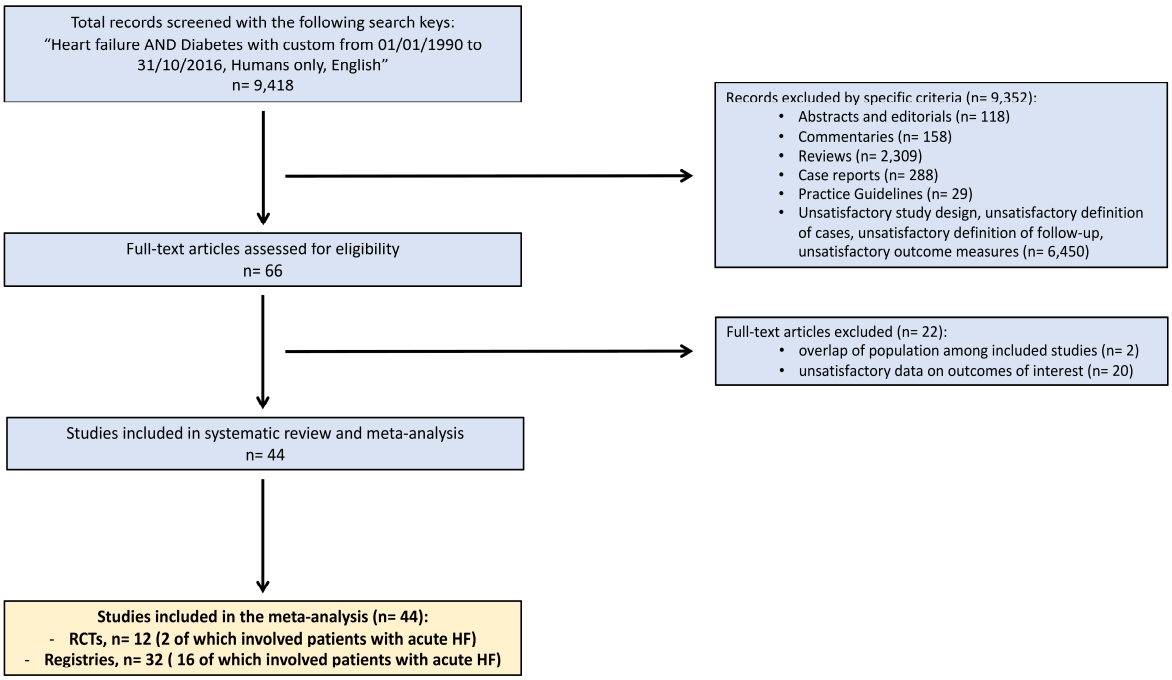
SUPPLEMENTARY DATA

Manuscript Title: Prognostic impact of diabetes mellitus on long-term survival outcomes in patients with heart failure. A meta-analysis.

Dauriz M *et al*.

Supplementary Figure S1. Study flow-chart: the MOOSE flow diagram.



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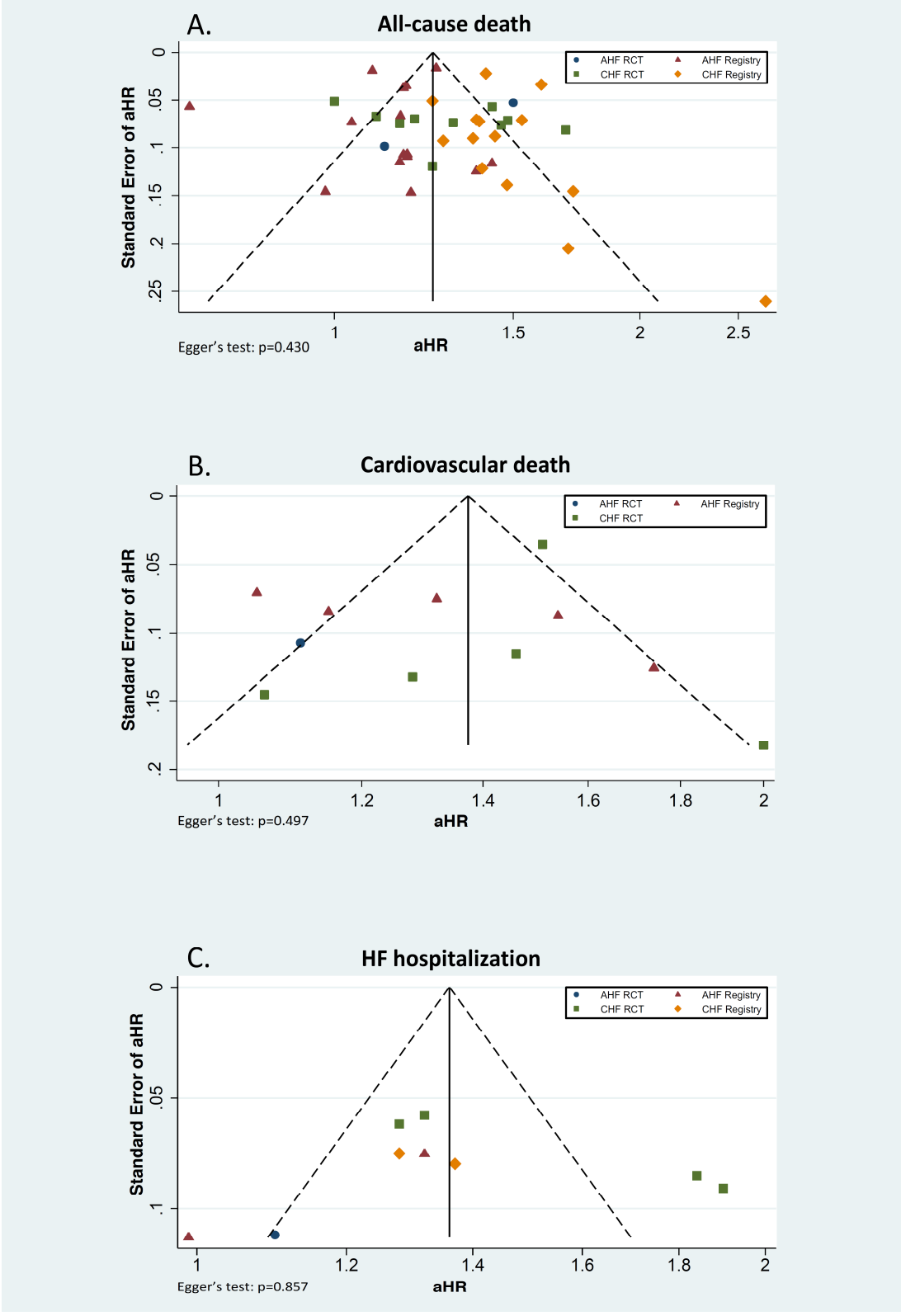
Supplementary Figure S2. Funnel plot of standard error by Log odds ratio for all-cause death (panel A), cardiovascular death (panel B) and hospitalization (panel C). Egger's regression test: *P*-value=0.430, 0.497 and 0.857, respectively.



