Title: The cost of prevalent and incident cardiovascular disease in people with type 2 diabetes in Scotland: Data from the Scottish Care Information - Diabetes Collaboration (SCI-Diabetes)

Running head: Cost of prevalent and incident CVD in type 2 diabetes

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What is already known:

- People with type 2 diabetes mellitus are at an elevated risk of being affected by cardiovascular disease (CVD).
- CVD is the leading cause of comorbidity and death among people with type 2 diabetes
- Cost comparisons are usually between two groups of people with type 2 diabetes: with and without CVD
- The majority of studies take a CVD prevalence-based approach to estimating the cost of illness

What this study adds:

- We present both, costs associated with prevalent CVD for three groups of people with type 2 diabetes and costs associated with incident CVD over a three-year period.
- The mean annual healthcare costs per person without CVD was £2,500, for a people at high risk of future CVD £3,300 and for a person with established CVD £6,900
- Total mean costs over three years following an incident CVD event were £25,000 vs. £5,900 for people with type 2 diabetes without an incident CVD event

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Abstract

Aims

There is a lack of generalisable studies based on large national population datasets on the economic burden of cardiovascular disease (CVD) in people with type 2 diabetes. Our study aims are twofold: we compare costs for three groups of people with type 2 diabetes: those at high risk of future CVD, those without CVD and those with established CVD. We also estimate costs incurred by people with type 2 diabetes with an incident CVD event and compare to those who remain incident event free over a three-year period.

Methods

Data about people with type 2 diabetes in Scotland were obtained from the Scottish Care Information Diabetes registry. Data linkage was used to retrieve information on healthcare utilisation, care home use and deaths. Productivity effects were estimated for those of non-pensionable age. We estimated costs over 12 months (prevalent CVD) and three years from incident CVD event.

Results

Mean annual cost per person with established CVD was £6,900, £3,300 for a person at high risk of future CVD and £2,500 for a person without CVD and not at high risk. In year one, the cost of an incident CVD event was £16,700 compared to £2,100 for people without an incident event. Over two years, the cumulative costs were £21,500 and £4,200, and by year three, £25,000 and £5,900 respectively.

Conclusions

Cardiovascular disease in people with type 2 diabetes places a significant financial burden on health care and the wider economy. Our results emphasise the financial consequences of CVD prevention strategies.

Keywords : Cardiovascular disease, Observational study, Healthcare costs, Type 2 diabetes mellitus

Introduction

Cardiovascular disease (CVD) is the leading cause of comorbidity and death among people with type 2 diabetes mellitus [1]. People with type 2 diabetes are at increased risk and are disproportionally affected by cardiovascular disease (CVD) [2-5]. In addition to a reduction in quality of life and life expectancy, morbidity associated with CVD places significant burden on health services and the wider economy, highlighted in a recent systematic review on the economic burden of CVD among people with type 2 diabetes [6]. This review concluded that only few of the studies included productivity costs.[6] The majority of studies were undertaken over a decade ago, however the treatment landscape in type 2 diabetes changes rapidly. In addition, comparisons that have been made in the literature were between people with and without CVD. Prevention is also important and hence, inclusion of a third group i.e., people at high risk of developing CVD will add significantly to the existing evidence on costs associated with prevalent CVD in people with type 2 diabetes. In addition, it is not known how costs and the composition of these develop over time after an incident CVD event.

Therefore, this study aims to provide a comprehensive analysis of both, the cost of prevalent and incident CVD in people with type 2 diabetes. For prevalent CVD, we compare the cost of illness for a 12 months period for three groups of people with type 2 diabetes: those with no CVD, those at high risk of developing CVD, and those with established CVD. The second analysis compares costs incurred by people with type 2 diabetes who experience an incident CVD event to those who remain CVD event free over a three-year period. We will also provide evidence on the composition of overall costs over that time period.

Methods

Data Sources

We utilised the population-wide Scottish Care Information – Diabetes (SCI-Diabetes) database to obtain information about people with type 2 diabetes [7]. SCI-Diabetes is a real-time clinical information system tracking clinical information with more than 99% case ascertainment. It also contains socio-demographic and prescribing data. The Community Health Index (CHI), a universal national health service identifier, allowed us to link individual patient-level data on inpatient admissions and mortality.

Cohort Definitions

Prevalent CVD

Using a cross-sectional study design, we included all people with type 2 diabetes who were alive on 1 July 2015. Based on a 10-year lookback period people were classified into three groups: i) having established CVD, ii) being at high risk of future CVD and iii) being CVD free and not at high risk of future CVD. Observations were censored at death or on incident CVD event. Prevalent CVD was established using inpatient admission and primary care records (see supplementary material for ICD-10 codes). Risk of future CVD was defined using SCI-Diabetes and primary care records (Read codes) if patients over the age of 60 years also met one of the following criteria: duration of type 2 diabetes for more than 5 years, HbA1c>9%, hypertension (defined as blood pressure >130/80 mm Hg (if no formal diagnosis of hypertensive disease)), dyslipidaemia (defined as total cholesterol >9.0 mmol/l, non-HDL >7.5 mmol/l, triglycerides 4.5-9.9 mmol/l, pure hypercholesterolemia (E78.0), pure hyperglyceridemia (E78.1), mixed hyperlipidemia (E78.2), other hyperlipidemia (E78.4), unspecified hyperlipidemia (E78.5), other lipoprotein metabolism disorders (E78.89), unspecified disorder of lipoprotein metabolism (E78.9)), albuminuria, smoking status (smoker vs. non-smoker), BMI >30kg/m^2, >2 drugs specific to CVD, eGFR<60 ml/min/1.73m2, diabetic retinopathy, left ventricular dysfunction, left ventricular hypertrophy or angina. For these variables, values that were nearest to 1st January were used with a lookback period of two years and the most recent value was used for each individual [8].

