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# Cardiovascular outcomes of patients with type 2 diabetes after myocardial infarction and the impact of diabetes duration: a nationwide registry study

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ABSTRACT

*Aims:* To study long-term cardiovascular outcomes following a myocardial infarction (MI) among patients with type 2 diabetes.
*Methods:* Patients surviving 90 days after MI with type 2 diabetes (n = 10,440) or without diabetes (n = 65,315) during 2004–2018 were identified from Finnish nationwide registries. The primary outcome, a major adverse cardiovascular event (MACE; recurrent MI, ischemic stroke, heart failure hospitalization, or cardiovascular death), was studied using competing risk Fine-Gray analyses. Median (maximum) follow-up was 3.7 (12) years. Differences between groups were balanced by multivariable adjustments and propensity score matching (n = 10,300 patient pairs).
*Results:* 12-year cumulative incidence of MACE was higher in patients with type 2 diabetes (68.8 %) compared to propensity score-matched patients without diabetes (56.1 %) (sub-distribution hazard ratio [sHR]: 1.36; 95 % CI: 1.31–1.41). Incidences of recurrent MI (sHR 1.49; 95 % CI 1.41–1.57), ischemic stroke (1.14; 1.05–1.23), heart failure hospitalization (1.48; 1.40–1.57), and cardiovascular death (1.30; 1.24–1.36) were higher in patients with type 2 diabetes. Longer diabetes duration was associated with MACE, recurrent MI, heart failure, and cardiovascular death.
*Conclusions:* Patients with type 2 diabetes have impaired long-term cardiovascular outcomes after an MI, underlining the importance of effective secondary prevention. Patients with a longer diabetes duration are at a particularly high risk.

## 1. Introduction

Type 2 diabetes is a world-wide epidemic, and it clearly increases the risk of cardiovascular diseases (CVD), including myocardial infarction (MI) [1,2]. Patients with type 2 diabetes without a prior MI have a risk of MI comparable to that of patients without diabetes who have had a prior MI [3]. MI patients with diabetes also have higher mortality rates compared to patients without diabetes [4,5]. Some earlier studies including the Framingham study indicate that MI patients with diabetes are also at a particularly high risk of recurrent MI and post-MI heart failure [6–8].

The treatment of acute coronary syndromes (ACS) has intensified with increasing rates of timely reperfusion and more aggressive secondary prevention, and case fatality rates after MI have improved in general and among patients with type 2 diabetes [9,10]. Diabetes care has also improved significantly with cardioprotective antidiabetic medications (i.e. sodium-glucose co-transporter 2 [SGLT2] inhibitors and glucagon-like peptide-1 [GLP-1] analogues), more precise insulin delivery [11], advancements in glucose monitoring [12], and more aggressive CVD risk management [13]. As better glycemic control and better CVD risk factor control are associated with a lower risk of macrovascular events [14,15], these changes may have potentially led to

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improvements in the prognosis of MI among patients with type 2 diabetes. Thus, up-to-date studies assessing cardiovascular outcomes after MI among patients with type 2 diabetes are warranted.

In this nationwide registry study between 2004 and 2018, we provide an update on several long-term cardiovascular outcomes after an MI (i.e. the risk of recurrent MI, ischemic stroke, heart failure hospitalization, and cardiovascular death) among patients with type 2 diabetes, compared to those among patients without diabetes. To enhance the reliability of our findings, we account for a comprehensive set of potential confounders by both propensity score matching and multivariable regression. Furthermore, we assess the impact of diabetes duration on MI prognosis.

## 2. Materials and methods

### 2.1. Study patients

Patients with incident MI admitted to hospitals in Finland between July 1st, 2004 −June 30st, 2018 were studied [16]. The study data were retrospectively retrieved from national registries in Finland covering the entire population. Patients with MI were identified from the Care Register for Health Care in Finland (CRHC) with the ICD-10 code I21 as the primary admission diagnosis [17]. The first time MI admission during the study period was included. Transfers between hospitals and wards were combined as a single admission. Exclusion criteria were death within 90 days after MI, admission duration >90 days, aortic or valvular surgery during index MI admission, and missing data on follow-up (0.5 %) (Supplement Fig. S1).

