Relation of Smoking with Total Mortality and Cardiovascular Events among Patients with Diabetes: A Meta-analysis and Systematic Review

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Online Supplemental Material

The following materials are included in the Online Supplemental Material.

1. Search strategies in PubMed and EMBASE.
2. List of papers that were included in the meta-analysis but were not found from the search of Pubmed and EMBASE
3. Supplemental Tables 1-5.
4. Supplemental Figures 1-2.
5. List of references that were included in the meta-analysis

Supplemental Table 1. Characteristics of Studies Included in the Meta-analysis of Smoking and Risk of Total and Cardiovascular Disease Mortality among Diabetic Patients

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Search strategies in PubMed (May 3, 2015)

#1 (diabetes mellitus[MeSH Terms]) OR (type 2 diabetes mellitus[MeSH Terms]) OR (prediabetic state[MeSH Terms]) OR (metabolic syndrome X[MeSH Terms]) OR (glucose intolerance [MeSH Terms]) OR (hyperglycemia [MeSH Terms]) OR (glucose metabolism disorders [MeSH Terms]) OR (insulin resistance [MeSH Terms]) OR (glucose tolerance test [MeSH Terms]) OR ("insulin sensitivity"[Text Word]) OR ("insulin resistance"[Text Word]) OR ("impaired fasting glucose"[Text Word]) OR ("impaired glucose tolerance"[Text Word]) OR ("IGT"[Text Word]) OR ("IFG"[Text Word]) OR ("diabetes*"[Text Word]) OR ("diabetic*"[Text Word])

#2 (smoking [MeSH Terms]) OR (smoking cessation [MeSH Terms]) OR (smoke inhalation injury [MeSH Terms]) OR (Tobacco Smoke Pollution[MeSH Terms]) OR (tobacco[MeSH Terms]) OR (smokeless[MeSH Terms]) OR (tobacco use cessation [MeSH Terms]) OR (tobacco use disorder [MeSH Terms]) OR (nicotine[MeSH Terms]) OR ("nicotine*"[Text Word]) OR ("tobacco*"[Text Word]) OR ("smok*"[Text Word]) OR ("cigarette*"[Text Word])

#3 (incidence[MeSH Terms]) OR (cohort studies[MeSH Terms]) OR (follow-up studies[MeSH Terms]) OR (prognosis[MeSH Terms]) OR (early diagnosis[MeSH Terms]) OR (survival analysis[MeSH Terms]) OR ("course"[Title/Abstract]) OR ("predict*"[Title/Abstract]) OR ("prognos*"[Title/Abstract]))

#4 NOT ((meta-analysis[MeSH Terms]) OR (review[publication type]) OR (case-control studies[MeSH term]))

#5 Search #1 AND #2 AND #3 AND #4

Search strategies in EMBASE (April 16, 2014)

#1 'diabetes mellitus'/exp OR 'prediabetic state'/exp OR 'metabolic syndrome x'/exp OR 'glucose intolerance'/exp OR 'hyperglycemia'/exp OR 'glucose metabolism disorders'/exp OR 'insulin resistance'/exp OR 'glucose tolerance test'/exp OR 'insulin sensitivity'/exp OR'impaired glucose tolerance'/exp AND [embase]/lim

#2 'smoke'/exp OR 'smoking'/exp OR 'smoking cessation'/exp OR 'smoke inhalation injury'/exp OR 'smokeless' OR 'tobacco use cessation'/exp OR 'tobacco use disorder'/exp OR 'tobacco'/exp OR 'nicotine dependence'/exp OR 'tobacco dependence'/exp OR 'smoking dependence' OR 'cigarette'/exp

#3 'incidence'/exp OR 'cohort studies'/exp OR 'follow-up studies'/exp OR 'prognosis'/exp OR 'early diagnosis'/exp OR 'survival analysis'/exp OR 'prediction'/exp

#4 Search #1 AND #2 AND #3 NOT 'meta-analysis'/exp NOT 'review'/exp NOT 'case-control studies'/exp AND [humans]/lim AND [embase]/lim

The following studies were further included by searching the reference lists of relevant papers and reviews:

1. Ford ES, DeStefano F. Risk factors for mortality from all causes and from coronary heart disease among persons with diabetes. Findings from the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study. *Am J Epidemiol*. 1991;133:1220-30.
2. Klein R, Klein BE, Moss SE. Incidence of gross proteinuria in older-onset diabetes. A population-based perspective. *Diabetes*. 1993;42:381-9.
3. Lehto S, Ronnemaa T, Pyorala K, Laakso M. Predictors of stroke in middle-aged patients with non-insulin-dependent diabetes. *Stroke*. 1996;27:63-8.
4. Muggeo M, Zoppini G, Bonora E, Brun E, Bonadonna RC, Moghetti P, Verlato G. Fasting plasma glucose variability predicts 10-year survival of type 2 diabetic patients: the Verona Diabetes Study. *Diabetes Care*. 2000;23:45-50.
5. Ostgren CJ, Lindblad U, Melander A, Rastam L. Survival in patients with type 2 diabetes in a Swedish community: Skaraborg Hypertension and Diabetes project. *Diabetes Care*. 2002;25:1297-302.
6. Klein BE, Klein R, McBride PE, Cruickshanks KJ, Palta M, Knudtson MD, Moss SE, Reinke JO. Cardiovascular disease, mortality, and retinal microvascular characteristics in type 1 diabetes: Wisconsin epidemiologic study of diabetic retinopathy. *Arch Intern Med*. 2004;164:1917-24.
7. Laing SP, Jones ME, Swerdlow AJ, Burden AC, Gatling W. Psychosocial and socioeconomic risk factors for premature death in young people with type 1 diabetes. *Diabetes Care*. 2005;28:1618-23.
8. Yang X, So WY, Kong AP, Ho CS, Lam CW, Stevens RJ, Lyu RR, Yin DD, Cockram CS, Tong PC, Wong V, Chan JC. Development and validation of stroke risk equation for

Hong Kong Chinese patients with type 2 diabetes: the Hong Kong Diabetes Registry. *Diabetes Care*. 2007;30:65-70.

9. Elley CR, Robinson E, Kenealy T, Bramley D, Drury PL. Derivation and validation of a new cardiovascular risk score for people with type 2 diabetes: the New Zealand diabetes cohort study. *Diabetes Care*. 2010;33:1347-52.
10. de Boer IH, Rue TC, Cleary PA, Lachin JM, Molitch ME, Steffes MW, Sun W, Zinman B, Brunzell JD; Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study Research Group, White NH, Danis RP, Davis MD, Hainsworth D, Hubbard LD, Nathan DM. Long-term renal outcomes of patients with type 1 diabetes mellitus and microalbuminuria: an analysis of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications cohort. *Arch Intern Med*. 2011;171:412-20.
11. Hayes AJ, Leal J, Gray AM, Holman RR, Clarke PM. UKPDS outcomes model 2: a new version of a model to simulate lifetime health outcomes of patients with type 2 diabetes mellitus using data from the 30 year United Kingdom Prospective Diabetes Study: UKPDS 82. *Diabetologia*. 2013;56:1925-33.
12. Pinies JA, Gonzalez-Carril F, Arteagoitia JM, Irigoien I, Altzibar JM, Rodriguez-Murua JL, Echevarriarteun L; Sentinel Practice Network of the Basque Country. Development of a prediction model for fatal and non-fatal coronary heart disease and cardiovascular disease in patients with newly diagnosed type 2 diabetes mellitus: the Basque Country Prospective Complications and Mortality Study risk engine (BASCORE). *Diabetologia*. 2014;57:2324-33.
13. Costanzo P, Cleland JG, Pellicori P, Clark AL, Hepburn D, Kilpatrick ES, Perrone-Filardi P, Zhang J, Atkin SL. The obesity paradox in type 2 diabetes mellitus:

relationship of body mass index to prognosis: a cohort study. *Ann Intern Med*. 2015;162:610-8.