Incident CVD

People alive with type 2 diabetes at any point between 1 January 2010 and 30 June 2015 were included and followed up for a maximum of three years during which occurrence of the first CVD event was recorded. A 10-year lookback period was used to exclude people with a previous history of CVD. CVD events were defined using standard definitions as defined for the prevalent cohort above [8]. Observations were censored at death or end of study (June 2016). For people not experiencing a CVD event during follow-up, the study mid-point (2013) was used as their inception date, allowing for the maximum follow-up of three years.

Health and Social Care Utilisation

Inpatient admissions and day cases including information on diagnostic codes (ICD-10), length of acute hospital stay, speciality, health board area and discharge destination were obtained from Scottish Morbidity Records (SMR01) [9]. Per diem costs [10] for 2015/2016 were obtained from the Scottish Health Service Costs ('Cost Book' (R040)) and mapped to health board and specialty. Prescribing data were retrieved from SCI-Diabetes. Unit costs per prescription were obtained from

the Information Services Division (ISD) [11] and were assigned to prescribed items using British National Formulary (BNF) codes. To derive an estimation of annual frequency of primary care visits we used a validated algorithm based on the Charlson Comorbidity Index (CCI). [12] Primary care costs were assigned to each visit using published costs from the Personal Social Services Research Unit [13]. Dependency status was derived from the discharge destination in SMR01. The Scottish Care Home census confirms that, once admitted to a care home only 5% of patients return to independent living. [14] Therefore, we applied 95% of the mean weekly care costs to all patients in care homes for the duration of the study or until death. [15] For people of working age we applied a weekly cost of £560 [16] (average adult wage) for the duration that patients were either in hospital or a care home and unable to work. Mortality data were obtained from National Records for Scotland (NRS).

Analyses

Generalised Linear Models (GLM) with a gamma distribution and an identity link function were employed to estimate the contribution of different cost categories to total costs for each of the three groups. No imputation was carried out in cases of missing data items except for comorbidity. We adjusted for clinical (duration of diabetes, blood pressure, HbA1c, total cholesterol and CCI) and demographic (age, sex, Scottish Index of Multiple Deprivation (SIMD) [17]) factors. Mean annual costs for prevalent CVD over a 12 months period and confidence intervals were obtained from predicted values of these regression models. Similarly, we obtained mean costs for year one, two and three since incident CVD event. All cost estimates were reported in 2015/16 prices. All analyses were carried out in R [18] and the dplyr package was used to prepare the data for analyses.

Results

Prevalent CVD

Of 244,752 people alive with type 2 diabetes as of 1 July 2015 (median duration of diabetes 7.7 years), we identified 73,037 people with type 2 diabetes with established CVD, 141,428 at high risk of CVD and 30,287 with no CVD and not at high risk (Table A1, supplementary online material). The mean annual cost for a person without CVD and not at high risk was £2,500 (95%CI: £700 - £8,000), £3,300 (95%CI: £1,000 - £16,100) for a person at high risk of future CVD and £6,900 (95%CI:£1,600 - £29,700) for a person with established CVD (Table 1). This pattern of increasing costs in connection with CVD was observed across all age groups. Across (non-exclusive) CVD categories and excluding the small number of people with hypertensive diseases, people with peripheral arterial disease and

heart failure as their first event incurred the highest costs over the 12 months study period and those that underwent revascularisation procedures the lowest (Table 2). However, the wide confidence intervals reflect the variation in costs.

[TABLE 1]

[TABLE 2]

For people with established CVD, hospital admissions accounted for the majority of annual costs (Figure 1). Costs related to hospital admission accounted for a smaller share of overall costs for people with no CVD, with prescription and primary care costs accounting for a larger proportion of total costs compared to people with established CVD (Figure 1). The distribution of individual cost elements for people at high risk of CVD is similar to that of people with no CVD except their hospital costs represented a greater share of overall costs and primary care costs a smaller share. Indirect costs due to lost productivity was found to be a very small component of overall costs for all groups (0.2% across all three groups). A breakdown of costs by CVD type and healthcare sector is provided in Table 3.

[Figure 1]

[TABLE 3]

Incident CVD

Our analysis included 245,428 people with type 2 diabetes with no previous history of CVD, 35,322 of whom experienced an incident CVD event during follow-up. Baseline characteristics are shown in Table A2 (online supplementary material). We present mean annual costs by subgroups of age and type of CVD incident event in Table 3 alongside three-year mortality and incidence rates. People experiencing an incident event were nine years older on average compared to individuals not experiencing a CVD event (Table A2). These people have also had their type 2 diabetes diagnosis for longer.

Mean costs per person after three years since the incident CVD event (£25,000) compared to costs for individuals, who do not experience an incident CVD event (£5,900) were substantially higher (Table 3). Although costs in year one include those incurred during the incident event, we find that this pattern persists and also that costs generally increase with increasing age. Cerebrovascular incident events were associated with the highest cost over three years (£37,900) and

revascularisation procedures were associated with the lowest cost (£17,500). Large cost increments between year one and three were found for transient ischaemic attack (TIA), where by year three costs had doubled compared to those incurred in year one since incident event. A different pattern is observed for incident events that may require a higher upfront cost, such as revascularisation procedures, where costs after three years show a smaller increase (Table 4). The overall CVD event rate was 30.81 per 1,000 person-years and was found to be highest for Ischaemic Heart Disease (15.35 per 1,000 person-years). The CVD categories in Table 4 are not exclusive, people may be counted in more than one depending on diagnosis made at incident event.