### 2.2. Definitions

A combination of national registries was used to identify patients with type 2 diabetes. Criteria for type 2 diabetes were ICD-10 code E11 in CRHC, no diagnosis of other diabetes types (ICD-10 code E10, E12-E14), entitlement for special reimbursement for antidiabetic medications (code 215 or 103), and use of peroral (p.o.) antidiabetic medication prior to index MI (Supplement Fig. S1) [4]. All patients with appropriately diagnosed diabetes patients are entitled to special reimbursement for their antidiabetic medications [18]. Reimbursement is provided and recorded by the Social Insurance Institution of Finland after review of a medical certificate issued by the treating physician that describes the rationale for the diagnosis of diabetes. Duration of diabetes was calculated from the date of entitlement of special reimbursement for antidiabetic medications. MI patients without a diagnosis of diabetes (ICD-10 codes E10-E14), no entitlement to special reimbursement for antidiabetic medications, and no purchases of antidiabetic medications within 6 months prior to MI served as controls without diabetes.

Comorbidities at baseline, ST-elevation MI, and revascularizations during index MI admission were identified by using data on diagnoses, procedure codes, and entitlements for special reimbursement for medications, as previously described [17,19]. Secondary preventive medication (beta-blocker, oral anticoagulant, P2Y12 inhibitor, renin-angiotensin-aldosterone system [RAAS] inhibitor, and statin) and antidiabetic medication within 90 days after MI were identified using Anatomical Therapeutical Chemical classification [4]. These medications are only available with prescription in Finland, distributed from pharmacies for a maximum period of three months per purchase, and each purchase recorded in a nationwide database [20]. We lack data on smoking and laboratory values such as lipid levels.

### 2.3. Outcomes

The primary outcome of interest was composite major adverse cardiovascular event (MACE) including hospitalization for recurrent MI, ischemic stroke, or heart failure, and cardiovascular death. Secondary outcomes were hospitalization for recurrent MI, ischemic stroke, heart failure, and cardiovascular death. Outcomes are defined in more detail in the Supplement. Follow-up started 90 days after the index MI and continued up to 12 years. Follow-up data was available up until the end of 2018. Median follow-up of primary outcome on all patients was 3.7 years (IQR 1.4–7.2).

### 2.4. Data sources and ethical considerations

Individual level data were collected from national databases of the National Institute of Health and Welfare (hospital admissions and major interventional procedures), the Finnish Cancer Registry (data on malignancies), the Social Insurance Institution of Finland (data on medication purchases and on entitlements to special reimbursements of medication expenses), and the Statistics Finland (mortality data). The included registries are mandatory by law and cover the entire Finnish population. Permissions for the use of registry data were obtained from Findata (permission THL/164/14.02.00/2021), and Statistics Finland (permission TK/923/07. 03.00/2022). Ethical board review and informed consent were waived by the applicable law due to retrospective design. The participants were not contacted at any point during the study. Legal grounds for the data handling are public interest and scientific research (EU General Data Protection Regulation 2016/679 (GDPR), Article 6(1)(e) and Article 9(2)(j); Data Protection Act, Sections 4 and 6).

### 2.5. Statistical analysis

Differences between study groups were analyzed with chi-squared and *t*-test (original cohort) or with McNemar's test and paired *t*-test (matched groups). The between-groups effect sizes in the baseline characteristics were evaluated by standardized mean differences (SMD). Time-dependent outcomes were studied using the cumulative incidence function and Fine-Gray regression to account for the competing risk of non-endpoint specific death [21].

To adjust for confounders, both multivariable regression and propensity score matching were used. Patients with type 2 diabetes patients were 1:1 matched with control patients without diabetes using the optimal matching method without replacement with a caliper set at 0.2 times the standard deviation (SD) of the estimated propensity score. Propensity score was created using logistic regression with age, sex, baseline comorbidities (hypertension, heart failure, atrial fibrillation, previous MI, cerebrovascular disease, chronic pulmonary disease, malignancy, depression, peripheral vascular disease, previous coronary artery bypass [CABG], valvular disease, rheumatic disease, dementia, psychotic disorder, renal failure, alcohol abuse, liver disease, paralysis, and coagulopathy), ST-elevation, revascularization (percutaneous coronary intervention (PCI) or CABG), secondary preventive medication usage after MI (beta-blocker, statin, RAAS inhibitor, P2Y12 inhibitor, and oral anticoagulation), calendar year of index MI, and treating hospital (university versus non-university).