14. Paul SK, Klein K, Majeed A, Khunti K. Association of smoking and concomitant use of metformin with cardiovascular events and mortality in people newly diagnosed with type 2 diabetes. *J Diabetes*. 2015 Apr 30 [Epub ahead of print]; http://dx.doi.org/10.1111/1753-0407.12302.
15. Vazquez-Benitez G, Desai JR, Xu S, Goodrich GK, Schroeder EB, Nichols GA, Segal J, Butler MG, Karter AJ, Steiner JF, Newton KM, Morales LS, Pathak RD, Thomas A, Reynolds K, Kirchner HL, Waitzfelder B, Elston Lafata J, Adibhatla R, Xu Z, O'Connor PJ. Preventable major cardiovascular events associated with uncontrolled glucose, blood pressure, and lipids and active smoking in adults with diabetes with and without cardiovascular disease: a contemporary analysis. *Diabetes Care*. 2015;38:905-12.

The following studies were included using the full text of the meeting abstracts:

1. Ruggenenti P, Porrini E, Motterlini N, Perna A, Ilieva AP, Iliev IP, Dodesini AR, Trevisan R, Bossi A, Sampietro G, Capitoni E, Gaspari F, Rubis N, Ene-Iordache B, Remuzzi G; BENEDICT Study Investigators. Measurable urinary albumin predicts cardiovascular risk among normoalbuminuric patients with type 2 diabetes. *J Am Soc Nephrol*. 2012;23:1717-24.
2. Yu TY, Li HY, Jiang YD, Chang TJ, Wei JN, Chuang LM. Proteinuria predicts 10-year cancer-related mortality in patients with type 2 diabetes. *J Diabetes Complications*. 2013;27:201-7.
3. Kelly PJ, Clarke PM, Hayes AJ, Gerdtham UG, Cederholm J, Nilsson P, Eliasson B, Gudbjornsdottir S. Predicting mortality in people with Type 2 diabetes mellitus after

major complications: a study using Swedish National Diabetes Register data. *Diabet Med*. 2014;31:954-62.

4. van Diepen M, Schroijen MA, Dekkers OM, otmans JI, Krediet RT, Boeschoten EW, Dekker FW. Predicting mortality in patients with diabetes starting dialysis. *PloS One*. 2014;9:e89744.

Supplemental Table 1. Characteristics of Studies Included in the Meta-analysis of Smoking and Risk of Total and Cardiovascular Mortality among Diabetic Patients

Reference, year	Study location	*n*	Male (%)	Mean baseline age	Diabetes category	Current smoking (%)	Mean follow-up years	Mortality outcome	n of cases	Reference group	Current smoking	Past smoking
Klein et al,[1] 1989	United States	996	50.7	>30	T1D	23.4	6	Total	91	Never + Past	2.36 (1.17-4.78)	
Klein et al,[1] 1989	United States	1370	46.2	65.4	T2D	14.0	6	Total	484	Never + Past	1.58 (1.13-2.22)	
Ford et al,[2] 1991	United States	602	37.3	>60	T2D	19.6	10	Total	233	Never	1.79 (1.10-2.91)	1.22 (0.72-2.07)
Rossing et al,[3] 1996	Denmark	886	52.5	About 39.5	T1D	59.3	9.2	Total	183	Never + Past	1.51 (1.09-2.08)	
Chaturvedi et al,[4] 1997	International	4427	About 48	About 47	T1D, T2D	38	13 (max)	Total	1037	Never	1.45 (1.30-1.62)	1.35 (1.16-1.57)
Hadden et al,[5] 1997	Ireland	432	56	55.8	T2D	36.8	10	Total	106	Never	2.50 (1.59-3.93)	
Adlerberth et al,[6] 1998	Sweden	249	100	56.1	T2D	41	16	Total	155	Never + Past	1.95 (1.40-2.63)	
Muggeo et al,[7] 2000	Italy	1409	46.3	66.4	T2D	21.9	10	Total	468	Never + Past	0.85 (0.66-1.10)	
Muhlhauser et al,[8] 2000	Germany	3570	49.7	27.3	T1D	42.7	10.3	Total	251	Never + Past	1.92 (1.43-2.57)	
Al-Delaimy et al,[9] 2001	United States	7401	0	About 62	T2D	20	20	Total	724	Never	1.66 (1.35-2.05)	1.31 (1.11-1.55)
Florkowski et al,[10] 2001	New Zealand	447	46.5	62	T2D	15	10	Total	187	Never + Past	1.57 (0.97-2.55)	
Ostgren et al,[11] 2002	Sweden	400	50.5	About 70	T2D	17	5.9	Total	131	Never + Past	1.66 (0.99-2.76)	
Church et al,[12] 2004	United States	2196	100	49.3	T2D	20.5	14.6	Total	275	Never	1.75 (1.24-2.46)	1.23 (0.92-1.64)
Davis et al,[13] 2004	Australia	1269	49.2	64.1	T2D	15.0	7	Total	312	Never + Past	1.47 (1.03-2.11)	
Raggi et al,[14] 2004	United States	903	57	57	T2D	44.1	5	Total	63	Never + Past	1.76 (0.99-3.11)	
Bo et al,[15] 2005	Italy	3892	51.7	69.7	T2D	22.3	4.5	Total	599	Never + Past	1.36 (1.09-1.69)	
Hu et al,[16] 2005	Finland	3708	Mixed	About 50	T2D	27.5	18.7	Total	1423	Never	1.50 (1.30-1.74)	1.00 (0.84-1.19)
Laing et al,[17] 2005	United Kingdom	235	54.1	Before 20	T1D	33.6	>10 (max)	Total	98	NR	1.5 (0.8-2.5)	
Saremi et al,[18] 2005	United States	628	35.4	51	T2D	9.2	11	Total	204	Never + Past	1.9 (0.8-4.3)	
Ko et al,[19] 2006	Hong Kong, China	5202	43.8	59.1	T2D	28.2	2.1	Total	189	Never	Four groups: 0.84 (0.35-2.02); 0.75 (0.34-1.67); 1.10 (0.63-1.92); 1.61 (1.04-2.49)	
Trichopoulou et al,[20] 2006	Greece	1013	41.9	About 65	T2D	17.4	4.5	Total	80	Never	1.41 (0.67-2.99)	2.06 (1.07-3.96)
Katakura et al,[21] 2007	Japan	388	45.4	72.9	T2D	22	6	Total	76	Never	1.96 (1.19-3.13)	
McAuley et al,[22] 2007	United States	831	100	61.3	T2D	16.0	4.8	Total	112	Never	1.93 (1.22-3.05)	0.79 (0.55-1.16)
Wells et al,[23] 2008	United States	33067	50.5	61.9	T2D	14.9	2.4	Total	3661	Never	1.46 (1.17-1.83)	1.17 (1.07-1.29)
Tseng et al,[24] 2008	Taiwan, China	358	53.4	66.6	T2D after lower-extremity amputation	40.2 (ever)	4	Total	214	Never	1.542 (1.021-2.329)	
Iversen et al,[25] 2009	Norway	1494	50.4	65.8	T2D	16.2	10 (max)	Total	547	Never + Past	1.75 (1.38-2.22)	
Nilsson et al,[26] 2009	Sweden	13087	55.7	60.3	T2D	16.4	5.7	Total	664	Never + Past	1.84 (1.51-2.22)	
Brown et al,[27] 2010	United States	300	49.7	51.1	T2D with serious mental illness	47	6.9	Total	63	Never + Past	1.79 (1.01-2.90)*	
de Fine Olivarius et	Denmark	1108	53.2	65.2	T2D	39.0	5.2	Total	224	Never	1.31 (0.88-1.95)	1.35 (0.93-1.96)