[TABLE 4]

In the 12 months period following the incident CVD event, hospital and residential care costs accounted for the largest share of total costs. In years 2 and 3, residential and primary care accounted for a larger proportion than in year one, with hospital care still being the main contributor (Figure 2). Prescription costs remained relatively proportionately constant over time for individuals experiencing an incident CVD event, but proportionately reduced in relation to other cost categories for those without an event, while hospital costs increased. For both groups, costs associated with lost productivity only accounted for one to two percent of total costs. (Figure 2). All analyses were age-adjusted.

Sector-specific costs by type of incident CVD event and year are presented in Table 5. Figure A1 (online supplementary material) provides an overview of the sector-specific cost contributions to overall costs at 3 years for people who experienced an incident event (Figure A1). People without a CVD event incurred costs distributed evenly between primary, hospital, residential care and prescriptions. With the exception of hypertensive diseases, the distribution of cost categories is very similar between CVD types (Figure A1).

[TABLE 5]

Discussion

Prevalent and incident CVD in people with type 2 diabetes place a significant financial burden on health and social care services and the wider economy. Using national population level data, we

identified both, prevalent CVD and incident CVD events in people with type 2 diabetes and estimated costs to the healthcare system and the wider economy. The magnitude of that burden varies between groups. Our findings suggest that a person with type 2 diabetes at high CVD risk costs the economy an additional £900 per year on average compared to a person with type 2 diabetes not at high risk. If CVD is present the additional annual cost rises to£4,400, excluding the costs associated with earlier CVD event(s).

To date, only a limited number of UK studies have analysed the economic burden of CVD in people with type 2 diabetes. [19,20] Hex et al reported costs for hospital admission and procedures at a population [19] and Alva et al [20] at an individual level. In comparison to our study the sample sizes were smaller and CVD categories differed. However, in terms of secondary care costs in the first year it is possible to make comparisons. For ischaemic heart disease, Alva et al. report a cost of £9,800 in 2012 prices (£10,100 inflated using the Hospital and community service index), which is close to our estimate of £11,000.

Rather than just comparing between people with and without CVD, we were able to identify a third group of people with type 2 diabetes at high risk of future CVD, thus providing a more comprehensive picture.

The type of incident CVD event also impacts on costs and the highest costs are incurred during the incident event. However substantial cost differentials between people with type 2 diabetes with and without CVD event continue to show beyond incident event over a three-year follow-up. This seems to be caused by the initial high costs associated with the incident event and by complications that develop once CVD is established. The composition of overall costs changes over a three-year follow-up for people with type 2 diabetes with an incident CVD event with hospital costs decreasing, and costs for residential care increasing over time. For people who remained CVD event free over a three-year period, hospital costs increased, whereas prescription costs decreased. Costs due to lost productivity are small, as a majority of patients is above pensionable age. We expanded on earlier research which reported overall annual costs of $3,400 and $9,700 for treating people with type 2 diabetes and CVD compared to those without CVD [6]. Our estimated cost differences were higher than those reported in the systematic review, however, most studies only considered direct costs and the time period for which cost differences were measured varied greatly [6].

Strengths and Limitations

We were able to include all main cost components for direct and indirect medical costs, estimated costs due to lost productivity and costs for care home stays. However, we appreciate that there may be uncertainty, in particular around the frequency of primary care contacts, as these were estimated using an existing algorithm from the literature and around costs due to lost productivity as the estimation relied on the assumption that only a hospitalisation would lead to days of work lost. Using a contemporary and representative cohort we were able to quantify the financial burden of CVD in type 2 diabetes, emphasising the importance of effective prevention strategies and providing guidance to inform risk stratification to guide treatment decisions.

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Ethics: Ethical approval for the use of SCI-DIABETES data linked to other datasets for research by the SDRN-Epidemiology team has been obtained under: Ethics 07/MRE00/118 Understanding the Impact of Diabetes in Scotland: A Project to Support Scottish Diabetes Register Data Linkage. Privacy Advisory Committee and Caldicott Guardian approval has been awarded under ref PAC 33/11 with amendment 1617-0147. Subsequent updated PBPP (which replace PAC and Caldicott) approval has been granted: reference number 1617-0147, November 2017.

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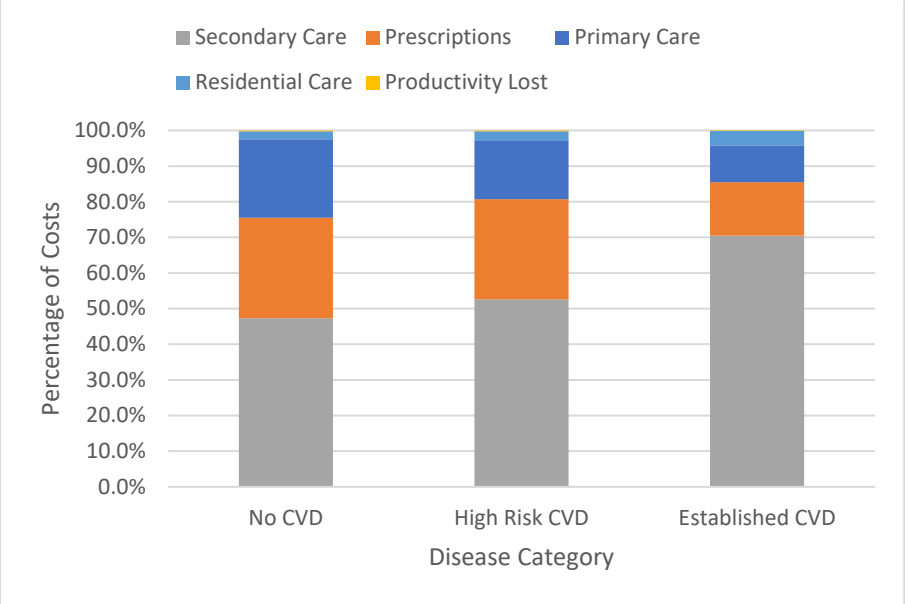
Table 1: Total mean cost for people with type 2 diabetes in Scotland for 2015-2016 by CVD status and age (rounded to the nearest £100)