Multivariable regression models included the same variables as in the propensity score (except for the year of index MI). Association of sex on primary outcome was studied using interaction analysis in multivariable model. Association of diabetes duration as both continuous and categorical (<5, 5–10, ≥10 years) variable with outcomes was studied

using multivariable regression. The extent of potential unmeasured confounding was estimated by calculating the E-value [22]. Results are given as the mean, median, percentage, or sub-distribution hazard ratio (sHR), with 95 % confidence interval (CI), interquartile range (IQR), or ±SD. A p value of <0.05 was considered as statistically significant. Analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

## 3. Results

The original study cohort included 10,440 MI patients with type 2 diabetes and 65,315 MI patients without diabetes. Patients with type 2 diabetes were older, more often female, and had a higher comorbidity burden than patients without diabetes (Table 1). Myocardial infarction with ST-elevation was less common in patients with diabetes, and revascularization was performed less frequently for patients with diabetes. Patients with type 2 diabetes used statins less frequently, but beta-blockers and RAAS inhibitors more frequently than patients without diabetes early after MI (Table 1). Metformin was the most used antidiabetic drug (85.4 %) early after MI, followed by insulin (34.9 %), dipeptidyl peptidase 4 inhibitors, and sulfonylureas (Supplemental Table S1). The use of GLP-1 analogues and SGLT2 inhibitors was infrequent (Supplemental Table S1). These drugs were used in the study cohort after MI since 2005 and 2013, respectively.

Baseline differences were balanced by propensity score matching, resulting in 10,300 matched pairs of patients with type 2 diabetes and patients without diabetes (Table 1).

### 3.1. Major adverse cardiovascular events

A total of 25,221 MACEs occurred during the follow-up of 346,529 person-years after MI (Supplement Table S2). Patients with type 2 diabetes had a higher probability of MACE compared to patients without diabetes in the original and in the propensity score matched cohorts (Fig. 1). In the original cohort, the 12-year cumulative incidence of MACE was 68.9 % in the type 2 diabetes group and 45.7 % in the group without diabetes (multivariable adjusted sHR 1.37; CI 1.33–1.42; p < 0.0001). There was no significant difference in 12-year incidence of MACE between sexes (interaction p = 0.087) with multivariable adjusted sHR 1.40 (CI 1.32–1.48) for men and sHR 1.30 (CI 1.21–1.38) for women.

In the matched cohort, the one-year cumulative incidence of MACE was 19.5 % in the type 2 diabetes group versus 15.3 % in the group without diabetes (p < 0.0001) and 45.5 % versus 36.7 %, respectively, at five years (p < 0.0001). During the 12-year follow-up, the cumulative incidence of MACE was 68.8 % in type 2 diabetes patients versus 56.1 % in matched controls (sHR 1.36; CI 1.31–1.41; p < 0.0001). The E-value was 2.06 (CI 1.94–2.17).

### 3.2. Secondary outcomes

The cumulative incidences of hospitalization for recurrent MI, ischemic stroke, heart failure, and cardiovascular death were all higher in patients with type 2 diabetes compared to matched control patients without diabetes (Fig. 2). At one year follow-up, the cumulative incidence of a recurrent MI was 8.1 % in the type 2 diabetes group versus 5.6 % in the matched control group (p < 0.0001) and at 12 years, it was