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Supplementary Table S1. Main characteristics of randomized clinical trials and registries assessing the impact of diabetes mellitus on the risk of all-cause death, cardiovascular death, hospitalization and the combined endpoint of all-cause death or hospitalization in patients with acute HF.

Author [Ref.], Year	Study Characteristics	Follow-up length	Diagnostic criteria for HF	Diagnosis of DM; prevalence of DM	Mean LVEF (%); proportion of patients with LVEF>35%	Total number of all-cause deaths	Covariate Adjustment	Main findings by outcomes (unadjusted or adjusted HRs [±95% CI])	Degree of adjustment§
Randomized Clinical Trials (RCTs)									
Gustafsson I *et al.*[1], 2004	RCT: The DIAMOND Study, n=5,491 (59.8% men) Danish patients consecutively hospitalized with new or worsening HF. Mean age 73 years	From 5 to 8 years	Clinical; ecochardiographic	Medical records; the prevalence of DM was 16.4%	NA	3,955	Age, sex, smoking status, IHD, hypertension, AF, NYHA class, wall motion index	DM was an independent risk factor for all-cause death (aHR 1.50 [1.30-1.60])	***
Deedwania PC *et al.*[2], 2011	RCT: The EPHESUS Trial, n=2,238 (68.8% men) multinational patients with acute HF. Mean age 66 years	1.3 years (median)	Clinical; ecochardiographic	Physician diagnosis; the prevalence of DM was 50.0%	Mean LVEF 33%	403	Age, sex, race, smoking status, Q-wave index, time to randomization, revascularization, IHD, history of HF, HF hospitalization, hypertension, medications, Killip-class, BMI, SBP, DBP, heart rate, electrolytes, LVEF, creatinine, urea, glucose, uric acid, total bilirubin, alkaline phosphatase, LDH, liver enzymes, albumin, total protein, total cholesterol, triglycerides, hemoglobin, WBC, platelets, red blood cells, hematocrit	DM was an independent risk factor for CV death (aHR 1.11 [0.90-1.37]) and CV hospitalization (aHR 1.11 [0.90-1.37]), but not for all-cause death (aHR 1.12 [0.93-1.37])	***
Observational Registries									
Varela-Roman A *et al.*[3], 2005	Registry: n= 1,659 (59.9% men) Spanish patients hospitalized for acute HF between 1991 and 2002 in the Cardiology Department of a tertiary hospital. Mean age 69 years	3.13 years	Clinical; radiologic (Framingham criteria)	Use of insulin and/oral glucose-lowering agents, or fasting glucose levels >7mmol/L, or random glucose levels >11.1 mmol/L during hospitalization; the prevalence of DM was 26.6%	Patients with LVEF>35% were 39.7%	846	Age, sex, hypertension, hyperlipidaemia, NYHA class, LVEF, AF, alveolar oedema, jugular vein distension	DM was an independent risk factor for all-cause death (aHR 1.43 [1.14-1.80])	**