Age Category/ CVD Type	**Costs (£) over 12 months per patient Mean (95% CI)**								
All (n=244,752)		**<60 years (n=72,055)**		**60-69 years (n=70,631)**		**70-79 years (n=64,839)**		**80+ years (n=37,227)**	
Established (n=73,037)	6,900 (1,600 – 29,700)	Established (n=10,024)	3,800 (1,300 – 15,300)	Established (n=19,451)	5,000 (1,500 – 22,700)	Established (n=25,345)	6,900 (1,700 – 30,800)	Established (n=18,217)	10,100 (2,100 – 40,400)
High Risk (n=141,428)	3,300 (1,000 – 16,100)	High Risk (n=49,094)	1,800 (900 – 4,900)	High Risk (n=42,182)	2,800 (1,100 – 13,200)	High Risk (n=33,403)	4,400 (1,400 - 22,900)	High Risk (n=16,749)	7,100 (1,800, - 38,800)
None (n=30,287)	2,500 (700 – 8,000)	None (n=12,937)	1,300 (700 – 2,600)	None (n=8,998)	2,300 (800 – 5,900)	None (n=6,091)	3,500 (1,100 – 19,400)	None (n=2,261)	5,900 (1,300 – 36,600)

Table 2: Total mean cost for people with type 2 diabetes in Scotland for 2015-2016 by CVD type (rounded to the nearest £100)

First CVD event	**N**	**Costs (£) over 12 months per patient Mean (95% CI)**
Ischaemic Heart Disease	44,948	5,800 (1,500 – 26,300)
Heart Failure	2,736	8,600 (1,500 – 38,300)
Cardiac Arrhythmia	9,855	8,100 (2,000 – 34,000)
Cerebrovascular Disease or Transient Ischaemic Attack	8,451	5,800 (1,400 – 21,700)
Cerebrovascular Disease	6,123	7,900 (1,900 – 32,000)
Transient Ischaemic Attack	2,328	6,200 (1,600 - 35,700)
Peripheral Arterial Disease	3,938	9,200 (1,800 – 40,900)
Revascularisation Procedures	3,104	4,700 (1,300 – 20,600)
Hypertensive Diseases	< 10	9,200 (2,700 – 19,800)



Caption for Figure 1. Contribution of cost categories to average total annual costs for patients with no CVD, at High Risk of CVD or with Established CVD

Table 3: Annual Costs by Cost Component and First CVD Type for people with type 2 diabetes in Scotland for 2015-2016 (rounded to the nearest £100)

	Costs (£) over 12 months - Mean (95% CI)				
CVD type	**Secondary care**	**Primary care**	**Residential care***	**Prescriptions**	**Productivity***
Cardiac Arrhythmia **n=9,855**	6,000 (60 – 53,300)	700 (175 – 1,300)	400 (0 – 1,400)	1,000 (0 – 3,200)	0 (0 – 0)
Cerebrovascular Disease **n=6,123**	5,300 (0 – 51,900)	700 (200 – 1,300)	500 (0 – 4,300)	900 (0 – 3,300)	0 (0, 0)
Cerebrovascular Disease or Transient Ischaemic Attack **n=8,451**	5,100 (0 – 49,000)	700 (200 – 1,300)	400 (0 – 2,100)	900 (0 – 3,300)	0 (0 – 0)
Heart Failure **n=2,736**	5,600 (0 – 50,700)	700 (200 – 1,400)	300 (0,0)	970 (0 - 3,300)	0 (0 – 0)
Hypertensive Diseases **n= 5**	5,700 (100 – 10,300)	700 (400 – 1,000)	0 (0 - 0)	1,300 (200 – 300)	0 (0 – 0)
Ischaemic Heart Disease **n=44,948**	3,900 (0 – 38,400)	700 (200 - 1,300)	200 (0 – 0)	1,000 (0, 3,400)	0 (0 – 0)
Peripheral Arterial Disease **n=3,938**	6,500 (0 – 58,700)	700 (200 – 1,300)	280 (0 - 0)	1,000 (1000 – 3,500)	0 (0 – 0)
Revascularisation Procedures **n=3,104**	3,400 (100 - 35,400)	600 (200 - 1,300)	200 (0 – 0)	900 (0 – 3,100)	0 (0 – 0)
Transient Ischaemic Attack **n=2,328**	4,600 (0 - 45,000)	700 (300 – 1,300)	200 (0 – 0)	900 (0 – 3,500)	0 (0 - 0)

*Notes: These values do not sum to the total costs given in the main text. They are regression based estimates. *These values reflect the age of incident event occurring typically after state pension eligibility age and the low numbers entering residential care.*