**Table 1**
Baseline features of myocardial infarction (MI) patients with type 2 diabetes and without diabetes.

| | Original cohort | | | | Propensity-score matched cohort | | | |
|---|---|---|---|---|---|---|---|---|
| Variable | Type 2 diabetes n = 10,440 | No diabetes n = 65,315 | *P*-value | \|SMD\| | Type 2 diabetes n = 10,300 | No diabetes n = 10,300 | *P*-value | \|SMD\| |
| Age, years (SD) | 72.5 (10.1) | 68.7 (12.8) | <0.0001 | 0.308 | 72.5 (10.1) | 72.6 (10.4) | 0.214 | 0.012 |
| Men | 61.6 % | 65.2 % | <0.0001 | 0.076 | 61.3 % | 60.9 % | 0.486 | 0.009 |
| Comorbidities | | | | | | | | |
| Hypertension | 75.6 % | 43.9 % | <0.0001 | 0.684 | 75.3 % | 75.5 % | 0.424 | 0.006 |
| Heart failure | 30.6 % | 16.1 % | <0.0001 | 0.347 | 29.8 % | 30.2 % | 0.523 | 0.007 |
| Atrial fibrillation | 20.0 % | 13.1 % | <0.0001 | 0.188 | 19.7 % | 20.0 % | 0.592 | 0.007 |
| Previous MI | 18.4 % | 12.9 % | <0.0001 | 0.153 | 18.1 % | 17.7 % | 0.450 | 0.010 |
| Cerebrovascular disease | 16.4 % | 9.6 % | <0.0001 | 0.203 | 16.1 % | 15.9 % | 0.641 | 0.006 |
| Chronic pulmonary disease | 15.3 % | 12.5 % | <0.0001 | 0.080 | 15.2 % | 14.6 % | 0.132 | 0.019 |
| Malignancy | 14.2 % | 11.6 % | <0.0001 | 0.076 | 14.2 % | 14.4 % | 0.675 | 0.006 |
| Depression | 12.3 % | 10.1 % | <0.0001 | 0.064 | 10.8 % | 10.8 % | 0.944 | 0.001 |
| Peripheral vascular disease | 11.9 % | 5.4 % | <0.0001 | 0.233 | 11.3 % | 11.0 % | 0.351 | 0.012 |
| Previous CABG | 6.5 % | 2.7 % | <0.0001 | 0.183 | 5.9 % | 5.8 % | 0.656 | 0.006 |
| Valvular disease | 6.4 % | 4.8 % | <0.0001 | 0.069 | 6.4 % | 6.4 % | 0.908 | 0.002 |
| Rheumatic disease | 6.1 % | 6.2 % | 0.741 | 0.003 | 6.1 % | 6.0 % | 0.631 | 0.007 |
| Dementia | 5.5 % | 4.2 % | <0.0001 | 0.062 | 5.5 % | 5.4 % | 0.703 | 0.005 |
| Psychotic disorder | 4.4 % | 2.9 % | <0.0001 | 0.080 | 4.2 % | 3.9 % | 0.194 | 0.018 |
| Renal failure | 3.6 % | 1.9 % | <0.0001 | 0.106 | 3.5 % | 3.4 % | 0.463 | 0.010 |
| Alcohol abuse | 2.3 % | 3.1 % | <0.0001 | 0.046 | 2.3 % | 2.3 % | 0.963 | 0.001 |
| Liver disease | 1.4 % | 0.9 % | <0.0001 | 0.050 | 1.3 % | 1.3 % | 0.803 | 0.003 |
| Paralysis | 0.4 % | 0.4 % | 0.344 | 0.010 | 0.4 % | 0.4 % | 0.491 | 0.009 |
| Coagulopathy | 0.4 % | 0.4 % | 0.279 | 0.011 | 0.4 % | 0.5 % | 0.835 | 0.003 |
| ST-elevation MI | 26.3 % | 39.8 % | <0.0001 | 0.291 | 26.6 % | 26.5 % | 0.862 | 0.862 |
| Revascularization | 55.9 % | 61.5 % | <0.0001 | 0.113 | 56.1 % | 56.0 % | 0.788 | 0.788 |
| PCI | 47.2 % | 55.2 % | <0.0001 | 0.160 | 47.4 % | 47.2 % | 0.698 | 0.005 |
| CABG | 9.3 % | 7.0 % | <0.0001 | 0.082 | 9.2 % | 9.2 % | 0.958 | 0.001 |
| Post-MI medication | | | | | | | | |
| Beta-blocker | 85.3 % | 84.4 % | 0.015 | 0.026 | 85.4 % | 85.5 % | 0.733 | 0.004 |
| Statin | 80.6 % | 83.6 % | <0.0001 | 0.079 | 80.7 % | 81.1 % | 0.491 | 0.009 |
| RAAS inhibitor | 75.6 % | 68.1 % | <0.0001 | 0.167 | 75.4 % | 75.8 % | 0.551 | 0.007 |
| $P2Y_{12}$ inhibitor | 63.8 % | 69.2 % | <0.0001 | 0.116 | 63.8 % | 63.4 % | 0.444 | 0.010 |
| Oral anticoagulant | 19.3 % | 13.0 % | <0.0001 | 0.174 | 19.0 % | 18.6 % | 0.459 | 0.010 |
| Treatment in University hospital | 48.6 % | 50.7 % | <0.0001 | 0.043 | 48.6 % | 48.5 % | 0.877 | 0.002 |
| Year of MI | | | <0.0001 | 0.174 | | | 0.437 | 0.023 |

CABG = coronary artery bypass surgery. PCI = percuteneus coronary intervention. SD = standard deviation. SMD = standardized mean difference. RAAS = renin-angiotensin-aldosterone system.

