabetes, respectively, when comparing 2005-2009 to 2000-2004 (**Table 2**). Maximally adjusted IRRs were marginally changed upon further adjustment for potential confounders: 0.85 (0.73-0.99) in both people with and without diabetes (**Table 2**).

Compared to men, women with type 2 diabetes had a more notable reduction in age-standardised rates for ischaemic HF with a diagnosis of diabetes between 2000-2009 (**Figure 1**): rates were 0.68 (0.62-0.75) per 1,000 person-years for 2000-2004 and 0.50 (0.45-0.55) for 2005-2009 (**Table 2**). Among women without diabetes, the age-standardised rates remained stable at 0.37 (0.34-0.40) for 2000-2004 to 0.27 (0.25-0.30) for 2005-2009. Comparing the time period 2005-2009 to 2000-2004, this resulted in age-adjusted IRR of 0.68 (0.59-0.78) and 0.76 (0.68-0.85) in women with type 2 diabetes and without diabetes, respectively (**Table 2**). Maximally adjusted IRRs were negligibly changed upon further adjustment for known potential confounders: 0.75 (0.61-0.91) and 0.74 (0.61-0.89) in women with type 2 diabetes and without diabetes, respectively.

Both men and women had generally higher rates for ischaemic HF in older age groups, with a slight reduction in individuals diagnosed between 70-79 years compared to 60-69 years; trends were broadly stable across all ages and irrespective of diabetes status (**Figure 2**). Deprivation-stratified analyses found marginally higher rates in the most vs. least deprived group; however, the estimates were overlapping with considerable uncertainty, showing no clear trend, and the overall rates were minimal. In men and women with type 2 diabetes, the highest rates observed in the most deprived group were 2.41 and 1.34 per 1,000 person-years, respectively, while the highest in the least deprived group were 1.71 and 1.28, respectively. Among men and women without diabetes, the highest rates were 1.06 and 0.58 per 1,000 person-years in the most deprived and 0.75 and 0.35 rates in the least deprived group, respectively (**Figure S3**).

**Trends in non-ischaemic heart failure**

During the same follow-up, 16,501 (2.24%) people experienced a first incident non-ischaemic HF; of these, 3,099 (2.91%) and 4,900 (2.00%) occurred in men with and without type 2 diabetes, respectively, and 3,259 (3.00%) and 5,243 (1.90%) in women with and without type 2 diabetes, respectively (**Table 2**).

In men with type 2 diabetes, age-standardised rates for non-ischaemic HF remained stable over-time (**Figure 1**): rates were 2.43 (2.30-2.55) per 1,000 person-years in those with type 2 diabetes diagnosed in 2000-2004 and 2.42 (2.30-2.54) in 2005-2009 (**Table 2**). This plateau was observed also in men without diabetes, with rates of 1.58 (1.51-1.65) in 2000-2004 and 1.58 (1.51-1.64) in 2005-2009. Comparing the diagnosis period 2005-2009 to 2000-2004, the corresponding age-adjusted IRRs were 1.03 (0.96-1.11) and 0.98 (0.93-1.04) in men with and without type 2 diabetes, respectively (**Table 2**). Maximally adjusted IRRs were marginally changed upon adjustment for potential confounders (**Table 2**).

In women with type 2 diabetes, age-standardised rates for non-ischaemic HF remained stable over-time (**Figure 1**): rates were 1.90 (1.80-2.00) per 1,000 person-years in those with type 2 diabetes diagnosis in 2000-2004 and 1.84 (1.75-1.94) in 2005-2009 (**Table 2**). Similarly, rates were stable in women without diabetes: 1.15 (1.10-1.20) in 2000-2004 and 1.12 (1.07-1.17) in 2005-2009. Comparing the diagnosis period 2005-2009 to 2000-2004, the age-adjusted IRRs were 0.95 (0.88-1.02) and 0.99 (0.94-1.04) in women with type 2 diabetes and without diabetes, respectively, with no meaningful changes upon adjustment for other confounders (**Table 2**).