Table 4: Mean annual costs; (cumulative); 3 year mortality; Incidence rates in people with type 2 diabetes without previous history of CVD in Scotland 2010-2015 – based on study entry date (rounded to the nearest £100)

	No incident CVD event Mean Cost £ and 95% CI	**Incident and subsequent CVD Mean Cost £ and 95% CI**
All n=245428		
3 year mortality		25.25%
Event Rate per 1,000 person years*		30.81
Year 1	2,100 (1,000 - 6,100)	16,700 (6,700 - 41,700)
Year 1&2	4,200 (2,000 - 11,900)	21,500 (9,000 - 50,900)
Year 1,2&3	5,900 (2,800 - 16,500)	25,000 (10,700 - 57,100)
< 60 years (n=104078)		
Year 1	1,400 (900 - 2,800)	11,200 (6,100 - 26,100)
Year 1&2	3,000 (2,000 - 5,600)	14,400 (8,100 - 31,300)
Year 1,2&3	4,000 (2,700 - 7,500)	16,800 (9,700 - 35,200)
60- 69 years (n=68626)		
Year 1	1,900 (1,200 - 4,900)	13,800 (7,100 - 31,000)
Year 1&2	4,000 (2,400 - 9,700)	17,400 (9,400 - 37,300)
Year 1,2&3	5,600 (3,500 - 13,400)	20,100 (11,100 - 41,700)
70- 79 years (n=51769)		
Year 1	2,900 (1,600 - 8,800)	17,400 (8,500 - 39,400)
Year 1&2	5,900 (3,200 - 16,600)	22,900 (12,000 - 48,900)
Year 1,2&3	8,300 (4,600 - 23,000)	27,000 (14,500 - 55,300)
80+ (n=20955)		
Year 1	4,100 (2,000 - 12,400)	25,200 (12,200 - 57,800)
Year 1&2	8,200 (4,200 - 23,400)	32,300 (16,700 - 68,700)
Year 1,2&3	11,500 (6,000 - 32,200)	37,300 (20,000 - 76,900)
Cerebrovascular Disease (n=4172)		
3 year mortality		30.37%
Event Rate per 1,000 person years*		3.64
Year 1		29,600 (14,700 - 62,300)
Year 1&2		34,600 (17,600 - 71,600)
Year 1,2&3		37,900 (19,400 - 78,700)
Ischaemic Heart Disease (n=17594)		
3 year mortality		21.26%
Event Rate per 1,000 person years*		15.35
Year 1		12,500 (6,500 - 27,500)
Year 1&2		16,700 (8,600 - 35,900)
Year 1,2&3		19,800 (10,200 - 42,100)
Transient Ischaemic Attack (n=1370)		
3 year mortality		17.88%
Event Rate per 1,000 person years*		1.2
Year 1		10,000 (5,100 - 21,400)
Year 1&2		14,800 (7,700 - 30,000)
Year 1,2&3		18,500 (9,700 - 36,700)
Peripheral Arterial Disease (n=3114)		
3 year mortality		27.65%
Event Rate per 1,000 person years*		2.72
Year 1		21,600 (10,300 - 47,900)
Year 1&2		28,200 (13,500 - 61,100)
Year 1,2&3		32,700 (15,700 - 69,100)
Heart Failure (n=4205)		

3 year mortality		38.10%
Event Rate per 1,000 person years*		3.67
Year 1		20,100 (9,200 - 43,300)
Year 1&2		25,900 (11,700 - 54,700)
Year 1,2&3		29,900 (13,600 - 62,000)
Cardiac Arrhythmia (n=10260)		
3 year mortality		30.02%
Event Rate per 1,000 person years*		8.95
Year 1		17,600 (8,400 - 38,600)
Year 1&2		22,900 (11,100 - 48,300)
Year 1,2&3		26,700 (13,100 - 55,200)
Hypertensive Diseases (n < 10)		
3 year mortality		66.67%
Event Rate per 1,000 person years*		0.00
Year 1		40,000 (28,700 - 50,600)
Year 1&2		40,000 (28,700 - 50,600)
Year 1,2&3		40,000 (28,700 - 50,600)
Revascularisation Procedures (n = 3636)		
3 year mortality		9.85%
Event Rate per 1,000 person years*		3.17
Year 1		12,100 (6,400 - 27,900)
Year 1&2		15,000 (8,100 - 33,600)
Year 1,2&3		17,500 (9,600 - 38,300)
Cerebrovascular Disease/Transient Ischaemic Attack (n= 5435)		
3 year mortality		27.28%
Event Rate per 1,000 person years*		1.2
Year 1		15,700 (8,900 - 31,800)
Year 1&2		21,000 (2,000 - 42,400)
Year 1,2&3		24,900 (13,500 - 48,700)