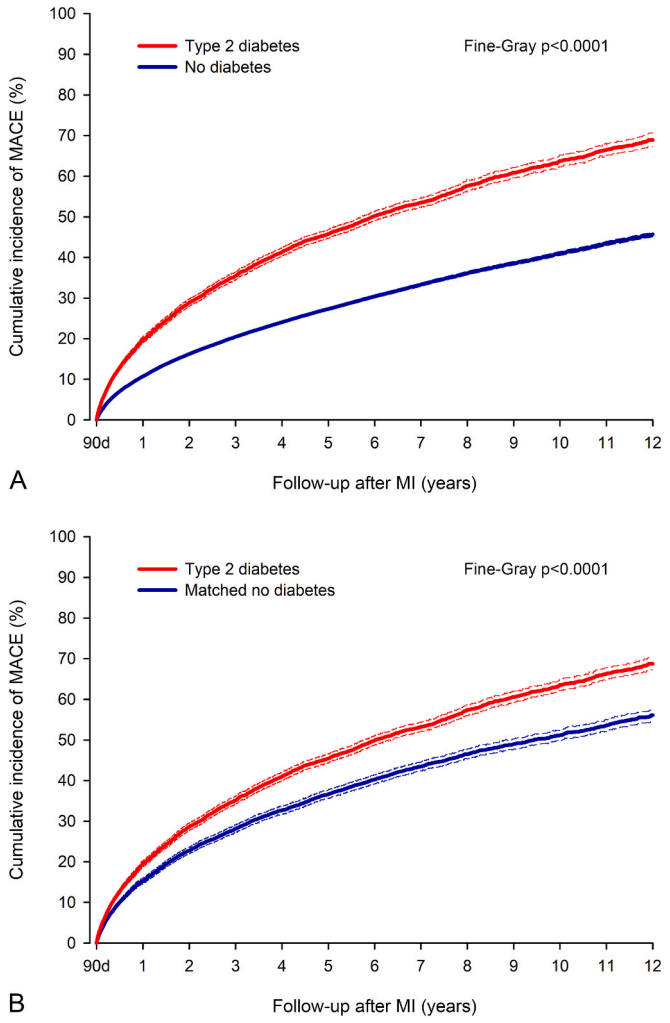


**Fig. 1.** Cumulative incidence of major adverse cardiovascular event (MACE) after myocardial infarction (MI) in patients with type 2 diabetes and in control patients without any type of diabetes in (A) original and (B) matched cohorts. Dashed lines represent 95% confidence interval.

26.4 % versus 19.9 %, respectively (sHR 1.49; CI 1.41–1.57; $p < 0.0001$). Correspondingly, the cumulative incidence of ischemic stroke was 2.6 % in both groups at one year ($p = 0.573$) and 14.0 % versus 12.2 % at 12 years (sHR 1.14; CI 1.05–1.23; $p = 0.001$). The cumulative incidence of heart failure hospitalization was 7.3 % in type 2 diabetes patients versus 5.2 % in controls at one year ($p < 0.0001$) and 29.7 % versus 20.9 % during the 12-year follow-up (sHR 1.48; CI 1.40–1.57; $p < 0.0001$). The cumulative incidence of cardiovascular death after MI was 7.5 % in type 2 diabetes patients versus 6.4 % in matched controls at one year ($p < 0.0001$) and 48.8 % versus 38.7 %, respectively, at 12 years (sHR 1.30; CI 1.24–1.36; $p < 0.0001$). The cumulative incidence of cardiovascular death after MI was 7.5 % in type 2 diabetes patients versus 6.4 % in patients without diabetes at one-year follow-up ($p < 0.0001$) and 48.8 % versus 38.7 %, respectively, during the complete 12-year follow-up (sHR 1.30; CI 1.24–1.36; $p < 0.0001$). Results of multivariable analyses in the total study cohort were comparable to results of the matched cohort (Table 2).

### 3.3. Duration of diabetes

The median duration of type 2 diabetes before the index MI was 7.2 years (IQR 3.4–12.5, range 0–45.1). Longer duration of diabetes was associated with MACE (sHR 1.02 per year; 95 % CI 1.01–1.03; $p < 0.0001$), recurrent MI ($p = 0.0002$), heart failure hospitalization ($p < 0.0001$), and cardiovascular death ($p < 0.0001$), but not with ischemic stroke ($p = 0.348$) in multivariable analyses. Results on categorized diabetes duration (<5 years in 28.4 %, 5–10 years in 36.0 %, and ≥ 10 years in 35.6 % of patients) are presented in Table 3.