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Owan TE *et al.*[4], 2006	Registry: n= 6,076 (55.4% men) American consecutive patients hospitalized with decompensated heart failure at Mayo Clinic Hospitals. Mean age 72.9 years	15 years	Clinical; radiologic (Framingham criteria)	Medical records; the prevalence of DM was 33.7%	Patients with LVEF>35% were 47.1%	3,691	Age, sex, creatinine, hemoglobin, hypertension, IHD, valve disease, year of admission, HFpEF	DM was an independent risk factor for all-cause death (aHR 1.09 [1.05-1.13])	***
Varadarajan P *et al.*[5], 2006	Registry: n= 2,246 (52% men) American patients with a discharge diagnosis of acute HF in a large tertiary care hospital from 1990 to 1999. Mean age 69 years	5 years (median)	Clinical; radiologic (Framingham criteria)	Fasting glucose levels >7 mmol/L or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 30%	Patients with LVEF>35% were 48%	1,613	Age, sex, hemoglobin, LVEF, hypertension, IHD, CKD, medications	DM was not an independent risk factor for all-cause death (aHR 1.17 [0.95-1.44])	***
Ouzounian M *et al.*[6], 2007	Registry: n= 7,816 (48% men) Canadian patients discharged with a primary diagnosis of acute HF. Mean age 76 years	2 years	Clinical	Medical records; the prevalence of DM was 44.9%	Median LVEF 40%; patients with LVEF>35% were 88.2%	2,841	Age, sex, smoking status, hyperlipidemia, peripheral vascular disease, creatinine, medications	DM was not an independent risk factor for all-cause death (aHR 1.16 [0.93-1.46])	***
MacDonald MR *et al.*[7], 2008	Registry: n= 116,556 (47.3% men) Scottish patients admitted to the hospital for the first time with HF between 1986 and 2003. Mean age 73 years	5 years	ICD codes	Medical records; the prevalence of DM was 13%	NA	34,369	Age, main comorbidities, year of admission, deprivation index	DM was an independent risk factor for all-cause death (aHR 1.26 [1.22-1.30]) and was associated with a lower in-hospital death (aHR 0.84 [0.78-0.89])	**
Barsheshet A *et al.*[8], 2010	Registry: HFSIS n= 2,336 (55.2% men) Israeli patients with acute HF. Mean age 75 years	Up to 4 years	Clinical; ecochardiographic	Medical records, admission fasting glucose levels ≥11.1 mmol/L, or use of insulin and/or oral glucose-lowering agents (on admission or discharge); the prevalence of DM was 51.6%	NA	1,403	Age, sex, IHD, AF, NYHA class, eGFR, SBP, Na, anemia, admission to an intensive care unit, etiology of HF, history of stroke, COPD, malignancy, hepatic cirrhosis, medications	DM was not an independent risk factor for in-hospital death (aHR 1.37 [0.71-2.71]) and for all-cause death (aHR 1.19 [0.90-1.60])	***
Harjola VP *et al.*[9], 2010	Registry: EHFS-II, n= 2,981 (61.3% men) European patients with acute HF. Mean age 71.7 years	1.02 year (median)	Clinical	Medical records; the prevalence of DM was 33.1%	Mean LVEF 34.6%	542	Age, living in special accommodation, acute decompensated chronic heart failure, history of IHD, valvular heart disease, stroke/TIA, hypertension, AF/flutter, QRS interval, creatinine, SBP, peripheral pitting oedema, anaemia, Na, length of hospitalization	DM was an independent risk factor for all-cause death (aHR 1.38 [1.08-1.76])	***
Shah R *et al.*[10], 2014	Registry: The GREAT Registry, n= 6,142 (55.8% men)	1 year	Clinical; ecochardiographic	Medical records, or use of insulin and/or oral glucose-lowering agents;	Mean LVEF 39.6%	1,269	Age, sex, BMI, eGFR, SBP, DBP, heart rate, Na, history of HF, IHD, AF	DM was not an independent risk factor for all-cause death (aHR 1.18	**

	multinational patients with acute decompensated HF. Mean age 73.4 years			the prevalence of DM was 38.3%				[0.96-1.46])	
AlHabib K.F. *et al.*[11], 2014	Registry: The HEARTS, n=2,610 (65.8% men) Arabs patients with acute decompensated HF admitted to 18 hospitals. Median age 61.4 years	3 years	Clinical; ecochardiographic; NT-proBNP	Medical records; the prevalence of DM was 64.1%	Patients with LVEF>35% were 27.1%	634	None	DM was not an independent risk factor for all-cause death (uHR 1.04 [0.90-1.20])	
Teng TH *et al.*[12], 2015	Registry: n= 16,366 (58.3% men) Australian non-Aboriginal patients hospitalized for acute HF. Mean age 71 years	1 year	ICD codes; clinical; ecochardiographic	Medical records; the prevalence of DM was 30.7%	NA	3,051	Age, sex, Charlson comorbidity index, hypertension, AF, rheumatic/valvular heart disease, CKD, IHD, cerebrovascular disease, history of PCI/CABG	DM was associated with a lower all-cause death (aHR 0.72 [0.64-0.80])	**
Helfand BK *et al.*[13], 2015	Registry: n= 9,748 (43.9% men) American patients hospitalized for acute decompensated HF. Mean age 76 years	Up to 10 years	ICD-9 codes; clinical; radiologic (Framingham criteria)	Medical records, or use of insulin and/or oral glucose-lowering agents at admission; the prevalence of DM was 39%	NA	4083	Age, sex, presenting symptoms, SBP, heart rate, eGFR	DM was an independent risk factor for all-cause death (aHR 1.17 [1.09-1.26]) but not for in-hospital death (aHR 1.03 [0.86-1.24])	**
Khafaji HA *et al.*[14], 2015	Registry: The Gulf CARE Registry, n= 5,005 (62.5% men) Arabian patients with acute HF. Mean age 60 years	1 year	Clinical; ecochardiographic	Medical records, or use of insulin and/or oral glucose-lowering agents, or fasting glucose levels >7 mmol/L, or HbA1c ≥6.5%; the prevalence of DM was 49.8%	Mean LVEF 37%; patients with LVEF>35% were 51.2%	313	Age, sex, CKD, COPD, asthma, STEMI, LVEF, valvular heart disease, stroke, peripheral vascular disease	DM was not an independent risk factor for in-hospital death (aHR 1.06 [0.79-1.41]) and for all-cause death (aHR 1.18 [0.95-1.46])	**
Spinar J *et al.*[15], 2016	Registry: The AHEAD Network Registry, n= 5,846 (56.6% men) Czech consecutive patients hospitalized for acute HF. Mean age 72 years	2.75 year (median)	Clinical; ecochardiographic	Medical records; the prevalence of DM was 44%	Mean LVEF 37%	1,888	Age, sex, AF, hypertension, COPD, IHD, creatinine, Na, anemia	DM was an independent risk factor for all-cause death (aHR 1.18 [1.09-1.26])	**
Targher G *et al.*[16], 2016	Registry: IN-HF Outcome Registry, n= 1,776 (60.2% men) Italian patients hospitalized with acute HF (worsening or de novo). Mean age 72.2 years	1 year	Clinical; ecochardiographic	Medical records, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 42.4%	Mean LVEF 37%	428	Age, sex, SBP, eGFR, LVEF, HF etiology, HF worsening/de novo presentation	DM was an independent risk factor for in-hospital death (aHR 1.86 [1.01-3.42]), but not for all-cause death (aHR 0.98 [0.74-1.31])	***
Targher G *et al.*[17], 2017	Registry: The ESC-HFA HF Long-Term Registry, n= 6,926 (62.9% men)	1 year	Clinical; ecochardiographic; NT-proBNP	Medical records, or use of insulin and/or oral glucose-lowering agent, or fasting glucose levels	Mean LVEF 39.2%; patients with	1,781	Age, sex, BMI, SBP, eGFR, LVEF, HF etiology, HF presentation, smoking status, hypertension, previous stroke,	DM was an independent risk factor for in-hospital death (aHR 1.78 [1.28-2.46]), HF hospitalization	***