al,[28] 2010												
Joergensen et al,[29] 2010	Denmark	289	61.2	54	T2D	43.6	15	Total	196	Never + Past	1.41 (1.05-1.89)	
Nelson et al,[30] 2010	United States	1507	43.8	About 65	T2D	16.4	7.6	Total	642	Never + Past	1.77 (1.15-2.73)	
Adams et al,[31] 2010	United States	337	49	58	T2D	19	10.9	Total	99	NR	1.2 (0.7-2.2)	
Ciechanowski et al,[32] 2010	United States	3535	46.7	63.3	T1D, T2D	7.8	4.5	Total	533	Never + Past	1.59 (1.12-2.25)	
Currie et al,[33] 2010	United Kingdom	27965	57	64.1	T2D	63 (ever)	5	Total	2035	Never	1.10 (1.03-1.18)	
Perman et al,[34] 2011	Argentina	1730	51	73	T2D	8.0	6.15	Total	363	Never + Past	1.48 (1.03-2.12)	
Thomas et al,[35] 2011	Finland	3100	About 52	About 39	T1D	24	9.1	Total	202	Never + Past	1.73 (1.211-2.479)	
Currie et al,[36] 2012	United Kingdom	13401	53.7	63.6	T2D	39.6	3.2	Total	2367	Never	1.47 (1.27-1.70)	1.14 (1.03-1.26)
Lin et al,[37] 2012	Taiwan, China	5686	51.9	About 58 y	T2D	20.0	4	Total	429	Never	1.31 (1.01-1.71)	
Ma et al,[38] 2012	Taiwan, China	881	47.9	59.7	T2D	14.6	4.7	Total	73	Never + Past	0.90 (0.43-1.90)	
Regidor et al,[39] 2012	Spain	667	41.8	>70	T2D	14.9 (M) 1.2 (F)	8 (max)	Total	222	Never	1.93 (1.03-3.63)	1.61 (1.03-2.52)
Fickley et al,[40] 2013	United States	506	49.4	29.1	T1D	38.7 (ever)	22 (max)	Total	128	Never	1.93 (1.35-2.76)	
Svendstrup et al,[41] 2013	Denmark	578	63	54	T1D, T2D	49	10.5	Total	219	Never + Past	1.56 (1.34-2.44)	
Yu et al,[42] 2013	Taiwan, China	646	49.5	62	T2D	17.2	10.4	Total	158	Never + Past	1.75 (1.11-2.78)	
Kelly et al,[43] 2014	Sweden	20836	56	75.7	T2D with a major complication	12	1.66	Total	7911	Never + Past	1.51 (1.40-1.63)	
Sluik et al,[44] 2014	Europe	6384	54	57.4	T2D	25	9.9	Total	830	Never	2.29 (1.91-3.01)	1.36 (1.13-1.64)
van Diepen et al,[45] 2014	The Netherlands	394	55	65.3	T2D with ESRD	21	1	Total	82	Never + Past	1.62 (0.93-2.52)*	
Costanzo et al,[46] 2015	UK	10568	63	29	T2D	16	10.6	Total	3728	Never + Past	1.45 (1.32-1.61)	
Paul et al,[47] 2015	UK	82205	55	62	T2D	17	5.4	Total	10003	Never	1.75 (1.65-1.86)	1.10 (1.05-1.15)
Vazquez-Benitez et al,[48] 2015	USA	859617	52.2	59	T2D	9.2	5.0	Total	66892	Never + Past	Those without history of CVD: 1.62 (1.55-1.69); those with history of CVD: 1.35 (1.31-1.40)	
Rossing et al,[3] 1996	Denmark	916	52.5	About 39.5	T1D	59.3	9.2	CVD	71	Never + Past	2.23 (1.31-3.79)	
Muggeo et al,[49] 1997	Italy	566	27.7	79.8	T2D	5.3	5	CVD	79	Never + Past	0.90 (0.34-2.41)	
Muggeo et al,[7] 2000	Italy	1409	46.3	66.4	T2D	21.9	10	CVD	180	Never + Past	1.00 (0.65-1.52)	
Fuller et al,[50] 2001	International	1661	100	47	T2D	NR	12	CVD	210	Never	1.1 (0.6-1.9)	1.6 (0.9-2.8)
Fuller et al,[50] 2001	International	1822	0	46.7	T2D	NR	12	CVD	156	Never	1.5 (0.9-2.4)	1.0 (0.5-1.9)
Fuller et al,[50] 2001	International	659	100	44.4	T1D	NR	12	CVD	95	Never	1.9 (0.9-4.0)	0.6 (0.2-1.6)
Fuller et al,[50] 2001	International	601	0	44.5	T1D	NR	12	CVD	62	Never	1.1 (0.4-3.1)	1.7 (0.5-5.1)
Al-Delaimy et al,[9] 2001	United States	7401	0	About 62	T2D	20.0	20	CVD	289	Never	Three dose categories: 1.58 (0.82-3.07); 2.56 (1.69-3.88); 1.85 (0.74-4.64)	1.30 (1.00-1.68)
Linnemann et al,[51]	Germany	475	36	64.7	T2D	20.4	5	CVD	57	NR	2.11 (1.27-3.30)*	

2003												
Hu et al,[16] 2005	Finland	3708	Mixed	About 50	T2D	27.5	18.7	CVD	906	Never	1.34 (1.11-1.63)	1.01 (0.81-1.26)
Church et al,[52] 2005	United States	2316	100	50.1	T2D	20.4	15.9	CVD	179	Never	1.26 (0.82-1.95)	1.05 (0.73-1.49)
Norman et al,[53] 2006	Australia	1294	48.8	64.1	T2D	15.0	5	CVD	363	Never + Past	1.75 (1.05-2.92)	
Ko et al,[19] 2006	Hong Kong, China	5202	43.8	59.1	T2D	28.2	2.1	CVD	164	Never	Four groups: 1.53 (0.25-9.22); 1.02 (0.23-4.56); 1.26 (0.54-2.94); 2.38 (1.23-4.60)	
Zoppini et al,[54] 2009	Italy	2726	55.3	67	T2D	23	4.7	CVD	145	Never + Past	1.18 (0.56-2.53)	
de Fine Olivarius et al,[28] 2010	Denmark	1108	53.2	65.2	T2D	39.0	5.2	CVD	124	Never	1.01 (0.58-1.75)	1.48 (0.91-2.41)
Lin et al,[37] 2012	Taiwan, China	5686	51.9	About 58	T2D	20.0	4	CVD	83	Never	1.56 (0.86-2.81)	

Abbreviations: CVD, cardiovascular disease; ESRD, end stage renal disease; F, female; M, male; NR, not reported; T1D, type 1 diabetes; T2D, type 2 diabetes;
[*]The relative risk (RR) was converted from odds ratio (OR) by the formula $RR=OR/[(1-P_o)+(P_o \times OR)]$, in which P_o is the incidence of the outcome of interest in the nonexposed group. (Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA*. 1998;280:1690-1.)

Supplemental Table 2. Characteristics of Studies Included in the Meta-analysis of Smoking and Risk of Cardiovascular Disease Outcomes among Diabetic Patients