## 4. Discussion

In this nationwide registry study, we demonstrated that even throughout the 2000s and 2010s, type 2 diabetes is independently associated with poorer long-term cardiovascular outcomes following an MI, including increased rates of cardiovascular death, recurrent MI, ischemic stroke, and heart failure. Compared to earlier studies with similar results [5,8], major advances in both treatment of MI and diabetes have occurred, including increased rates of revascularization, optimized secondary prevention strategies, and intensified glycemic control [23,24]. Numerous previous studies have confirmed that short- and long-term mortality rates following and MI are increased among patients with diabetes [4,5,9,25,26], but contemporary studies on long-term cardiovascular outcomes are more limited.

Our study design and methodology has several strengths. The nationwide MI cohort is representative of the entire Finnish population, and the diagnoses for fatal and non-fatal CHD events, heart failure, and stroke in the CRHC have been validated with PPVs of 86–90 % [27–29]. The MI diagnoses in the CRHC have been between 1998 and 2002 compared to a clinical MI registry (FINMONICA/FINAMI), and the sensitivity was 78 % in women and 81 % in men [28]. Potential confounding by numerous comorbidities and other baseline features was addressed with both propensity score matching and multivariable-adjusted analyses, with comparable results. The study has inherent limitations typical of health registry research, including the possibility of incomplete data on comorbidities, coding errors, and the absence of many important clinical parameters. We cannot exclude unmeasured confounding by factors such as smoking, lipid levels, body mass index, the stage or progression of chronic kidney disease, and the extent of coronary artery disease. The analysis of E-value [22], however, showed that unmeasured confounding factor would need to have an association of at least 2.06 on the risk ratio scale with both type 2 diabetes and MACE to be able to fully explain our main finding.

Our findings are in line with previous investigations showing that diabetes is a strong risk factor for MI recurrence and post-MI heart failure [6,7,30]. In a SWEDEHEART registry study, MI patients with diabetes were characterized by a 1.5–1.6-fold risk of heart failure compared to patients without diabetes during a mean follow-up of 3.4 years [7]. Diabetes is a risk factor for CVD recurrence also among populations with a broader spectrum of ASCVD: A study within the international REACH registry showed that patients with diabetes have higher rates of cardiovascular events among those with ASCVD, among those at high risk for ASCVD, and also among those with prior ischemic events [31]. Diabetes was also independently associated with cardiovascular events, including heart failure, in a multinational prospective cohort study of patients with chronic coronary syndromes [32].

Additional explanations for the observed worse MI prognosis among patients with diabetes are numerous. Patients with diabetes more often have multivessel disease, multiple coronary lesions, and more vulnerable atherosclerotic plaques compared to patients without diabetes [33]. These changes may be explained by differences in plaque histopathologic features: diabetes is associated with larger necrotic core size, greater inflammatory infiltrates, and enhanced calcification [34]. Changes in the myocardium and coronary microvasculature may also play a role [35]. ACS patients with diabetes have more often non-specific symptoms and longer delays in diagnosis and treatment compared to patients without diabetes [36,37]. They may also be at increased risk of developing cardiogenic shock and sudden cardiac death [38,39]. In addition, MI patients with diabetes are less likely to attain lifestyle-related cardiac rehabilitation targets, including smoking cessation and exercise training attendance, compared to MI patients