In age-stratified analyses, crude rates of non-ischaemic HF were stable over-time regardless of diabetes status, age or sex. As for ischaemic HF, there were slightly reduced rates in individuals diagnosed between ages of 70-79 years compared to 60-69 years (**Figure 2**). In both men and women, deprivation-stratified analyses indicated higher rates in the most vs least deprived group but without a clear trend (**Figure S3**). For men and women with type 2 diabetes, the highest rates observed in the most deprived group were 4.26 and 4.19 per 1,000 person-years were, respectively, and 2.92 and 2.66 in the least deprived group. Corresponding figures in those without diabetes were 2.08 and 1.44 in the most deprived and 1.30 and 1.04 rates in the least deprived group (**Figure S3**).

**Sensitivity analyses**

When defining incident HF as either inpatient HF or HF death, the age-standardised rates of both ischaemic and non-ischaemic HF were slightly attenuated, but the overall findings remained consistent with those of the main analysis indicating stable trends (**Figure S4**). Following the inclusion of individuals with prevalent IHD at index date, age-standardised rates of ischaemic HF slightly increased, although trends were largely similar to the main results (**Figure S5**). Additionally, trends mirrored those of the main analysis when using a maximum follow-up time of 5 years, but with lower age-standardised rates (**Figure S6**).

**Discussion**

This large, retrospective UK cohort study investigated trends in incident ischaemic and non-ischaemic HF between 1st January 2000 and 31st December 2019 in individuals with type 2 diabetes and without diabetes. Comparing the diagnosis periods 2005-2009 and 2000-2004, the age-standardized rates for ischaemic HF showed modest differences: 0.15 per 1,000 person-years in men with diabetes, 0.90 in men without diabetes, 0.18 in women with type 2 diabetes, and 0.10 in women without diabetes. In contrast, the age-standardised rates for non-ischaemic HF were higher and broadly more stable than ischaemic HF, with differences of 0.01 per 1,000 person-years in men with type 2 diabetes; no differences in men without type 2 diabetes; 0.06 in women with type 2 diabetes; and 0.03 in women without diabetes.

We observed marginally decreasing trends in ischaemic HF over-time, which aligns with UK trend studies reporting decreasing rates of IHD (23–25) and incident HF (11,26) over-time. Trend studies investigating incident HF by ischaemic vs. non-ischaemic aetiology are sparse. A 2022 New Zealand study by Chan et al. found declining age-standardized incident HF rates from 2006 to 2013, a plateau from 2013 to 2018, and a reduction in the proportion of incident HF cases associated with IHD from 35.1% in 2006 to 28.0% in 2018 (15). However, the author’s defined HF as hospitalized HF, which hinders representativeness to the general population, a limitation that our study addresses.

Additionally, our findings are somewhat consistent with a 2021 Danish investigation by Schwartz et al. reporting declining trends in crude incident HF rates in people with type 2 diabetes, whereby those with IHD had a greater reduction in incident HF over-time vs. those without IHD (1995 vs. 2018, 0.25 vs. 0.37) (18). In contrast, we observed a plateau for non-ischaemic HF, possibly related to restricting survival time at 10-years of follow-up to reduce the potential bias arising for varying diabetes durations.

The small decreasing trends observed for ischaemic HF could reflect the parallel declining trends in smoking (27) and hypertension (28), as well as improvements in cardiovascular disease management and prevention strategies, such as sodium-glucose co-transporter-2 (SGLT-2) inhibitors (29). However, after adjusting for all available confounders—including smoking, hypertension, demographics, comorbidities, and medications—we observed that these adjustments had minimal impact on the trends for both ischaemic and non-ischaemic HF. Therefore, these trends might be driven by other risk factors that were unaccounted for, such as physical activity (30) or dietary factors (30). Further research is needed to explore if, and to what extent, these risk factors could have impacted the trends in ischaemic and non-ischaemic HF. The plateau observed for non-ischaemic HF might reflect increasing trends in cardiomyopathies (31) and non-atherosclerotic cardiovascular diseases (heart block and aortic stenosis) (25) in the UK as potential aetiological mechanisms underpinning HF. However, further research, ideally with further phenotyping of HF (i.e., based on ejection fraction), should be conducted to clarify the reasons for these stable trends, with implications for the development of preventative and therapeutic strategies.