	European hospitalized patients with acute HF. Mean age 69 years			≥7.0 mmol/L or HbA1c ≥6.5%; the prevalence of DM was 49.4%	LVEF>35% were 29.8%		COPD, haemoglobin, Na, medicationss	(aHR 1.32 [1.14-1.53]) and for all-cause death (aHR 1.16 [1.02-1.32])	

Note: §Degree of adjustment: 0 unadjusted; *adjusted for age and/or sex; **adjustment for age, sex, blood pressure, HF etiology and LVEF; ***, further adjustment for traditional and/or non-traditional CVD risk factors.
Abbreviations: AF, atrial fibrillation; AHF, acute heart, failure; aHR, adjusted hazard ratio; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; DM diabetes mellitus; eGFR, estimated glomerular filtrate rate; HbA1c, hemoglobin A1c; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; LDH, lactate dehydrogenase; Na, sodium; NA, not available; NT-proBNP, N-terminal probrain natriuretic peptide; RCT, randomized controlled trial; SBP, systolic blood pressure; TIA, transient ischaemic attack; WBC, white blood cell, uHR, unadjusted hazard ratio.

Supplementary Table S2. Main characteristics of randomized clinical trials (RCTs) and registries assessing the impact of diabetes mellitus (DM) on the risk of all-cause death, cardiovascular death, hospitalization and the combined endpoint of all-cause death or hospitalization in patients with chronic HF.

Author [Ref.], Year	Study Characteristics	Follow-up length	Diagnostic criteria for HF	Diagnosis of DM; prevalence of DM	Mean LVEF (%); proportion of patients with LVEF >35%	Total number of all-cause deaths	Covariate Adjustment	Main findings by outcomes (unadjusted or adjusted HRs [±95% CI])	Degree of adjustment§
Randomized Clinical Trials (RCTs)									
Torp-Pedersen C *et al.*[18], 2007	RCT: The COMET Study, n= 3,029 (79.7% men) American patients with chronic HF. Mean age: 62 years	From 3.9 to 6 years	Clinical; ecochardiographic	Medical records, or use of insulin and/or oral glucose-lowering agents, or random glucose levels >11.1 mmol/L; the prevalence of DM was 24.1%	Mean LVEF 26%	1,157	Age, sex, SBP, NYHA class, duration of HF, LVEF, previous IHD, stroke, AF, hemoglobin, Na, creatinine, medications,	DM was an independent risk factor for all-cause death (aHR 1.20 [1.05-1.38])	***
MacDonald MR *et al.*[19], 2008	RCT: CHARM Trial, n= 7,599 (68.4% men) American and Canadian patients with symptomatic chronic HF. Mean age: 66 years	3.14 years (median)	Clinical; ecochardiographic	Medical records, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 28.5%	Percentage of patients with LVEF>35% was 39.8%	1,831	Age, sex, BMI, NYHA class, LVEF, heart rate, SBP, DBP, HF hospitalization, previous IHD, current angina, stroke, hypertension, AF, pacemaker, implantable cardioverter defibrillator, smoking status, PCI, CAGB, previous cancer,	DM was an independent risk factor for all-cause death (aHR 1.69 [1.43-1.97]), CV death (aHR 1.74 [1.32-2.16]), HF hospitalization (aHR 1.84 [1.54-2.15]) and for the combined of CV death or HF hospitalization (aHR 1.80 [1.55-2.05])	***