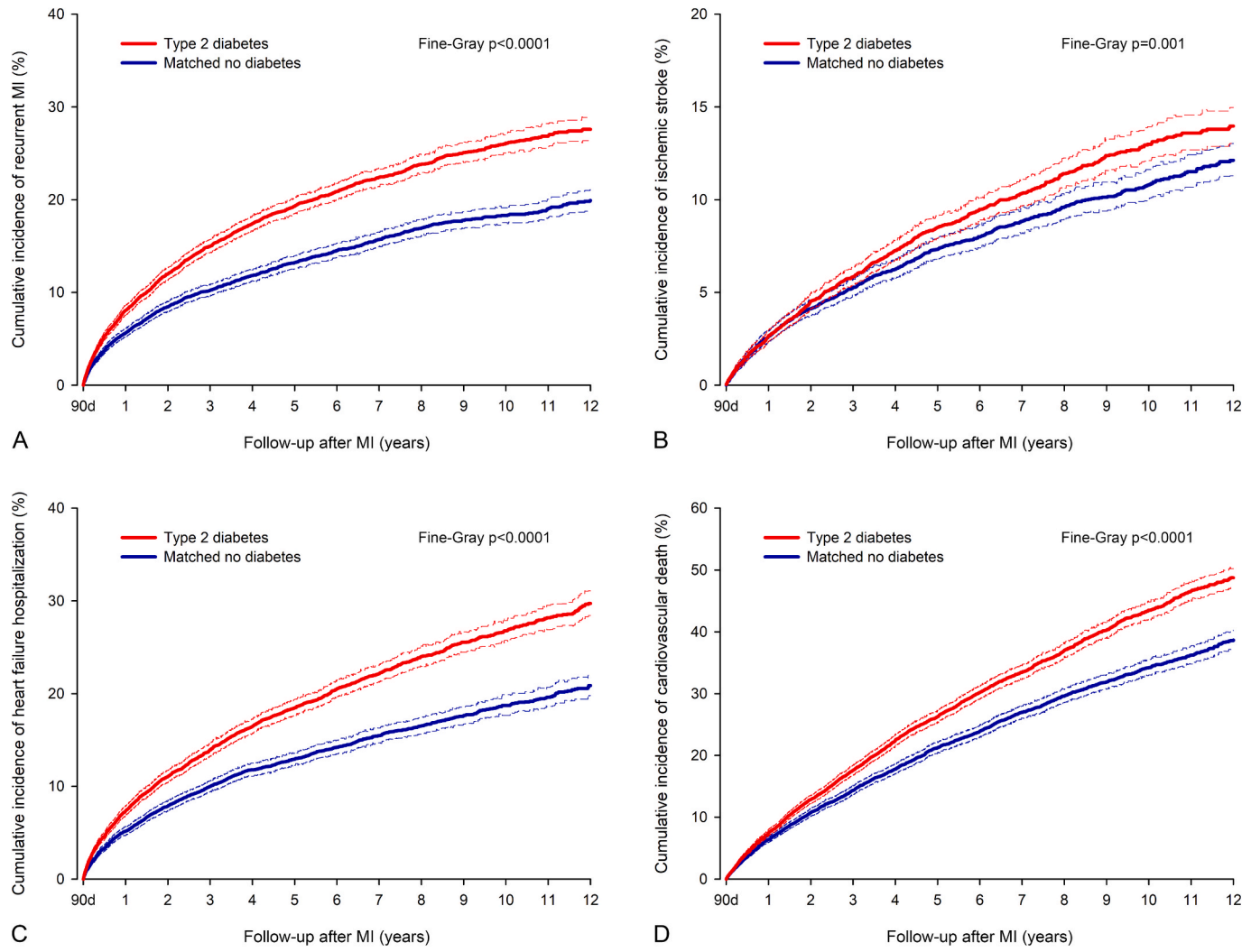


**Fig. 2.** Cumulative incidences of (A) recurrent myocardial infarction (MI), (B) ischemic stroke, (C) hospitalization for heart failure, and (D) cardiovascular death after index myocardial infarction in patients with type 2 diabetes and in matched controls without any type of diabetes. Dashed lines represent 95% confidence interval. Please note the differences in y-axis.

**Table 2**
Cumulative incidences of outcomes in the total study cohort during the 12-year follow-up. Results of unadjusted and multivariable adjusted Fine-Gray models (see methods for details). sHR = subdistribution hazard ratio.

| Outcome | Cumulative incidence | | Univariable | | Multivariable | |
|---|---|---|---|---|---|---|
| | Type 2 diabetes | No diabetes | sHR (95 %CI) | *P*-value | sHR (95 %CI) | *P*-value |
| Major adverse cardiovascular event | 68.9 % | 45.7 % | 1.90 (1.84–1.96) | <0.0001 | 1.37 (1.33–1.42) | <0.0001 |
| Recurrent myocardial infarction* | 27.7 % | 17.0 % | 1.84 (1.75–1.93) | <0.0001 | 1.49 (1.41–1.56) | <0.0001 |
| Ischemic stroke* | 14.0 % | 10.1 % | 1.50 (1.39–1.61) | <0.0001 | 1.18 (1.09–1.27) | <0.0001 |
| Heart failure* | 29.9 % | 14.8 % | 2.24 (2.13–2.35) | <0.0001 | 1.53 (1.45–1.62) | <0.0001 |
| Cardiovascular death | 48.8 % | 38.7 % | 1.89 (1.82–1.97) | <0.0001 | 1.35 (1.29–1.41) | <0.0001 |

* Hospitalization.

without diabetes [40].