*Event rates refer to the cardiovascular event rather than mortality

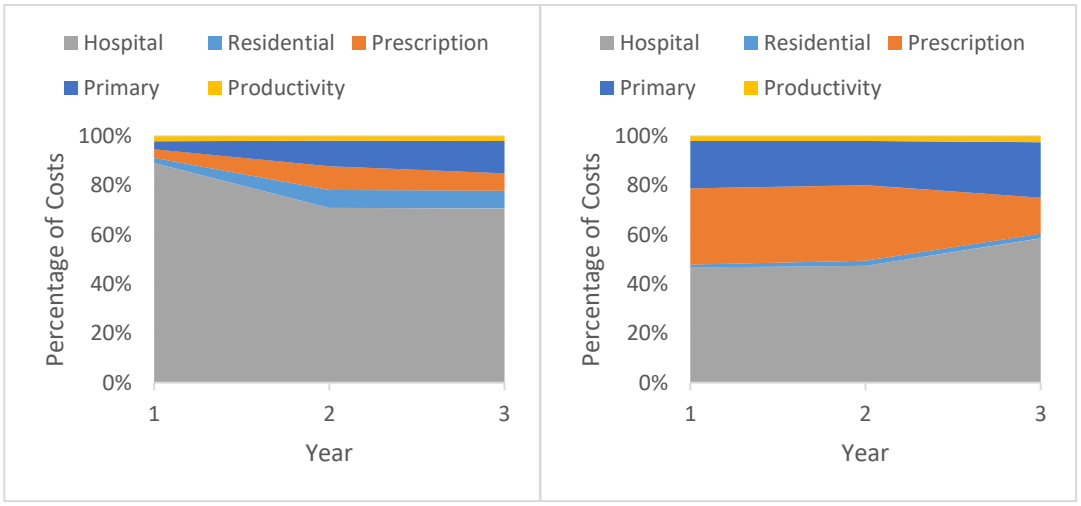
Table 5: Mean cost (cumulative) by cost component and CVD type (rounded to the nearest £100)

Cost Type / CVD type	Costs (£) over 12 months Mean (95% CI)*	Costs (£) over 24 months Mean (95% CI)*	Costs (£) over 36 months Mean (95% CI)*
Secondary care			
Cerebrovascular Disease	25,000 (700 - 114,900)	28,300 (700 - 129,500)	30,600 (800 - 139,100)
Ischaemic Heart Disease	11,000 (100 - 63,400)	13,900 (100 - 80,600)	16,100 (200 - 91,200)
Transient Ischaemic Attack	8,600 (100 - 65,200)	12,000 (100 - 78,900)	14,700 (200 - 90,200)
Peripheral Arterial Disease	18,500 (100 - 98,300)	23,400 (100 - 116,800)	26,500 (200 - 131,300)
Heart Failure	17,000 (100 - 79,900)	21,100 (200 - 101,900)	24,000 (400 - 112,600)
Cardiac Arrhythmia	15,600 (100 - 84,200)	19,300 (100 - 100,700)	22,100 (200 - 122,500)
Hypertensive Diseases	16,200 (3,800 - 32,000)	27,100 (14,600 - 34,300)	27,200 (14,700 - 34,400)
Revascularisation Procedures	11,200 (100 - 74,800)	13,100 (100 - 86,300)	14,700 (200 - 99,200)
Cerebrovascular Disease or TIA	21,100 (100 - 105,800)	24,500 (200 - 121,100)	26,900 (400 - 130,000)
Primary care			
Cerebrovascular Disease	600 (0 - 1,200)	1,100 (0 - 2,300)	1,500 (0 - 3,500)
Ischaemic Heart Disease	500 (0 - 1,200)	1,000 (0 - 2,200)	1,500 (0 - 3,300)
Transient Ischaemic Attack	600 (200 - 1,200)	1,200 (200 - 2,500)	1,800 (200 - 3,600)
Peripheral Arterial Disease	600 (0 - 1,200)	1,100 (0 - 2,400)	1,600 (0 - 3,500)
Heart Failure	600 (0 - 1,200)	1,100 (0 - 2,500)	1,600 (0 - 3,700)
Cardiac Arrhythmia	600 (0 - 1,200)	1,100 (0 - 2,300)	1,500 (0 - 3,300)
Hypertensive Diseases	500 (100 - 700)	800 (200 - 1,400)	1,100 (200 - 2,100)
Revascularisation Procedures	500 (100 - 1,000)	1,000 (100 - 2,100)	1,400 (100 - 3,100)
Cerebrovascular Disease or TIA	600 (0 - 1,200)	1,100 (0 - 2,300)	1,600 (0 - 3,500)
Residential care			
Cerebrovascular Disease	700 (0 - 13,500)	1,300 (0 - 20,000)	1,700 (0 - 25,000)
Ischaemic Heart Disease	300 (0 - 0)	500 (0 - 0)	700 (0 - 0)
Transient Ischaemic Attack	300 (0 - 0)	500 (0 - 0)	700 (0 - 0)
Peripheral Arterial Disease	300 (0 - 0)	500 (0 - 1,400)	800 (0 - 3,900)
Heart Failure	400 (0 - 1,300)	600 (0 - 4,000)	800 (0 - 5,300)
Cardiac Arrhythmia	500 (0 - 3,200)	900 (0 - 7,100)	1,200 (0 - 10,800)
Hypertensive Diseases	0 (0 - 0)	4,100 (0 - 11,600)	4,100 (0 - 11,600)
Revascularisation Procedures	100 (0 - 0)	300 (0 - 0)	400 (0 - 0)
Cerebrovascular Disease or TIA	600 (0 - 10,200)	1,100 (0 - 15,600)	1,500 (0 - 19,300)
Prescriptions			
Cerebrovascular Disease	800 (0 - 2,900)	1,300 (0 - 5,200)	1,600 (0 - 6,800)
Ischaemic Heart Disease	900 (0 - 3,100)	1,600 (0 - 5,900)	1,900 (0 - 7,700)
Transient Ischaemic Attack	800 (0 - 3,200)	1,500 (0 - 6,400)	1,800 (0 - 7,700)
Peripheral Arterial Disease	900 (0 - 3,100)	1,600 (0 - 5,900)	2,000 (0 - 7,900)
Heart Failure	900 (0 - 3,500)	1,600 (0 - 6,500)	2,000 (0 - 8,400)
Cardiac Arrhythmia	800 (0 - 3,000)	1,400 (0 - 5,400)	1,700 (0 - 7,000)
Hypertensive Diseases	2,000 (900 - 3,000)	3,000 (3,000 - 3,100)	4,100 (3,200 - 5,000)
Revascularisation Procedures	800 (0 - 3,000)	1,300 (0 - 5,200)	1,700 (0 - 6,800)
Cerebrovascular Disease or TIA	800 (0 - 3,000)	1,400 (0 - 5,500)	1,700 (0 - 7,100)
Productivity			