Reference, year	Study location	*n*	Male (%)	Mean baseline age	Diabetes category	Current smoking (%)	Mean follow-up years	Outcome	n of cases	Reference group	Current smoking	Past smoking
Fu et al,[55] 1993	Taiwan, China	479	41.3	67.4	T2D	25.5	4	CVD	114	Never+past	1.44 (0.84-2.43)	
Al-Delaimy et al,[56] 2002	United States	6547	0	About 62	T2D	20.0	20	CVD	NR	Never	Two dose categories: 1.46 (1.02-2.10); 2.42 (1.94-3.02)	1.03 (0.86-1.25)
Bonora et al,[57] 2002	Italy	627	About 48	about 64	T2D	38.1	4.5	CVD	126	NR	1.42 (1.00-1.96)*	
Targher et al,[58] 2005	Italy	744	62	65	T2D (nested C-C)	20	5	CVD	248	Never + Past	1.40 (1.1-1.9)	
Hayes et al,[59] 2008	Australian and New Zealand	7348	62	66	T2D	9.1	2.4	CVD	453	Never + Past	1.58 (1.18-2.11)	
Zethelius et al,[60] 2011	Sweden	24288	60.1	61.6	T2D	17.8	5	CVD	2488	Never + Past	1.35 (1.22-1.49)	
Elley et al,[61] 2010	New Zealand	36127	49	59.2	T2D	15	3.9	CVD	6479	Never	1.26 (1.17-1.37)	1.11 (1.04-1.18)
Sasso et al,[62] 2012	Italy	742	46.6	65.8	T2D with nephropathy	23.3	4.6	CVD	202	Never + Past	1.53 (1.08-2.17)	
Ruggenenti et al,[63] 2012	Italy	1208	52.8	62.3	T2D with hypertension	12.1	9.2	CVD	189	Never	1.25 (0.81-1.92)	
Clair et al,[64] 2013	United States	445	NR	About 50	T2D	33.3	25	CVD	125	Never	2.07 (0.94-4.56)	1.17 (0.65-2.09)
Mukamal et al,[65] 2013	United States	782	45.5	About 73	T2D	10.4	10	CVD	265	Never	1.64 (1.08-2.50)	1.29 (0.98-1.70)
Mukamal et al,[65] 2013	United States	843	52.7	About 65	T2D	13.0	7	CVD	71	Never	1.05 (0.45-2.43)	1.24 (0.74-2.07)
Den Ruijter et al,[66] 2013	International	4220	Mixed	61	T2D	18	8.7	CVD	684	Never + Past	1.36 (1.13-1.63)	
Pinis et al,[67] 2014	Spain	659	52.8	63.5	T2D	16.1	8	CVD	192	Never	1.56 (1.03-2.38)	
Paul et al,[47] 2015	UK	82205	55	62	T2D	17	5.4	CVD	6865	Never	1.27 (1.18-1.37)	1.07 (1.02-1.13)
Vazquez-Benitez et al,[48] 2015	USA	859617	52.2	59	T2D	9.2	5.0	CVD	76318	Never + Past	Without CVD: 1.53 (1.47-1.61); with CVD: 1.30 (1.25-1.36)	
Swaminathan et al,[68] 2004	Scotland, United Kingdom	2101	55.4	<35	T1D	33	9 (max)	CVD	110	Never	2.26 (1.42-3.60)	1.39 (0.79-2.45)
Ford et al,[2] 1991	United States	492	37.3	>60 y	T2D	19.6	10	CHD deaths	62	Never	2.49 (0.94-6.59)	0.46 (0.10-2.13)
Hadden et al,[5] 1997	Ireland	405	56	55.8	T2D	36.8	10	MI	112	Never	2.09 (1.37-3.18)	
Adlerberth et al,[6] 1998	Sweden	249	100	56.1	T2D	41	16	CHD deaths	77	Never + Past	1.74 (1.09-2.77)	
Fuller et al,[50] 2001	International	1661	100	47	T2D	NR	12	MI	206	Never	1.2 (0.9-1.7)	1.2 (0.8-1.8)
Fuller et al,[50] 2001	International	1822	0	46.7	T2D	NR	12	MI	159	Never	1.4 (1.1-2.0)	0.8 (0.5-1.4)
Fuller et al,[50] 2001	International	659	100	44.4	T1D	NR	12	MI	64	Never	0.8 (0.4-1.6)	1.2 (0.6-2.4)
Fuller et al,[50] 2001	International	601	0	44.5	T1D	NR	12	MI	49	Never	1.0 (0.5-1.8)	0.3 (0.1-1.3)
Abu-Lebdeh et al,[69] 2001	United States	449	47	57	T2D	46	13	CHD	216	Never	1.45 (1.10-1.91)	

Florkowski et al,[10] 2001	New Zealand	344	46.5	62	T2D	15	10	CHD deaths	130	Never + Past	2.63 (1.20-5.77)	
Al-Delaimy et al,[56] 2002	United States	6547	0	About 62	T2D	20.0	20	CHD	458	Never	Two dose categories: 1.66 (1.10-2.52); 2.68 (2.07-3.48)	1.21 (0.97-1.51)
Aronow et al,[70] 2002	United States	529	32.3	79	T2D with prior MI	18.3	2.4	CHD	405	Never + Past	1.78 (1.40-2.26)	
Klein et al,[71] 2004	United States	899	50.7	About 30	T1D	23.4	20 (max)	Non-fatal CHD	225	Never	1.43 (1.10-1.81)[*]	1.82 (1.42-2.26)[a]
Soedamah-Muthu et al,[72] 2004	Europe	2329	51.6	32.1	T1D	30.9	7	CHD	151	Never	1.30 (0.93-1.83)	0.70 (0.46-1.09)
Donnan et al,[73] 2006	United Kingdom	4569	52.6	59.5	T2D	23.5	4.1	CHD	243	Never	1.31 (1.09-1.57)	1.01 (0.83-1.23)
Yang et al,[74] 2007	Hong Kong, China	7067	45.4	57	T2D	20.6	5.4	CHD	351	Never	1.58 (1.11-2.26)	1.13 (0.78-1.64)
Miller et al,[75] 2009	United States	448	49.3	25.4	T1D	19.4	18	CHD	80	Never	1.98 (1.15-3.43)	
Nilsson et al,[26] 2009	Sweden	13087	55.7	60.3	T2D	16.4	5.7	MI	1019	Never + Past	1.67 (1.43-1.95)	
Xu et al,[76] 2012	United States	1872	34	About 57	T2D	27.4	12.2	CHD	546	Never	1.58 (1.23-2.02)	1.13 (0.89-1.44)
Hayes et al,[77] 2013	United Kingdom	2910	100	about 52	T2D	34	17.6	MI	619	Never + Past	1.32 (1.10-1.58)	
Hayes et al,[77] 2013	United Kingdom	2042	0	about 52	T2D	25	17.6	MI	334	Never + Past	1.41 (1.08-1.85)	
Luo et al,[78] 2013	United States	6338	0	>60	T2D	4.1	8.8	CHD	492	Never	3.07 (2.15-4.39)	1.26 (1.03-1.53)
Tanaka et al,[79] 2013	Japan	1748	50.1	62.1	T2D	24.4	7.2	CHD	96	Never + Past	1.67 (1.00-2.81)	
Costanzo et al,[46] 2015	UK	10568	63	29	T2D	16	10.6	ACS	912	Never + Past	1.45 (1.21-1.73)	
Paul et al,[47] 2015	UK	82205	55	62	T2D	17	5.4	MI	2797	Never	1.31 (1.16-1.47)	1.19 (1.09-1.30)
Vazquez-Benitez et al,[48] 2015	USA	859617	52.2	59	T2D	9.2	5.0	CHD	28969	Never + Past	Without CVD: 1.64 (1.55-1.74); with CVD: 1.39 (1.32-1.46)	
Lehto et al,[80] 1996	Finland	1059	54.9	58.2	T2D	14.2	7	Stroke	125	Never + Past	1.50 (0.91-2.21)[*]	
Fuller et al,[50] 2001	International	1661	100	47	T2D	NR	12	Stroke	103	Never	2.2 (1.2-3.9)	2.1 (1.1-4.0)
Fuller et al,[50] 2001	International	1822	0	46.7	T2D	NR	12	Stroke	123	Never	1.3 (0.9-2.0)	1.2 (0.8-2.0)
Fuller et al,[50] 2001	International	659	100	44.4	T1D	NR	12	Stroke	37	Never	1.9 (0.8-5.1)	1.0 (0.3-3.2)
Fuller et al,[50] 2001	International	601	0	44.5	T1D	NR	12	Stroke	30	Never	1.1 (0.5-2.5)	1.3 (0.5-3.7)
Abu-Lebdeh et al,[69] 2001	United States	449	47	57	T2D	46	13	Stroke	115	Never	1.57 (1.07-2.30)	
Al-Delaimy et al,[56] 2002	United States	6547	0	About 62	T2D	20.0	20	Stroke	NR	Never	Two dose categories: 1.04 (0.50-2.17); 1.84 (1.21-2.81)	0.69 (0.48-1.00)
Aronow et al,[70] 2002	United States	529	32.3	79	T2D with prior MI	18.3	2.4	Stroke	157	Never + Past	3.44 (2.44-4.86)	
Giorda et al,[81] 2007	Italy	11644	48.2	65	T2D	14.0	4	Stroke	188	Never	M: 2.29 (1.36-3.87); F: 1.18 (0.47-2.94)	M: 1.17 (0.70-1.96); F: 0.71 (0.22-2.26)