Our findings underline the importance of meticulous secondary prevention, both pharmacological and non-pharmacological, among MI patients with type 2 diabetes. This includes lifestyle modifications, optimal diabetes management targeting HbA1c < 53 mmol/mol, high-intensity statins and other lipid-lowering drugs, blood pressure control targeting generally < 130/80 mmHg, and antithrombotic therapy according to recent recommendations [10,33]. Specifically in patients with type 2 diabetes and atherosclerotic CVD, the use of SGLT2 inhibitors and GLP-1 receptor agonists should be prioritized over other antidiabetic medications and used independent of glucose control, since they reduce the risk of future CVD events [33,41,42]. In normotensive patients with diabetes and MI, ACE inhibitors or angiotensin receptor blockers are also recommended to reduce the risk of cardiovascular events, especially in patients with HF or chronic kidney disease [33].

Patients with diabetes are likely not a homogeneous group with regard to MI outcomes [43], but risks of recurrent cardiovascular events may vary by levels of modifiable risk factors, including glycated hemoglobin [44]. In our study, the risk of MACE was more pronounced among patients with longer duration of diabetes. Our previous findings

**Table 3**
Association of diabetes duration with 12-year cardiovascular outcomes after myocardial infarction (MI) in baseline features-adjusted competing risk analyses among 10,440 patients with type 2 diabetes.

| Outcome | Duration of type 2 diabetes before index MI | | | | | |
|---|---|---|---|---|---|---|
| | <5 years | 5–10 years | | >10 years | | |
| | | adj.sHR (95 %CI) | *P*-value | adj.sHR (95 %CI) | *P*-value | Type 3 test *P*-value |
| MACE | Reference | 1.10 (1.02–1.19) | 0.010 | 1.28 (1.20–1.38) | <0.0001 | <0.0001 |
| Recurrent MI | Reference | 1.12 (1.01–1.26) | 0.048 | 1.27 (1.14–1.42) | <0.0001 | <0.0001 |
| Ischemic stroke | Reference | 1.07 (0.91–1.26) | 0.411 | 1.07 (0.91–1.25) | 0.416 | 0.638 |
| Hert failure hospitalization | Reference | 1.14 (1.02–1.28) | 0.026 | 1.21 (1.09–1.35) | 0.001 | 0.002 |
| Cardiovascular death | Reference | 1.08 (0.98–1.19) | 0.116 | 1.31 (1.20–1.43) | <0.0001 | <0.0001 |

MI, myocardial infarction; sHR, subdistribution hazard ratio; MACE, major adverse cardiovascular event.

and those of others indicate that diabetes duration is associated with increased mortality rates after MI [4,45], and with increased MACE rates after PCI [46]. Recognizing diabetes duration as a prognostic factor for MI may allow individualized risk stratification, which may in turn be translated into, for example, more frequent follow-ups among patients with long-standing diabetes and more individualized patient counseling.

In conclusion, even throughout the 2000s and 2010s, patients with type 2 diabetes suffering from an MI are at increased risk for recurrent MI, ischemic stroke, heart failure, and cardiovascular death compared to MI patients without diabetes. This persistent gap in MI prognosis among patients with diabetes needs to be addressed by both lifestyle modifications and pharmacotherapy, including active use of cardioprotective antidiabetic medications. Longer duration of diabetes was identified as an additional prognostic risk factor.

## CRediT authorship contribution statement

**Anne M Kerola:** Writing – original draft, Investigation, Conceptualization. **Markus Juonala:** Writing – review & editing, Investigation, Conceptualization. **Ville Kytö:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation.

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## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: AK: speaker fees from Abbvie, Boehringer-Ingelheim, Novartis, and Sanofi, advisory board fees from Boehringer-Ingelheim and Pfizer, and congress sponsorship from Abbvie, Johnson & Johnson, and UCB Pharma. MJ: speaker fees from AstraZeneca, Amgen, Boehringer-Ingelheim, Novartis, and NovoNordisk. VK: None

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## Appendix A. Supplementary data

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