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							medications		
Wedel H *et al.*[20], 2009	RCT: CORONA Study, n= 3,342 (74.8% men) European patients with chronic HF. Mean age: 72.5 years	3 years	Clinical; ecochardiographic	Medical records; the prevalence of DM was 29%	Mean LVEF 31%	934	Age, sex, BMI, LVEF, NYHA class, CABG, AF, ApoA-1, NT-proBNP creatinine, intermittent claudicatio, heart rate, IHD	DM was an independent risk factor for all-cause death (aHR 1.31 [1.13-1.51])	***
de Boer RA *et al.*[21], 2010	RCT SENIORS Trial, n= 2,128 (26% men) European patients with chronic HF. Mean age: 76.1 years	1.75 years	Clinical; ecochardiographic	Medical records, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 26.1%	Mean LVEF 33%	361	Age, sex, LVEF, NYHA class, creatinine, blood pressure, medications, hypertension, and previous IHD	DM was an independent risk factor for the combined of all-cause death or CV hospitalization (aHR 1.36 [1.15-1.60]), but not for all-cause death (aHR 1.25 [0.99-1.58])	***
Komajda M *et al.*[22], 2011	RCT: The I-PRESERVE Trial, n= 4,128 (39.7% men) multinational patients with chronic HF. Mean age: 72 years	Up to 5.5 years	Clinical; ecochardiographic; NT-proBNP	Medical records; the prevalence of DM was 27%	Mean LVEF 59%	881	Age, LVEF, heart rate, neutrophiles count, NT-proBNP, hospitalization for HF, quality of life, COPD asthma, eGFR, HF etiology, IHD	DM was an independent risk factor for all-cause death (aHR 1.48 [1.29-1.71]) and for the combined of all-cause death or CV hospitalization (aHR 1.43 [1.29-1.60])	***
Sarma S *et al.*[23], 2013	RCT: The EVEREST Study, n= 4,113 (74.4% men) multinational patients with HF. Mean age: 65 years	Up to 2.5 years		Medical records, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 40.1%	Mean LVEF 28%	1,092	Age, sex, BMI, LVEF, Na, blood urea nitrogen, SBP, QRS interval, NT-proBNP, geographical region, smoking status, AF, flutter, hypertension, CKD, stroke, medications	DM was an independent risk factor for all-cause death (aHR 1.16 [1.00-1.34]), but not for CV death (aHR 1.15 [0.97-1.35])	***
Böhm M *et al.*[24], 2014	RCT: The SOLVD-treatment Trial, n= 2,569 (80.4% men) multinational patients	3.12 years	Clinical; ecochardiographic	Medical records; the prevalence of DM was 25.8%	Mean LVEF 24.9%	961	None	DM was an independent risk factor for all-cause death (uHR 1.30 [1.13-1.50]), CV death uHR 1.32 [1.14-1.53]), HF hospitalization (uHR 1.32 [1.18-1.48]) and for the combined of all-cause death	

	with chronic HF. Mean age: 61.1 years							or HF hospitalization (uHR 1.43 [1.27-1.61])	
Komajda M *et al.*[25], 2015	RCT: SHIFT Trial, n= 6,505 (76.4% men) European patients with chronic HF. Mean age: 61 years	3 years	Clinical; ecochardiographic	Medical records; the prevalence of DM was 30%	Mean LVEF 29%	1,055	Age, SBP, heart rate, eGFR, LVEF, NYHA class, IHD, medications	DM was an independent risk factor for HF hospitalization (aHR 1.28 [1.13-1.44]) but not for all-cause death (aHR 1.10 [0.96-1.25]) and for CV death (aHR 1.05 [0.91-1.20])	***
Kristensen SL *et al.*[26], 2016	RCT The PARADIGM-HF Trial, n= 8,399 (78.3% men) multinational patients with chronic HF. Mean age: 63years	2.16 years (median)	Clinical; ecochardiographic; NT-proBNP	Medical records or HbA1c ≥6.5%; the prevalence of DM was 35%	Mean LVEF 30%	1,525	Age, sex, race, geographical region, heart failure duration, NYHA class, LVEF, heart rate, KCCQ score, BMI, eGFR, NT-proBNP, previous IHD, stroke, AF	DM was an independent risk factor for all-cause death (aHR 1.46 [1.26-1.70]), CV death (aHR 1.54 [1.30-1.83]), HF hospitalization (aHR 1.90 [1.59-2.27]) and for the combined of CV death or HF hospitalization (uHR 1.73 [1.54-1.95])	***
Dauriz M *et al.*[27], 2017	RCT: GISSI-HF Trial, n= 6,935 (78.5% men) Italian patients with chronic HF. Mean age: 67 years	3.9 years (median)	Clinical; ecochardiographic	Medical records, or use insulin and/or oral glucose-lowering agents, or fasting glucose levels ≥7 mmol/L or HbA1c ≥6.5%; the prevalence of DM was 41.1%	Mean LVEF 33%; the percentage of patients with LVEF>35% was 9.5%	1,958	Age, sex, BMI, heart rate, SBP, creatinine, total cholesterol, smoking status, hypertension, AF, COPD, NYHA class, HF etiology, LVEF	DM was an independent risk factor for all-cause death (aHR 1.43 [1.28-1.60]) and for the combined of all-cause death or CV hospitalization (aHR 1.23 [1.13-1.32])	***
Registries									
O'Connor CM *et al.*[28], 2000	Registry: The Duke Cardiovascular Databank, n= 2,498 (45% men) American consecutive patients with HF, who underwent cardiac catheterization between 1984 1996.	5 years	Clinical; ecochardiographic	Medical records, use of insulin and/or oral glucose-lowering agents, fasting glucose levels ≥7 mmol/L; the prevalence of DM was 28%	Median LVEF 58%	699	IHD, race, NYHA class, peripheral vascular disease, LVEF	DM was an independent risk factor for all-cause death (aHR 1.38 [1.19-1.57])	*