Hitman et al,[82] 2007	UK and Ireland	2709	68	62.1	T2D	23	3.9	Stroke	57	Never	2.58 (1.24-5.35)	1.12 (0.56-2.23)
Yang et al,[83] 2007	Hong Kong, China	3668	45.5	57	T2D	20.0	5	stroke	190	Never + Past	1.34 (0.94-1.90)	
Nilsson et al,[26] 2009	Sweden	13087	55.7	60.3	T2D	16.4	5.7	Stroke	756	Never + Past	1.84 (1.51-2.22)	
Palmer et al,[84] 2010	United Kingdom	2123	52.6	64.5	T2D	50.8 (ever)	6.2	Stroke	104	Never	1.52 (1.0-2.3)	
Hankey et al,[85] 2013	Australia, New Zealand and Finland	9795	62.7	62.2	T2D	9.4	5	Stroke	333	Never + Past	1.52 (1.07-2.18)	
Hayes et al,[77] 2013	United Kingdom	4981	59	About 52	T2D	30.3	17.6	Stroke	490	Never + Past	1.39 (1.12-1.73)	
Costanzo et al,[46] 2015	UK	10568	63	29	T2D	16	10.6	ACS	760	Never + Past	1.24 (1.00-1.53)	
Paul et al,[47] 2015	UK	82205	55	62	T2D	17	5.4	Stroke	4380	Never	1.26 (1.15-1.38)	1.01 (0.94-1.08)
Vazquez-Benitez et al,[48] 2015	USA	859617	52.2	59	T2D	9.2	5.0	Stroke	25688	Never + Past	Without CVD: 1.53 (1.43-1.64); with CVD: 1.29 (1.22-1.36)	
Wattanakit et al,[86] 2005	United States	1651	46	56	T2D	21.5	10.3	PAD	238	Never	1.86 (1.26-2.75)	1.02 (0.69-1.51)
Norman et al,[53] 2006	Australia	474	48 8	64.1	T2D	15.0	5	PAD	75	Never	3.00 (1.78-4.38)[*]	1.13 (0.65-1.85)[a]
Althouse et al,[87] 2014	International	1479	72	61.9	T2D with CAD	11.5	4 6	PAD	303	Never + past	1.92 (1.67-3.41)	
Vaur et al,[88] 2003	Europe	4912	70	65	T2D	18	3 9	CHF	187	Never + Past	1.98 (1.15-3.40)	
Lind et al,[89] 2011	Sweden	20985	55	38 6	T1D	NR	9	HF	635	Never + Past	Two dose categories: 1.90 (1.52-2.38); 1.11 (0.84-1.47)	
Costanzo et al,[46] 2015	UK	10568	63	29	T2D	16	10.6	HF	598	Never + Past	1.32 (1.05-1.67)	
Vazquez-Benitez et al,[48] 2015	USA	859617	52.2	59	T2D	9.2	5.0	HF	33076	Never + Past	Without CVD: 1.53 (1.42-1.64); with CVD: 1.12 (1.07-1.18)	

Abbreviations: ACS: acute coronary syndrome; C-C, case-control; CHD, coronary heart disease; CHF: congestive heart failure; CVD, cardiovascular disease; HF: heart failure; MI, myocardial infarction; NR, not reported; PAD, peripheral arterial disease; T1D, type 1 diabetes; T2D, type 2 diabetes.

[*]The relative risk (RR) was converted from odds ratio (OR) by the formula $RR=OR/[(1-P_o)+(P_o \times OR)]$, in which P_o is the incidence of the outcome of interest in the nonexposed group. (Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA*. 1998;280:1690-1.)

Supplemental Table 3. Stratified Analyses of Smoking Status and Risk of Total and Cardiovascular Mortality among Diabetic Patients*

	Total mortality				**CVD mortality**			
	RR (95% CI)	*n* of reports	I^2 (%)	*P* for Heterogeneity	RR (95% CI)	*n* of reports	I^2 (%)	*P* for Heterogeneity
Overall results	1.55 (1.46-1.64)	50	77.6	<0.001	1.49 (1.29-1.71)	16	26.5	0.16
Trim and fill method	1.45 (1.38-1.53)	(65)	NA	NA	NA	NA	NA	NA
Former vs. never	1.19 (1.11-1.28)	13	53.8	0.01	1.15 (1.00-1.32)	8	0	0.44
Current vs. never	1.62 (1.49-1.76)	13	51.1	0.02	1.43 (1.18-1.73)	8	31.7	0.18
Ever vs. never	1.51 (1.20-1.90)	7	78.8	<0.001	1.67 (1.15-2.41)	2	0	0.78
Current vs. non-current	1.53 (1.43-1.63)	30	65.9	<0.001	1.51 (1.10-2.08)	6	46.6	0.10
Smoking exposure								
As a main exposure	1.66 (1.46-1.86)	4	68.5	0.02	2.18 (1.57-3.03)	1	NA	NA
As co-risk factor	1.58 (1.46-1.71)	18	75.5	<0.001	1.33 (1.15-1.55)	7	27.6	0.15
As a confounder	1.50 (1.36-1.66)	28	68.4	<0.001	1.51 (1.20-1.89)	8	32.6	0.17
Sex								
Men	1.87 (1.52-2.30)	3	0	0.89	1.30 (0.95-1.78)	3	0	0.51
Women	1.66 (1.35-2.05)	1	NA	NA	1.80 (1.29-2.51)	3	24.4	0.27
Mixed	1.53 (1.44-1.62)	46	78.8	<0.001	1.45 (1.21-1.72)	10	27.2	0.19
Type of diabetes								
T1D	1.77 (1.52-2.07)	6	0	0.79	1.91 (1.29-2.85)	3	0	0.49
T2D	1.53 (1.44-1.63)	41	81.0	<0.001	1.44 (1.24-1.68)	13	30.0	0.14
Unspecified, mixed	1.47 (1.33-1.63)	3	0	0.82	NA	NA	NA	NA
Study Location								
US	1.60 (1.46-1.76)	16	72.9	<0.001	1.69 (0.99-2.89)	2	74.4	0.048
Europe or Oceania	1.55 (1.41-1.71)	26	84.1	<0.001	1.41 (1.13-1.74)	8	38.7	0.12
Asia	1.40 (1.18-1.64)	6	8.9	0.36	1.67 (1.15-2.41)	2	0	0.78
International, others	1.45 (1.31-1.61)	2	0	0.92	1.38 (1.01-1.90)	4†	0	0.66
Ethnicity								
Caucasian Whites	1.61 (1.48-1.74)	27	50.1	0.002	1.45 (1.17-1.81)	9	54.7	0.02
East Asians	1.40 (1.18-1.64)	6	8.9	0.36	1.67 (1.15-2.41)	2	0	0.78
Others, mixed	1.51 (1.38-1.65)	17	89.4	<0.001	1.48 (1.13-1.93)	5	0	0.70
Mean age groups								
<60 years	1.55 (1.42-1.68)	24	77.0	<0.001	1.43 (1.25-1.64)	9	0	0.67