Our age-stratified analyses mostly found stable trends in ischaemic and non-ischaemic HF among all subgroups, except for a slight decline for ischaemic HF in men and women with type 2 diabetes diagnosed at ages ≥ 80 years and in women with type 2 diabetes diagnosed between 70-79 years. This is consistent with the 2022 New Zealand study by Chan et al, reporting declining trends in ischaemic HF for people aged ≥ 80 years and a plateau for non-ischaemic HF in people aged ≥ 80 years (15). In contrast, a 2017 Danish cohort study by Christiansen et al. reported decreasing trends in both ischaemic HF and non-ischaemic HF among older groups (>50 years), but increasing trends in younger aged groups (<50 years); though, neither this nor the previously mentioned study stratified by age, diabetes status and sex, which the current study addresses to provide more novel insights (19). We also found an increase in crude rates from those aged <60 (lowest rates) to 60-69 years, then a slight reduction between 70-79, followed by a further increase at ≥80 (highest). Given that our definition of incident HF includes HF death, this could suggest an increase in non-HF mortality among those aged 70-79, which could have led to lower rates of HF incidence.

We used CPRD GOLD and Aurum primary care databases linked with HES and ONS databases; this allowed for a large population sample size and facilitated subgroup analysis by sex and diabetes status, alongside further stratification by age and deprivation. Moreover, we defined our key exposure and outcomes variables as incident type 2 diabetes and incident HF, enabling us to understand these associations in temporality more accurately. Our analysis was also conducted using a 10-year survival time interval to account for the potential time-varying effect of diabetes duration.   
  
Nevertheless, the current study has various limitations. Firstly, a few well-known confounding variables (i.e., body fat distribution, physical activity, dietary factors) were unmeasured in CPRD and HES databases, for which residual confounding cannot be ruled out. We used routinely collected health records, which might have led to measurement error in defining variables and subsequently misclassification bias. Due to the observational nature of the study, causality cannot be definitively inferred; furthermore, some individuals may have had undiagnosed type 2 diabetes and thus being incorrectly classified in the subcohort of individuals without diabetes. While diagnostic criteria are formalised in several guidance documents, including national guidelines, the specific clinical-diagnostic pathways may have varied, as well as the accuracy of HF coding, which was based on clinical judgment. Despite matching people with type 2 diabetes to those without diabetes and adjusting for several potential confounders in regression models, residual confounding should be considered when interpreting maximally adjusted IRRs comparing periods of diagnosis. The increased use of NT-proBNP testing in the UK from 2004 to 2018 (32) may have impacted the number of HF cases captured in our study over-time. The observed trends in ischaemic and non-ischaemic HF should also be considered in light of the increasing use of CT coronary angiography (CTCA) from 2011 to 2017 in the UK (33), leading to potentially higher numbers of IHD (and hence, ischaemic HF) captured in the current study over-time. Due to the large sample size, it was computationally challenging to impute missing data, so a complete case approach was used. Lastly, the unavailability of echocardiography data prevented us from differentiating between HF phenotypes (with and without preserved ejection fraction), which could have been useful in further tailoring HF prevention and management strategies.

Our findings show only slight declines in ischaemic HF and stable non-ischaemic HF trends in the UK from 2000 to 2019, regardless of diabetes status and sex; notably, these trends were not meaningfully impacted by various demographic, comorbidities, or medication factors. Furthermore, the higher rates of both ischaemic and non-ischaemic HF in individuals with vs without type 2 diabetes indicate that improvements to cardiovascular disease prevention and treatments in the last two decades have not yet been effective in reducing this persistent diabetes-related risk gap.

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**CRediT authorship contribution statement**

KP contributed to the conception and design of work, data cleaning, data analysis, validation, and interpretation of results, including drafting the original article and revising the draft for important intellectual content. CL and FZ contributed to the conception and design of work, supervision, data cleaning, data analysis, validation, and interpretation of the results, including revising the draft for important intellectual content. KK contributed to the conception and design of work, interpretation of the results and revising the draft for important intellectual content. SS contributed to the data cleaning and analysis, interpretation of the results and revising the draft for important intellectual content.

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