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	Mean age: 63 years								
Bobbio M *et al.*[29], 2003	Registry: BRING-UP Study, n= 2,843 (73.7% men) Italian patients with chronic HF. Mean age: 63.7 years	1 year	Clinical; ecochardiographic	Hypoglycemic diet, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 21.8%	Mean LVEF 34%	341	Age, SBP, heart rate, NYHA class, LVEF, medications	DM was an independent risk factor for all-cause death (aHR 1.40 [1.10-1.78]), all-cause hospitalization (uHR 1.28 [1.11-1.49]) and for the combined all-cause death or all-cause hospitalization (uHR 1.35 [1.19-1.51])	*
De Groote P *et al.*[30], 2004	Registry: n= 1,246 (84.7% men) French consecutive patients with chronic HF. Mean age: 53.8 years	3.29 years (median)	Clinical; ecochardiographic	Medical records, use of insulin and/or oral glucose-lowering agents, fasting glucose levels >7 mmol/L; the prevalence of DM was 22.4%	Mean LVEF 33%	385	Age, HF etiology, NYHA class, LVEF, peak VO_2, medications	DM was not an independent risk factor for CV death (aHR 1.06 [0.80-1.41])	*
Henkel DM *et al.*[31], 2008	Registry: n= 1,063 (46% men) American community patients with HF. Mean age: 76.4 years	4.3 years (median)	ICD-9 codes; clinical; radiologic (Framingham criteria)	Two consecutive fasting glucose levels ≥7.7 mmol/L, or 2-hour glucose levels ≥11.1 mmol/L; the prevalence of DM was 19%	The percentage of patients with LVEF>35% was 45%	917	Age, sex, smoking status, IHD, CKD, LVEF	DM was an independent risk factor for all-cause death (aHR 1.44 [1.21-1.71]) and for CV death (aHR 1.46 [1.16-1.82])	*
Gustafsson F *et al.*[32], 2009	Registry: n= 4,012 (71% men) Danish consecutive outpatients referred for HF management in 18 HF clinics. Mean age: 69 years	1.58 years	Clinical; ecochardiographic	Medical records; the prevalence of DM was 17%	The percentage of patients with LVEF>35% was 17%	703	Age, sex, NYHA, class, creatinine, LVEF, HF duration and etiology, SBP, heart rate, hospitalization within the last 90 days	DM was an independent risk factor for the combined of all-cause death or HF hospitalization (aHR 1.21 [1.03-1.42])	**
Lee R *et al.*[33], 2010	Registry: National Healthcare Group Multi-disciplinary Heart Failure Disease Management Program, n= 1,668 (67% men)	3 years	Clinical	Medical records, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 50.2%	The percentage of patients with LVEF>35% was 11.8%	223	Age, marital status, education, IHD, hypertension, stroke, eGFR, NYHA class, medications	DM was an independent risk factor for all-cause death (aHR 1.70 [1.19-2.66])	**

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	Singaporean patients with chronic HF. Mean age: 64.9 years								
De Blois J *et al.*[34], 2010	Registry: Norwegian Heart Failure Registry n= 4,132 (71% men) Norwegian patients with HF from 22 hospitals. Mean age: 71 years	1.1 years	Clinical; ecochardiographic	Medical records; the prevalence of DM was 20.1%	Mean LVEF 32%	1,083	Age, NYHA class, COPD, creatinine, medications	DM was an independent risk factor for all-cause death (aHR 1.39 [1.20-1.60])	*
Ather S *et al.*[35], 2012	Registry: n= 9,442 (94.8% men) American patients with chronic HF. Mean age: 70 years	Up to 2 years	ICD-9 codes; clinical; ecochardiographic	Medical records; the prevalence of DM was 41.5%	The percentage of patients with LVEF>35% was 30%	2,243	Age, sex, SBP, Na, previous HF hospitalization, hypertension, peripheral vascular disease, stroke, CKD, aenemia, COPD, obesity, liver disease, cancer, AIDS, dementia, psychiatric disorder, rheumatological disorder, peptic ulcer disease, medications	DM was an independent risk factor for all-cause death in patients with HFrEF (aHR 1.25[1.13-1.38]) but not in those with HFpEF (aHR 1.03 [0.86-1.24])	**
MAGGIC Investigators[36], 2012	MAGGIC Meta-analysis, n= 41,972 (61.2% men) multinational patients with chronic HF. Mean age: 68 years	2.75 years (median)	Clinical; ecochardiographic	Medical records; the prevalence of DM was 23.0%	Mean LVEF 38%	10,754	Age, sex, HF etiology, AF, hypertension, LVEF	DM was an independent risk factor for all-cause death (aHR 1.41 [1.35-1.47]) and for CV death (aHR 1.51 [1.41-1.62])	***
Cubbon RM *et al.*[37], 2013	Registry: n= 1,091 (73.6% men) British patients with chronic HF. Mean age: 68 years	2.63 years	Clinical; ecochardiographic	Medical records, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 25.7%	Mean LVEF 32%	251	Age, sex, HF etiology, NYHA class, LVEF, hemoglobin, Na, eGFR, medications	DM was an independent risk factor for all-cause death (aHR 1.72 [1.29-2.28]) and for CV death (aHR 2.00 [1.40-2.86])	**
Frigola-Capell E *et al.*[38], 2013	Registry: n= 5,659 (40% men) Spanish outpatients	Up to 3 years	ICD-10 codes	Medical records; the prevalence of DM was 29.8%	NA	950	Age, hypertension, IHD, CKD	DM was an independent risk factor for all-cause death (aHR 1.53 [1.33-1.76])	*