≥60 years	1.56 (1.42-1.70)	26	78.9	<0.001	1.45 (1.07-1.96)	7	57.0	0.03
Follow-up years								
<10 years	1.54 (1.43-1.66)	31	83.4	<0.001	1.62 (1.31-1.99)	8	8.3	0.37
≥10 years	1.56 (1.43-1.71)	19	51.8	0.005	1.41 (1.16-1.71)	8	38.6	0.12
Sample size								
<2000	1.58 (1.45-1.73)	30	26.6	0.09	1.43 (1.16-1.78)	10	28.5	0.18
≥2000	1.52 (1.41-1.64)	20	89.2	<0.001	1.54 (1.26-1.89)	6	35.0	0.17
Publication year								
≤2000	1.62 (1.32-1.98)	9	74.8	<0.001	2.23 (1.31-3.79)	1	NA	NA
2001-2009	1.57 (1.47-1.69)	18	0	0.82	1.48 (1.27-1.72)	13	26.0	0.18
≥2010	1.52 (1.40-1.65)	23	87.1	<0.001	1.24 (0.81-1.89)	2	9.7	0.29
Study quality[‡]								
High (8-9)	1.59 (1.47-1.72)	31	48.9	0.001	1.68 (1.04-2.70)	2	84.1	0.01
Low (≤7)	1.50 (1.38-1.64)	19	88.2	<0.001	1.44 (1.23-1.68)	14	6.5	0.38
Adjustment for BMI								
Yes	1.58 (1.50-1.66)	28	28.6	0.08	1.47 (1.12-1.93)	5	53.2	0.07
No	1.51 (1.38-1.66)	22	85.7	<0.001	1.49 (1.24-1.78)	11	15.5	0.30
Adjustment for blood pressures								
Yes	1.51 (1.43-1.60)	34	63.8	<0.001	1.44 (1.22-1.70)	13	29.9	0.15
No	1.64 (1.40-1.92)	16	88.2	<0.001	1.64 (1.22-2.22)	3	21.6	0.28
Adjustment for blood lipids								
Yes	1.47 (1.37-1.58)	30	80.1	<0.001	1.47 (1.24-1.73)	12	31.7	0.14
No	1.67 (1.56-1.80)	20	31.8	0.09	1.56 (1.13-2.16)	4	26.4	0.25
Adjustment for glycemic parameters								
Yes	1.52 (1.41-1.63)	32	84.8	<0.001	1.44 (1.12-1.85)	8	44.5	0.08
No	1.59 (1.48-1.70)	18	0	0.89	1.47 (1.25-1.72)	8	8.2	0.37
Adjustment for CVD								
Yes	1.57 (1.43-1.71)	27	80.8	<0.001	1.41 (1.01-1.97)	3	9.1	0.33
No	1.53 (1.41-1.67)	23	73.5	<0.001	1.50 (1.27-1.77)	13	33.8	0.11
Baseline CVD excluded								
Yes	NA	NA	NA	NA	1.44 (1.13-1.84)	7	55.9	0.03
No	NA	NA	NA	NA	1.54 (1.28-1.86)	9	0	0.60
Adjustment for								

microvascular complications								
Yes	1.52 (1.44-1.61)	23	64.1	<0.001	1.56 (1.29-1.87)	10	0	0.48
No	1.58 (1.40-1.78)	27	83.5	<0.001	1.42 (1.12-1.81)	6	55.9	0.045
Adjustment for physical activity								
Yes	1.65 (1.46-1.85)	11	35.7	0.11	1.50 (1.10-2.05)	4	63.5	0.042
No	1.52 (1.43-1.63)	39	80.7	<0.001	1.47 (1.24-1.74)	12	9.7	0.35
Adjustment for alcohol intake								
Yes	1.71 (1.36-2.16)	5	62.4	0.03	2.02 (1.51-2.69)	2	0	0.33
No	1.53 (1.44-1.62)	45	78.1	<0.001	1.40 (1.23-1.60)	14	7.7	0.37
Adjustment for dietary intake								
Yes	1.78 (1.17-2.71)	3	79.9	0.007	1.56 (0.86-2.82)	1	NA	NA
No	1.53 (1.45-1.63)	47	77.3	<0.001	1.48 (1.27-1.72)	15	31.3	0.12

Abbreviations: CI, confidence interval; RR, relative risk; CVD, cardiovascular disease; NA, not available; T1D, type 1 diabetes; T2D, type 2 diabetes.
[*]The results are presented using the random-effects model.
[†]The 4 reports were from the same study by Fuller et al.[50]
[‡]The study quality scored from 0 to 9, with higher score indicating higher quality.

Supplemental Table 4. Stratified Analyses of Smoking Status and Risk of Cardiovascular Disease Outcomes among Diabetic Patients*

	Total CVD				**CHD**				**Stroke**			
	RR (95% CI)	*n* of reports	I^2 (%)	*P* for Heterogeneity	RR (95% CI)	*n* of reports	I^2 (%)	*P* for Heterogeneity	RR (95% CI)	*n* of reports	I^2 (%)	*P* for Heterogeneity
Overall results	1.44 (1.34-1.54)	18	73.9	<0.001	1.51 (1.41-1.62)	26	60.7	<0.001	1.54 (1.41-1.69)	20	70.9	<0.001
Trim and fill method	1.37 (1.27-1.48)	(22)	NA	NA	1.48 (1.37-1.59)	(29)	NA	NA	1.40 (1.26-1.54)	(26)	NA	NA
Former vs. never	1.09 (1.05-1.13)	7	3.6	0.73	1.14 (1.00-1.30)	13	58.7	0.004	1.04 (0.87-1.23)	9	24.6	0.22
Current vs. never	1.55 (1.30-1.86)	7	82.3	<0.001	1.47 (1.29-1.69)	13	61.4	0.002	1.54 (1.26-1.88)	9	39.8	0.10
Ever vs. never	1.40 (1.04-1.89)	2	58.1	0.003	1.70 (1.33-2.18)	3	19.1	0.29	1.55 (1.17-2.05)	2	0	0.91
Current vs. non-current	1.41 (1.30-1.53)	9	71.5	<0.001	1.53 (1.41-1.65)	10	66.3	0.002	1.56 (1.39-1.77)	9	83.8	<0.001
Smoking exposure												
As a main exposure	1.70 (1.09-2.63)	3	92.1	<0.001	1.87 (1.37-2.55)	4	87.8	<0.001	1.53 (1.15-2.03)	3	84.5	0.002
As co-risk factor	1.39 (1.28-1.51)	10	76.6	<0.001	1.43 (1.33-1.55)	17	50.5	0.009	1.46 (1.33-1.61)	14	48.3	0.02
As a confounder	1.45 (1.26-1.68)	5	0	0.92	1.62 (1.41-1.86)	5	28.6	0.23	1.95 (1.13-3.35)	3	91.0	<0.001
Sex												
Men	2.07 (0.94-4.56)	1	NA	NA	1.37 (1.22-1.53)	6†	0	0.42	2.19 (1.53-3.14)	3	0	0.94
Women	2.11 (1.75-2.55)	1	NA	NA	1.69 (1.28-2.22)	7†	75.4	<0.001	1.40 (1.09-1.79)	4	0	0.77
Mixed	1.38 (1.30-1.47)	16	66.3	<0.001	1.50 (1.40-1.62)	15†	58.5	0.002	1.53 (1.39-1.69)	13	79.4	<0.001
Type of diabetes												
T1D	2.26 (1.42-3.60)	1	NA	NA	1.33 (1.07-1.66)	5	22.7	0.27	1.39 (0.76-2.56)	2	0	0.38
T2D	1.42 (1.32-1.52)	17	73.7	<0.001	1.53 (1.43-1.65)	21	65.1	<0.001	1.55 (1.41-1.70)	18	73.7	<0.001
Study Location												
US	1.57 (1.35-	6	89.1	<0.001	1.67 (1.48-	10	77.4	<0.001	1.68 (1.41-	7	86.6	<0.001