Cerebrovascular Disease	600 (0 - 6,200)	700 (0 - 7,000)	700 (0 - 7,700)
Ischaemic Heart Disease	300 (0 - 2,200)	300 (0 - 2,700)	400 (0 - 3,100)
Transient Ischaemic Attack	100 (0 - 1,000)	200 (0 - 1,700)	200 (0 - 2,400)
Peripheral Arterial Disease	600 (0 - 6,100)	800 (0 - 7,700)	900 (0 - 8,800)
Heart Failure	300 (0 - 3,500)	400 (0 - 4,300)	500 (0 - 5,000)
Cardiac Arrhythmia	200 (0 - 2,300)	300 (0 - 2,900)	300 (0 - 3,300)
Hypertensive Diseases	100 (0 - 400)	4,800 (0 - 13,800)	4,800 (0 - 13,800)
Revascularisation Procedures	600 (0 - 5,400)	700 (0 - 6,200)	800 (0 - 7,100)
Cerebrovascular Disease or TIA	500 (0 - 5,600)	600 (0 - 6,100)	600 (0 - 6,900)

*Non-parametric CIs have been estimated

Caption for Figure 2. Contribution to average total costs of different cost categories over years 1,2&3 for people experiencing an index CVD event (left panel) and those not experiencing an index CVD event (right panel)



Supplementary material

Definition of established CVD

Established CVD was defined as having codes for any cause of admission for chronic ischaemic heart disease (ICD-10 I20-I25), cerebrovascular disease including transient ischaemic attack (ICD-10 I60-63, I66, I69 & G45), peripheral arterial disease (ICD-I70.2 and I73.9), heart failure (I11.0, I13 I50), cardiac arrhythmia (I48, I49), hypertensive heart disease (I13.0, I15.0) or procedure codes for revascularisation procedures of coronary, carotid or lower limb arteries. In addition, primary care records were also queried for corresponding Read codes for coronary heart disease, cerebrovascular disease and revascularisation procedures, peripheral vascular disease and atrial fibrillation.

Table A1: Demographic characteristics and risk factors by CVD status in people with Type 2 diabetes