	with HF. Mean age: 77 years								
Gotsman I *et al.*[39], 2014	Registry: n=6,067 (51% men) Israeli patients with chronic HF. Mean age: 75 years	1.33 years (median)	ICD-9 codes; clinical; ecochardiographic	Medical records; the prevalence of DM was 50.5%	The percentage of patients with LVEF>35% was 85.9%	761	Age, sex, hyperlipidaemia, hypertension, BMI, heart rate, urea, eGFR, Na, hemoglobin, medications	DM was an independent risk factor for all-cause death (aHR 1.48 [1.13-1.95]) and for the combined of all-cause or CV hospitalization (aHR 1.27 [1.12-1.43])	*
Johansson I *et al.*[40], 2014	Registry: Swedish Heart Failure Registry, n= 36,276 (60.6% men) Swedish patients with chronic HF. Mean age: 75 years	1.9 years (median)	Clinical; ecochardiographic	Medical records, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was 24.2%	The percentage of patients with LVEF>35% was 18.5%	7,244	Age, sex, duration of HF, SBP, DBP, IHD, hypertension, AF, pulmonary disease, revascularization, valvular surgery, creatinine, hemoglobin, weight, medications	DM was an independent risk factor for all-cause death (aHR 1.6 [1.5-1.71])	**
Ushigome R *et al.*[41], 2015	Registry: CHART study, n= 4,682 (65.2% men) Japanese patients with chronic HF. Mean age: 69 years	3 years	Clinical; ecochardiographic; NT-proBNP	Medical records, or use of insulin and/or oral glucose-lowering agents; the prevalence of DM was %	The percentage of patients with LVEF>35% was 59.4%	771	Age, BMI, heart rate, SBP, NYHA class, hyperlipidaemia, LV end-diastolic diameter, NT-proBNP, eGFR	DM was an independent risk factor for all-cause death (aHR 1.37 [1.15-1.64])	*
Sengeløv M *et al.*[42], 2015	Registry: n= 1,065 (73.6% men) Danish patients with chronic HF. Mean age: 67 years	3.33 years (median)	Clinical; ecochardiographic	Medical records; the prevalence of DM was 12%	Mean LVEF 27.5%	177	Age, hypertension, IHD, global longitudinal strain (on echocardiography)	DM was an independent risk factor for all-cause death (aHR 2.66 [1.55-4.30])	*
Dauriz M *et al.*[43], 2017	Registry: ESC-HFA Long-Term HF Registry, n= 9,428 (72% men) European patients with chronic HF.	1 year	Clinical; ecochardiographic; NT-proBNP	Medical records, or use of insulin and/or oral glucose-lowering agents, or a fasting glucose levels ≥7.0 mmol/L and/or HbA1c level ≥6.5%; the prevalence of DM was 36.5%	Mean LVEF 37%; the percentage of patients with LVEF>35% was 23.9%	757	Age, sex, BMI, hemoglobin, SBP, eGFR, LVEF, HF etiology, smoking status, hypertension, previous stroke, COPD, medications	DM was independent risk factor for all-cause death (aHR 1.28 [1.07-1.54]) and for HF hospitalization (aHR 1.37 [1.17-1.60]), but not for CV death (aHR 1.28 [0.99-1.66])	***

	Mean age: 64.9 years								

Note: §Degree of adjustment: 0 unadjusted; *adjusted for age and/or sex; **adjustment for age, sex, blood pressure, HF etiology and LVEF; ***, further adjustment for traditional and/or non-traditional CVD risk factors.
Abbreviations: AF, atrial fibrillation; aHR, adjusted hazard ratio; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; DM diabetes mellitus; eGFR, estimated glomerular filtrate rate; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction IHD, ischemic heart disease; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; Na, sodium; NA, not available; NT-proBNP, N-terminal probrain natriuretic peptide; RCT, randomized controlled trial; SBP, systolic blood pressure; uHR, unadjusted hazard ratio; VO_2, Oxygen Consumption.

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Supplementary Table S3. Sensitivity analyses – Prognostic impact of diabetes *per se* on the risk of all-cause death, cardiovascular death or hospitalization in all studies stratified by either left ventricular ejection fraction, ischemic etiology of HF or country at the study entry as well as in 'high-quality' observational registries according to the Newcastle-Ottawa Scale (i.e., NOS score >7).