	1.82)				1.88)				2.01)			
Europe or Oceania	1.33 (1.25-1.40)	10	16.2	0.29	1.44 (1.33-1.56)	10	36.1	0.12	1.48 (1.30-1.69)	7	64.6	0.009
Asia	1.44 (0.85-2.45)	1	NA	NA	1.61 (1.20-2.16)	2	0	0.86	1.34 (0.94-1.91)	1	NA	NA
International, others	1.36 (1.13-1.63)	1	NA	NA	1.22 (1.00-1.49)	4‡	0	0.45	1.51 (1.20-1.89)	5	0	0.57
Ethnicity												
Caucasian Whites	1.58 (1.37-1.82)	10	58.6	0.01	1.53 (1.33-1.76)	8	30.4	0.19	1.74 (1.53-1.98)	8	0	0.72
East Asians	1.44 (0.85-2.45)	1	NA	NA	1.61 (1.20-2.16)	2	0	0.86	1.34 (0.94-1.91)	1	NA	NA
Others, mixed	1.35 (1.24-1.47)	7	84.2	<0.001	1.50 (1.39-1.63)	16	71.8	<0.001	1.49 (1.33-1.66)	11	79.9	<0.001
Mean age groups												
<60 years	1.42 (1.25-1.60)	5	89.4	<0.001	1.45 (1.34-1.56)	17	51.3	0.008	1.44 (1.31-1.59)	12	48.7	0.03
≥60 years	1.46 (1.32-1.61)	13	56.0	0.007	1.74 (1.49-2.05)	9	73.4	<0.001	1.71 (1.41-2.07)	8	83.5	<0.001
Follow-up years												
<10 years	1.38 (1.29-1.47)	15	68.0	<0.001	1.55 (1.40-1.72)	10	80.1	<0.001	1.59 (1.40-1.81)	12	81.9	<0.001
≥10 years	2.03 (1.71-2.40)	3	0	0.56	1.47 (1.35-1.59)	16	17.0	0.26	1.46 (1.34-1.58)	8	0	0.83
Sample size												
<2000	1.47 (1.26-1.73)	8	0	0.94	1.54 (1.38-1.72)	14	17.5	0.26	1.79 (1.28-2.49)	7	68.2	0.004
≥2000	1.43 (1.32-1.55)	10	85.5	<0.001	1.50 (1.38-1.63)	12	76.8	<0.001	1.46 (1.34-1.58)	13	66.2	<0.001
Publication year												
≤2000	1.44 (0.85-2.45)	1	NA	NA	1.97 (1.46-2.66)	3	0	0.75	1.50 (0.96-2.34)	1	NA	NA
2001-2009	1.71 (1.40-2.09)	5	57.7	0.05	1.49 (1.34-1.64)	14	31.5	0.12	1.80 (1.48-2.18)	12	54.5	0.01
≥2010	1.36 (1.27-1.46)	12	72.5	<0.001	1.50 (1.37-1.66)	9	80.2	<0.001	1.39 (1.28-1.50)	7	69.7	0.003
Baseline outcome cases excluded												

Yes	1.56 (1.37-1.78)	10	75.5	<0.001	1.59 (1.45-1.74)	16	51.5	0.009	1.56 (1.46-1.66)	13	1.4	0.43
No	1.31 (1.26-1.54)	6	0	0.63	1.41 (1.31-1.53)	10	37.2	0.11	1.51 (1.31-1.74)	7	83.2	<0.001
Unclear	1.37 (1.15-1.63)	2	0	0.85								
Study quality[§]												
High (8-9)	2.03 (1.71-2.40)	3	0	0.56	1.84 (1.56-2.17)	9	45.6	0.07	1.64 (1.43-1.88)	6	12.6	0.33
Low (≤7)	1.38 (1.29-1.47)	15	68.0	<0.001	1.43 (1.34-1.54)	17	57.9	0.002	1.51 (1.36-1.67)	14	75.5	<0.001
Adjustment for BMI												
Yes	1.51 (1.29-1.76)	7	77.6	<0.001	1.69 (1.49-1.93)	12	64.7	0.001	1.71 (1.41-2.08)	8	83.6	<0.001
No	1.40 (1.29-1.53)	11	73.9	<0.001	1.43 (1.32-1.55)	14	59.0	0.003	1.44 (1.31-1.58)	12	48.4	0.03
Adjustment for blood pressures												
Yes	1.46 (1.35-1.59)	16	74.8	<0.001	1.58 (1.46-1.70)	19	65.0	<0.001	1.60 (1.43-1.78)	14	76.7	<0.001
No	1.28 (1.19-1.37)	2	0	0.53	1.31 (1.19-1.43)	7	0	0.65	1.29 (1.18-1.40)	6	0	0.46
Adjustment for blood lipids												
Yes	1.46 (1.35-1.58)	17	73.2	<0.001	1.63 (1.48-1.79)	16	67.4	<0.001	1.59 (1.40-1.82)	10	81.9	<0.001
No	1.27 (1.18-1.37)	1	NA	NA	1.37 (1.28-1.47)	10	10.2	0.35	1.45 (1.27-1.64)	10	38.6	0.10
Adjustment for glycemic parameters												
Yes	1.44 (1.33-1.55)	16	76.6	<0.001	1.49 (1.39-1.59)	15	61.0	0.001	1.46 (1.35-1.59)	13	66.4	<0.001
No	1.40 (1.14-1.71)	2	3.1	0.31	1.55 (1.28-1.88)	11	62.8	0.003	1.78 (1.27-2.50)	7	68.5	0.004
Adjustment for CVD												
Yes	1.31 (1.24-1.39)	5	0	0.49	1.43 (1.30-1.57)	7	32.2	0.18	1.58 (1.31-1.92)	6	84.4	<0.001
No	1.48 (1.35-	13	79.3	<0.001	1.54 (1.42-	19	65.2	<0.001	1.54 (1.37-	14	60.8	0.002

	1.63)				1.68)				1.72)			
Adjustment for microvascular complications												
Yes	1.40 (1.25-1.57)	4	89.0	<0.001	1.50 (1.39-1.62)	10	63.3	0.004	1.51 (1.36-1.67)	9	73.0	<0.001
No	1.47 (1.32-1.64)	14	63.9	0.001	1.56 (1.36-1.78)	16	61.3	0.001	1.61 (1.31-1.98)	11	71.8	<0.001
Adjustment for physical activity												
Yes	2.11 (1.75-2.55)	1	NA	NA	2.07 (1.53-2.82)	5	59.0	0.045	1.60 (1.11-2.30)	1	NA	NA
No	1.38 (1.30-1.48)	17	64.8	<0.001	1.46 (1.37-1.56)	21	53.9	0.002	1.54 (1.40-1.69)	19	72.2	<0.001
Adjustment for alcohol intake												
Yes	2.11 (1.75-2.55)	1	NA	NA	2.67 (1.91-3.73)	2	25.3	0.25	1.60 (1.11-2.30)	1	NA	NA
No	1.38 (1.30-1.48)	17	64.8	<0.001	1.47 (1.39-1.56)	24	48.9	0.004	1.54 (1.40-1.69)	19	72.2	<0.001
Adjustment for dietary intake												
Yes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
No	1.44 (1.34-1.54)	18	73.9	<0.001	1.51 (1.41-1.62)	26	60.7	<0.001	1.54 (1.41-1.69)	20	70.9	<0.001

Abbreviations: CHD, coronary heart disease; CI, confidence interval; RR, relative risk; CVD, cardiovascular disease; NA, not available; T1D, type 1 diabetes; T2D, type 2 diabetes.

[*]The results are presented using the random-effects model.

[†]Two studies[26,72] further reported their results separately for men and women, in addition to the overall results; thus there are 28 reports from 21 studies.

[‡]The 4 reports are from the same study by Fuller et al.[50]

[§]The study quality scored from 0 to 9, with higher score indicating higher quality.

