



# A systematic review and meta-regression of temporal trends in the excess mortality associated with diabetes mellitus after myocardial infarction



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## ABSTRACT

**Background/objectives:** It is not well known whether the gap in outcomes after myocardial infarction (MI) between patients with and without diabetes mellitus (DM) has changed over time. We performed a systematic review and meta-regression of temporal trends in the excess mortality associated with DM after MI.

**Methods:** We searched the PubMed database for studies reporting mortality data according to diabetic status in patients hospitalized for MI or acute coronary syndromes (ACS). We included 139 studies/cohorts for analysis (432,066 diabetic patients and 1,182,108 nondiabetic patients).

**Results:** When compared to their non-diabetic counterparts, patients with DM had an odds ratio (OR) [95% CI] of 1.66 [1.59–1.74] ( $P < 0.0001$ ) for early mortality, and of 1.86 [1.75–1.97] ( $P < 0.0001$ ) for 6–12 months mortality. When all data from the 116 studies reporting early mortality were pooled, there was no significant relationship between calendar year and Log (OR). Likewise, when considering the 61 studies reporting 6–12 months mortality, there was no significant relationship between calendar year and Log (OR). Similar to the overall pooled analysis, no significant relationship between inclusion year and Log (OR) for mortality in diabetic patients was observed in sensitivity analyses performed in studies with ST-elevation MI as inclusion criteria, in randomized trials, in studies including >2000 patients, and in studies with DM prevalence >20%.

**Conclusions:** We found no evidence for temporal changes in the incremental mortality risk associated with DM in the setting of MI. The improvements in management of MI patients during the last decades have not been associated with a reduction of the gap between diabetic and non-diabetic patients.

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## 1. Introduction

Besides being a major risk factor for cardiovascular disease development, diabetes mellitus (DM) is also a strong prognostic indicator in patients with established coronary artery disease [1–5]. This fact is especially important because the prevalence of DM is projected to increase substantially [6].

In particular, there have been numerous studies reporting incremental rates of in-hospital and post-discharge mortality after myocardial infarction (MI) in patients with DM. In recent years however, the management of patients with MI has improved significantly and one important question is to know to what extent diabetic patients may have benefited from these advances when compared to non-diabetic patients. Although this question has previously been addressed, the results have not been concordant in all studies [7–13]. In the present paper, we present

a systematic review and meta-regression of temporal trends in the excess mortality associated with DM after MI. Our aim was to address whether the gap in outcomes after MI between patients with and without DM has changed over time.

## 2. Methods

### 2.1. Study objective

The objective of this systematic review and meta-regression was to analyze temporal trends in the effect of diabetes mellitus on mortality in patients hospitalized for MI or acute coronary syndrome (ACS).

### 2.2. Search strategy

The PubMed database was searched for eligible studies with no restriction of time in July 2015 by using the terms « ((myocardial infarction OR acute coronary syndrome) AND diabetes) AND mortality » and the filters « Humans » and « English ».

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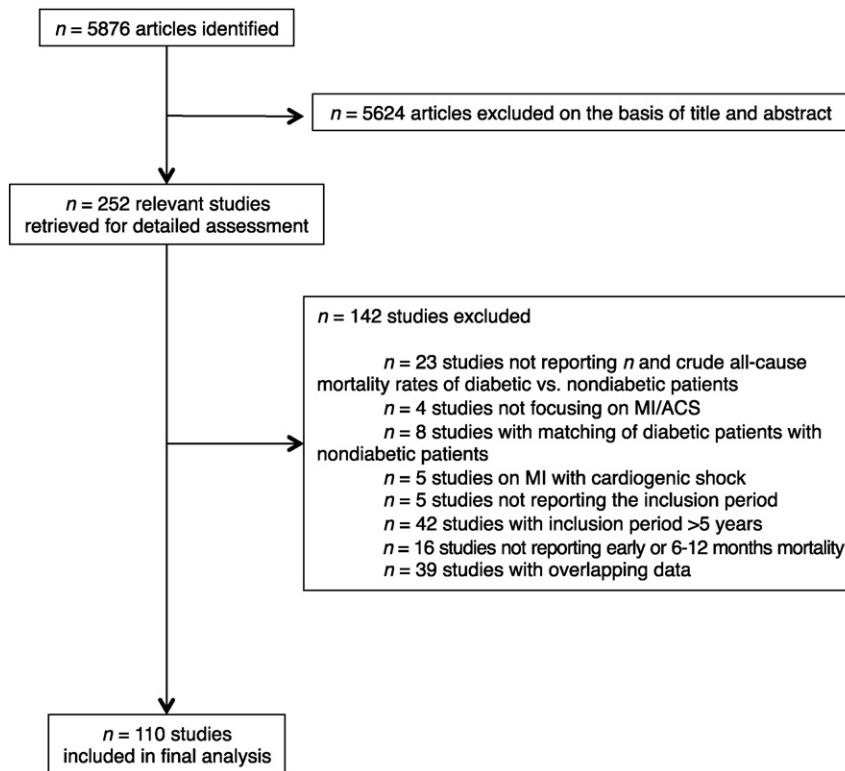