	All-cause death	Cardiovascular death	Hospitalization
Left ventricular ejection fraction (LVEF) [§]			
LVEF ≤35%	HR 1.26 (1.16-1.38) I^2 =74.3 number of studies: 12 *N*=47,344	HR 1.26 (1.09-1.44) I^2 =73.1 number of studies: 7 *N*=26,165	HR 1.35 (1.17-1.56) I^2 =78.8 number of studies: 3 *N*=20,554
LVEF >35%	HR 1.27 (1.18-1.36) I^2 =70.9 number of studies: 11 *N*=94,012	HR 1.46 (1.28-1.66) I^2 =31.7 number of studies: 2 *N*=51,400	HR 1.24 (1.04-1.47) I^2 =66.8 number of studies: 3 *N*=18,130
HF ischemic etiology [§#]			
Ischemic HF etiology ≥50% of sample	HR 1.35 (1.24-1.47) I^2 =88.9 number of studies: 16 *N*=108,899	HR 1.49 (1.23-1.80) I^2 =85.7 number of studies: 5 *N*=65,566	HR 1.55 (1.26-1.90) I^2 =86.3 number of studies: 4 *N*=29,429
Ischemic HF etiology <50% of sample	HR 1.34 (1.18-1.52) I^2 =82.2 number of studies: 8 *N*=66,900	HR 1.17 (0.97-1.42) I^2 =0.00 number of studies: 2 *N*=10,658	HR 1.22 (1.03-1.45) I^2 =64.8 number of studies: 3 *N*=12,047
Study countries [§]			
Europe	HR 1.34 (1.25-1.43) I^2 =80.9 number of studies: 17 *N*=219,066	HR 1.26 (0.98-1.61) I^2 =74.7 number of studies: 4 *N*=18,254	HR 1.27 (1.16-1.38) I^2 =33.8 number of studies: 5 *N*=25,478
Middle East	HR 1.18 (1.02-1.36) I^2 =42.9 number of studies: 4 *N*=15,518	not available	not available
North America	HR 1.26 (1.16-1.38) I^2 =82.9 number of studies: 9 *N*=43,717	HR 1.58 (1.33-1.88) I^2 =5.8 number of studies: 2 *N*=8,662	HR 1.84 (0.54-2.15) number of studies: 1 *N*=7,599
Western Pacific	HR 1.42 (1.21-1.67) I^2 =0.00 number of studies: 2 *N*=6,350	not available	not available
International	HR 1.32 (1.20-1.44) I^2 = 87.9 number of studies: 6 *N*=69,581	HR 1.33 (1.17-1.52) I^2 =75.5 number of studies: 5 *N*=59,311	HR 1.41 (1.06-1.86) I^2 =88.2 number of studies: 3 *N*=13,206
High-quality studies on NOS score			
N*=21 studies	HR 1.29 (1.19-1.40) I^2 =89.4 number of studies: 18 *N*=153,786*	HR 1.31 (1.06-1.63) I^2 =70.5 number of studies: 3 *N*=52,630	HR 1.26 (1.12-1.41) I^2 =50.3 number of studies: 4 *N*=18,973
N*=22 studies*	HR 1.24 (1.13-1.36) I^2 =92.9 number of studies: 19 *N*=170,152**	HR 1.31 (1.06-1.63) I^2 =70.5 number of studies: 3 *N*=52,630	HR 1.26 (1.12-1.41) I^2 =50.3 number of studies: 4 *N*=18,973

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[§] Without Sengeløv M. *et al.*[42] and Teng TH et al.[12]; [#]The 50% prevalence cut-off for ischemic HF etiology was calculated as median prevalence among the 28 studies with available data. *Without Teng TH *et al.*[12]; **With Teng TH *et al.*

Supplementary Table S4. Newcastle-Ottawa quality assessment scale (NOS) for observational registries.

Author	Selection	Comparability	Exposure/outcome
Varadarajan P. *et al.*[5], 2006	✶✶✶✶	✶✶	✶✶✶
Harjola V.P. *et al.*[9], 2010	✶✶✶✶	✶✶	✶✶✶
Ather S. *et al.*[35], 2012	✶✶✶✶	✶✶	✶✶✶
MAGGIC Investigators [36], 2012	✶✶✶✶	✶✶	✶✶✶
Spinar J. *et al* [15], 2016	✶✶✶✶	✶✶	✶✶✶
Targher G. *et al.*[17], 2017	✶✶✶✶	✶✶	✶✶✶
Targher G. *et al.*[16], 2016	✶✶✶✶	✶✶	✶✶✶
Dauriz M. *et al.*[43], 2017	✶✶✶✶	✶✶	✶✶✶
Bobbio M. *et al.*[29], 2003	✶✶✶✶	✶	✶✶✶
De Groote P. *et al.*[30], 2004	✶✶✶✶	✶	✶✶✶
Varela-Roman A. *et al.*[3], 2005	✶✶✶✶	✶✶	✶✶
Owan T.E. *et al.*[4], 2006	✶✶✶	✶✶	✶✶✶
Ouzounian M. *et al.*[6], 2007	✶✶✶✶	✶	✶✶✶
Gustafsson F. *et al.*[32], 2009	✶✶✶✶	✶✶	✶✶✶
Barsheshet A. *et al.*[8], 2010	✶✶✶✶	✶✶	✶✶
Lee R. *et al.*[33], 2010	✶✶✶	✶✶	✶✶✶
Frigola-Capell E. *et al.*[38], 2013	✶✶✶✶	✶	✶✶✶
Johansson I. *et al.*[40], 2014	✶✶✶	✶✶	✶✶✶
Shah R. *et al.*[10], 2014	✶✶✶	✶✶	✶✶✶
Ushigome R. *et al.*[41], 2015	✶✶✶✶	✶	✶✶✶
Teng T.H. *et al.*[12], 2015	✶✶✶	✶✶	✶✶✶
O'Connor C.M. *et al.*[28], 2000	✶✶	✶	✶✶✶
Henkel D.M. *et al.*[31], 2008	✶✶✶✶	✶	✶✶✶
MacDonald M.R. *et al.*[7], 2008	✶✶✶	✶	✶✶
De Blois J. *et al.*[34], 2010	✶✶✶✶	✶	✶✶
Cubbon R.M. *et al.*[37], 2013	✶✶	✶✶	✶✶✶
Alhabib K. *et al.*[11], 2014	✶✶✶	✶	✶✶
Gotsman I. *et al.*[39], 2014	✶✶✶	✶	✶✶✶
Helfand B.K. *et al.*[13], 2015	✶✶✶	✶	✶✶✶
Khafaji H.A. *et al.*[14], 2015	✶✶	✶✶	✶✶
Sengeløv M. *et al.*[42], 2015	✶✶	✶	✶✶✶

Note: Comparability category: age, sex, blood pressure, HF etiology and baseline LVEF were arbitrarily considered as the minimum required number of covariates for adjustment to assess the quality of individual studies.

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