Parameter	Established CVD	High Risk CVD	No CVD	Total
Male N (%)	44363(60.74)	75951(53.70)	17664(58.32)	137978(56.37)
Female N (%)	28674(39.26)	65477(46.30)	12623(41.68)	106774(43.63)
Mean (SD)				
Age at index date (years)	72.2(10.6)	64.9(12.5)	62.2(12.6)	66.7(12.5)
Age at diabetes diagnosis (years)	61.6(11.8)	55.8(12.5)	57.5(12.6)	57.7(12.6)
Diabetes duration (years)	10.6(7.6)	9.2(6.5)	4.7(4.6)	9.0(6.9)
Systolic BP (mmHg)	132.0(16.2)	135.0(14.4)	125.6(12.1)	133.0(15.0)
Diastolic BP (mmHg)	72.7(9.8)	76.3(9.5)	73.9(8.1)	75.0(9.6)
Total Cholesterol (mmol/L)	4.0(1.1)	4.3(1.1)	4.4(1.0)	4.3(1.1)
LDL Cholesterol (mmol/L)	2.0(0.8)	2.2(0.9)	2.3(0.9)	2.1(0.9)
HDL Cholesterol (mmol/L)	1.1(0.3)	1.2(0.4)	1.3(0.4)	1.2(0.4)
HbA1c (mmol/mol)	58.6(17.5)	60.5(18.2)	52.0(11.4)	59.0(17.5)
HbA1c (%)	9.3(3.5)	9.7(3.5)	8.4(2.5)	9.3(3.5)
Weight (Kg)	89.3(19.0)	92.8(20.6)	83.3(17.8)	90.7(20.1)
BMI (Kg/m2)	31.4(6.0)	32.8(6.5)	28.8(5.4)	31.9(6.4)
Albumin Creatinine Ratio	1.5(0.5,5.1)	1.1(0.3,3.0)	0.6(0.0,1.2)	1.1(0.3,3.1)
Albuminuric Status N (%)				
Normo	42093(68.43)	92326(77.26)	21718(98.28)	156137(76.87)
Micro	15941(25.91)	23907(20.01)	363(1.64)	40211(19.80)
Macro	3482(5.66)	3261(2.73)	16(0.07)	6759(3.33)
Renal status N (%)				
CKDEpi CKD Stage 1	12944(18.22)	49593(35.90)	12175(44.03)	74712(31.54)
CKDEpi CKD Stage 2	33587(47.27)	61661(44.63)	14985(54.19)	110233(46.54)
CKDEpi CKD Stage 3	21477(30.23)	24790(17.94)	479(1.73)	46746(19.73)
CKDEpi CKD Stage 4/5	3049(4.29)	2117(1.53)	15(0.05)	5181(2.19)
Current Smoker N (%)	13283(18.22)	29502(20.88)	1828(6.20)	44613(18.31)
Socio-Economic Status[1] N (%)				
Not known	198(0.27)	472(0.33)	115(0.38)	785(0.32)
SIMD-1	9509(13.02)	16718(11.82)	2979(9.84)	29206(11.93)
SIMD-2	9352(12.80)	16696(11.81)	3141(10.37)	29189(11.93)
SIMD-3	8906(12.19)	16542(11.70)	3022(9.98)	28470(11.63)
SIMD-4	8304(11.37)	15683(11.09)	3094(10.22)	27081(11.06)
SIMD-5	7587(10.39)	14522(10.27)	3069(10.13)	25178(10.29)
SIMD-6	6949(9.51)	14132(9.99)	2956(9.76)	24037(9.82)
SIMD-7	6451(8.83)	13375(9.46)	3094(10.22)	22920(9.36)
SIMD-8	5954(8.15)	12301(8.70)	3082(10.18)	21337(8.72)
SIMD-9	5445(7.46)	11498(8.13)	2960(9.77)	19903(8.13)
SIMD-10	4382(6.00)	9489(6.71)	2775(9.16)	16646(6.80)
Health Board				
Argyll	6240(8.54)	11730(8.30)	2526(8.34)	20496(8.38)
Ayrshire and Arran	6484(8.88)	11142(7.88)	2282(7.54)	19908(8.14)
Borders	1672(2.29)	3204(2.27)	838(2.77)	5714(2.34)
Dumfries & Galloway	2280(3.12)	4530(3.20)	815(2.69)	7625(3.12)
England / Wales / Northern Ireland	<10(0.01)	45(0.03)	<10(0.02)	61(0.02)
Fife	5344(7.32)	10711(7.58)	2282(7.54)	18337(7.49)
Forth Valley	4077(5.58)	8253(5.84)	1516(5.01)	13846(5.66)
Glasgow	11378(15.58)	20770(14.69)	4558(15.05)	36706(15.00)
Grampian	6960(9.53)	14000(9.90)	3203(10.58)	24163(9.87)
Highland	3070(4.20)	5626(3.98)	1017(3.36)	9713(3.97)
Lanarkshire	9406(12.88)	18234(12.90)	3957(13.07)	31597(12.91)
Lothian	9388(12.85)	19645(13.90)	4360(14.40)	33393(13.65)
Orkney	240(0.33)	499(0.35)	144(0.48)	883(0.36)
Shetland	258(0.35)	599(0.42)	108(0.36)	965(0.39)
Tayside	5926(8.11)	11745(8.31)	2555(8.44)	20226(8.27)
Western Isles	304(0.42)	645(0.46)	117(0.39)	1066(0.44)

[1]Socio-Economic status is measured using the Scottish Index of Multiple Deprivation (SIMD), represented as deciles, where 1 represents the most deprived areas and 10 represents the least deprived areas.

Table A2: Patient characteristics at study entry (mean (SD); %)

	No CVD	**Incident CVD**
Sex Female %	46.00	43.73
Mean (SD)		
Age at index date	60.9 (13.1)	69.2 (11.3)
Age at diabetes diagnosis	56.8 (13.0)	62.2 (12.4)
Diabetes duration (years) (Median, IQR)	1.5(0.0,6.6)	5.3(0.8,10.5)
Systolic BP (mmHg)	136.1(16.5)	137.4(17.8)
Diastolic BP (mmHg)	78.8(10.3)	75.9(10.7)
Total Cholesterol (mmol/L)	4.8(1.3)	4.4(1.2)
LDL Cholesterol (mmol/L)	2.4(1.0)	2.3(1.0)
HDL Cholesterol (mmol/L)	1.2(0.4)	1.2(0.4)
HbA1c (mmol/mol)	60.7(20.3)	59.2(19.2)
HbA1c (%)	7.7(4.0)	7.6(3.9)
Weight (Kg)	91.0(21.1)	87.9(20.2)
BMI Kg/m^2	32.2(6.7)	31.4(6.4)
Albumin Creatinine Ratio (µg/mg)	1.0(0.4,2.5)	1.3(0.6,3.8)
Renal Status		
CKDEpi CKD Stage 1	79832(38.46)	7068(20.44)
CKDEpi CKD Stage 2	96202(46.35)	16762(48.46)
CKDEpi CKD Stage 3	29545(14.23)	9768(28.24)
CKDEpi CKD Stage 4/5	1997(0.96)	989(2.86)
Current Smoker	52638(25.05)	9377(26.55)
SIMD Decile[1] (N, %)		
SIMD-1	4342(12.29)	24657(11.74)
SIMD-2	4399(12.45)	24543(11.68)
SIMD-3	4204(11.90)	24064(11.45)
SIMD-4	3955(11.20)	23065(10.98)
SIMD-5	3778(10.70)	21496(10.23)
SIMD-6	3384(9.58)	20730(9.87)
SIMD-7	3228(9.14)	20037(9.54)
SIMD-8	3052(8.64)	18505(8.81)
SIMD-9	2645(7.49)	17495(8.33)
SIMD-10	2232(6.32)	14781(7.04)
Not known	103(0.29)	733(0.35)

[1]Socio-Economic status is measured using the Scottish Index of Multiple Deprivation (SIMD), represented as deciles, where 1 represents the most deprived areas and 10 represents the least deprived areas.

Caption for Figure A1: Percentage Share of Cost Categories by CVD Event Type at 3 Years