Fig. 1. Flow chart of the study selection process.

**Table 1**

Study characteristics for the 139 studies/cohorts included in the meta-analysis.

Study/cohort	Median inclusion year	No. patients	Inclusion criteria	Analysis restricted to T2DM	Study population	Follow-up
Abbud, 1995 [15]	1986	42,595	MI	No	Multicentric cohort, USA	In-hosp
Abid, 2005 [16]	2003	448	STEMI	No	Monocentric cohort, Pakistan	In-hosp
Aguilar, 2004 [17]	2000	14,699	MI	No	Valsartan in Acute Myocardial Infarction (VALIANT) trial	1 yr
Ainla, 2005 [18]	2001	779	MI	No	Monocentric cohort, Estonia	6 mo
Alegria, 2007 [19]	1994	1164	STEMI	No	Multicentric Collaborative Organisation of RheothRx Evaluation (CORE) trial	6 mo
Alfaleh, 2014 [20]	2009	6362	ACS	No	Gulf Registry of Acute Coronary Events-2 (Gulf RACE-2)	In-hosp/1 yr
Antoniucci, 2004 [21]	2000	1061	STEMI	No	Monocentric cohort, Italy	6 mo
Bakhai, 2005 [22]	1998	1046	Non-ST elevation ACS	No	Multicentric Prospective Registry of Acute Ischaemic Syndromes in the United Kingdom (PRAIS-UK)	6 mo
Barbash, 1993 [23]	1989	8055	STEMI	No	International Tissue Plasminogen Activator/Streptokinase Mortality trial	In-hosp/6 mo
Behar, 1997 [24]	1982	5255	MI	No	Multicentric cohort, Israel	In-hosp/1 yr
Bhadriraju, 2006 [25]	1998	9020	ACS	No	Orbofiban in Patients with Unstable Coronary Syndromes-Thrombolysis In Myocardial Infarction (OPUS-TIMI 16) trial	10 mo
Bolk, 2001 [26]	1996	336	MI	No	Monocentric cohort, The Netherlands	1 yr
Bolognese, 2003 [27]	1996	720	STEMI	No	Monocentric cohort, Italy	1 mo/6 mo
Bonnefoy, 2005 [28]	1999	834	STEMI	No	CAPTIM trial, France	1 mo
Casella, 2005 [29]	2001	1959	MI	No	Multicentric cohort, Italy	In-hosp
Chyun, 2002a [30]	1992	2050	MI	No	Registry of Medicare beneficiaries, USA	1 yr
Chyun, 2002b [31]	1992	2050	MI	No	Registry of Medicare beneficiaries, USA	1 mo
Cubbon, 2007/Cohort 1995 [7]	1995	1762	MI	No	Multicentric cohort, UK	1 mo
Cubbon, 2007/Cohort 2003 [7]	2003	1642	MI	No	Multicentric cohort, UK	1 mo
David, 2014 [32]	2011	740	STEMI	No	Monocentric cohort, Brazil	1 mo
de Gevigney, 2002 [33]	1994	2297	MI	No	Multicentric cohort, France	In-hosp/1 yr
Demir, 2003 [34]	1999	774	STEMI	No	Monocentric cohort, Turkey	In-hosp
Donahue, 1993/Cohort 1975 [2]	1975	780	MI	No	Multicentric cohort, USA	In-hosp
Donahue, 1993/Cohort 1978 [2]	1978	845	MI	No	Multicentric cohort, USA	In-hosp
Donahue, 1993/Cohort 1981 [2]	1981	999	MI	No	Multicentric cohort, USA	In-hosp
Donahue, 1993/Cohort 1984 [2]	1984	719	MI	No	Multicentric cohort, USA	In-hosp
Donahue, 1993/Cohort 1986 [2]	1986	766	MI	No	Multicentric cohort, USA	In-hosp

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