Supplemental Table 5. Calculation of Population Attributable Fraction for Various Health Outcomes Associated with Smoking among Type 2 Diabetic Patients*

	Total mortality	CVD mortality	Total CVD	CHD	Stroke
Global					
Smoking prevalence (%)†	31.1 (M) 6.2 (F)	31.1 (M) 6.2 (F)	31.1 (M) 6.2 (F)	31.1 (M) 6.2 (F)	31.1 (M) 6.2 (F)
RR (95% CI)	1.55 (1.46-1.64)	1.49 (1.29-1.71)	1.44 (1.34-1.55)	1.51 (1.41-1.62)	1.54 (1.41-1.69)
PAF (%)	14.6 (12.5-16.6) (M) 3.3 (2.8-3.8) (F)	13.2 (8.3-18.1) (M) 2.9 (1.8-4.2) (F)	12.0 (9.6-14.4) (M) 2.7 (2.1-3.2) (F)	13.7 (11.3-16.2) (M) 3.1 (2.5-3.7) (F)	14.4 (11.3-17.7) (M) 3.2 (2.5-4.1) (F)
United States					
Smoking prevalence (%)†	17.2 (M) 14.3 (F)	17.2 (M) 14.3 (F)	17.2 (M) 14.3 (F)	17.2 (M) 14.3 (F)	17.2 (M) 14.3 (F)
RR (95% CI)	1.60 (1.46-1.76)	1.49 (1.29-1.71)‡	1.57 (1.35-1.82)	1.67 (1.48-1.8)	1.68 (1.41-2.01)
PAF (%)	9.4 (7.3-11.6) (M) 7.9 (6.2-9.8) (F)	7.8 (4.8-10.9) (M) 6.5 (4.0-9.2) (F)	8.9 (5.7-12.4) (M) 7.5 (4.8-10.5) (F)	10.3 (7.6-13.1) (M) 8.7 (6.4-11.2) (F)	10.5 (6.6-14.8) (M) 8.9 (5.5-12.6) (F)
United Kingdome					
Smoking prevalence (%)†	23.0 (M) 20.1 (F)	23.0 (M) 20.1 (F)	23.0 (M) 20.1 (F)	23.0 (M) 20.1 (F)	23.0 (M) 20.1 (F)
RR (95% CI)	1.55 (1.41-1.71)	1.41 (1.13-1.74)	1.33 (1.25-1.40)	1.44 (1.33-1.56)	1.48 (1.30-1.69)
PAF (%)	11.2 (8.6-14.0) (M) 10.0 (7.6-12.5) (F)	8.6 (2.5-14.5) (M) 7.6 (2.5-12.9) (F)	7.1 (5.4-8.4) (M) 6.2 (4.8-7.4) (F)	9.2 (7.1-11.4) (M) 8.1 (6.2-10.1) (F)	9.9 (6.5-13.7) (M) 8.8 (5.7-12.2) (F)
China					
Smoking prevalence (%)†	45.1 (M) 2.1 (F)	45.1 (M) 2.1 (F)	45.1 (M) 2.1 (F)	45.1 (M) 2.1 (F)	45.1 (M) 2.1 (F)
RR (95% CI)	1.40 (1.18-1.64)	1.49 (1.29-1.71)‡	1.44 (1.34-1.55)‡	1.51 (1.41-1.62)‡	1.54 (1.41-1.69)
PAF (%)	15.3 (7.5-22.4) (M) 0.8 (0.4-1.3) (F)	18.1 (11.6-24.3) (M) 1.0 (0.6-1.5) (F)	16.6 (13.3-19.6) (M) 0.9 (0.7-1.1) (F)	18.7 (15.6-21.9) (M) 1.1 (0.9-1.3) (F)	19.6 (15.6-23.7) (M) 1.1 (0.9-1.4) (F)

Abbreviations: CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; F, female; RR, relative risk; M, male; PAF, population attributable fraction.

*Population attributable fraction was calculated as $PAF=100\% \times P_e(RR-1)/(P_e[RR-1]+1)$, where P_e was the prevalence of smoking in the population and RR was derived from this meta-analysis.

†The smoking prevalence data were from the a recent JAMA paper about global prevalence of daily smoking among 187 countries (Ng M, Freeman MK, Fleming TD, et al. Smoking prevalence and cigarette consumption in 187 countries, 1980-2012. *JAMA* 2014;311:183–92).

‡For risk estimates pooled from less than 3 studies, we used the overall pooled RR to achieve a stable estimate; otherwise, country/region specific risk estimates were used.

Supplemental Figure 1. Adjusted Relative Risks of Smoking with (A) Peripheral Arterial Disease and (B) Heart Failure among Diabetic Participants

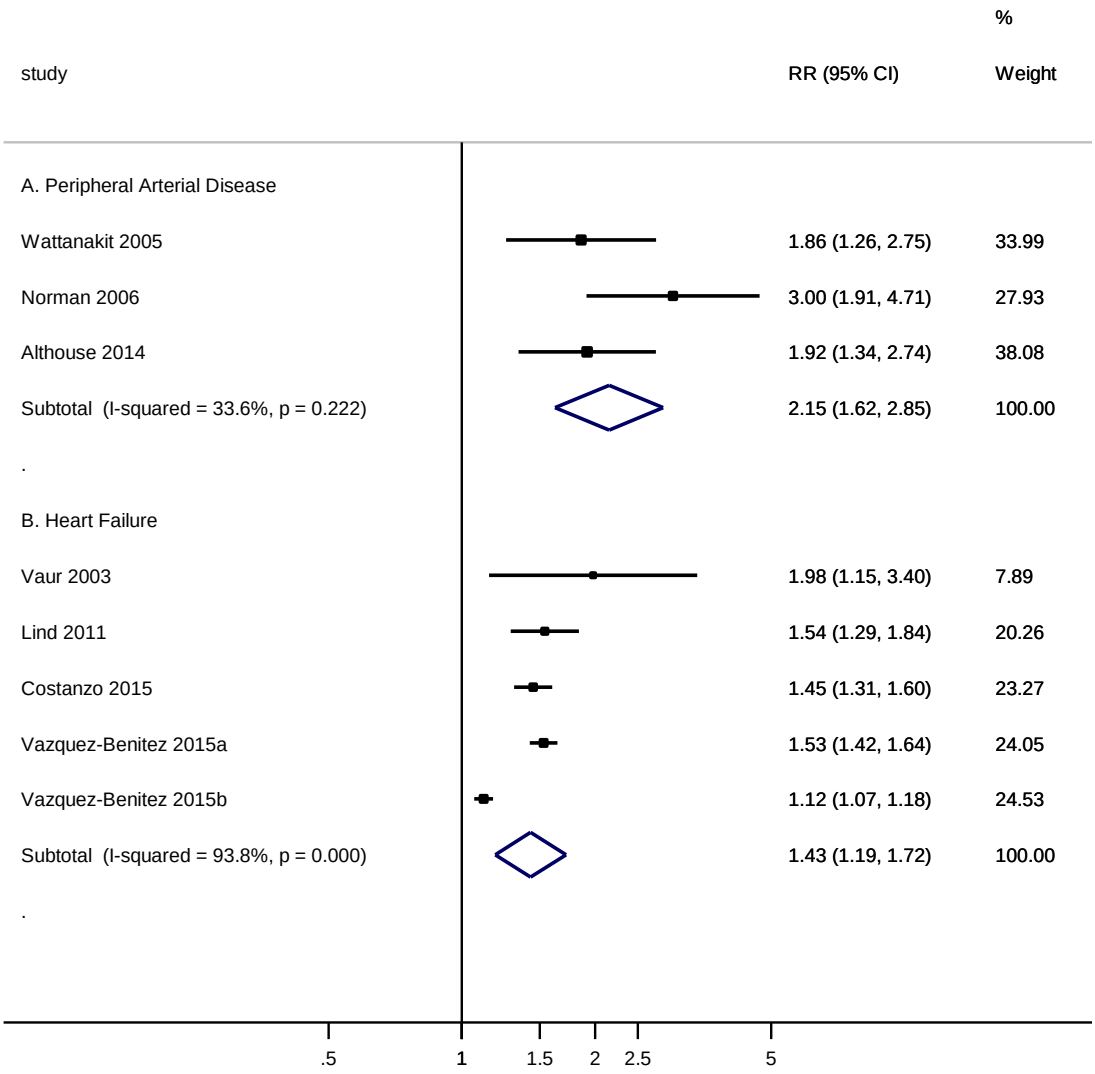

Figure legend

The summary estimates were obtained using a random-effects model. The data markers indicate the adjusted relative risks (RRs) comparing smoking to no smoking. The size of the data markers indicates the weight of the study, which is the inverse variance of the effect estimate. The diamond data markers indicate the pooled RRs. CI indicates confidence interval.

Supplemental Figure 2. Funnel Plots for (A) Detection of Publication Bias and (B) Trim-and-Fill Correction for Publication Bias for Total Mortality

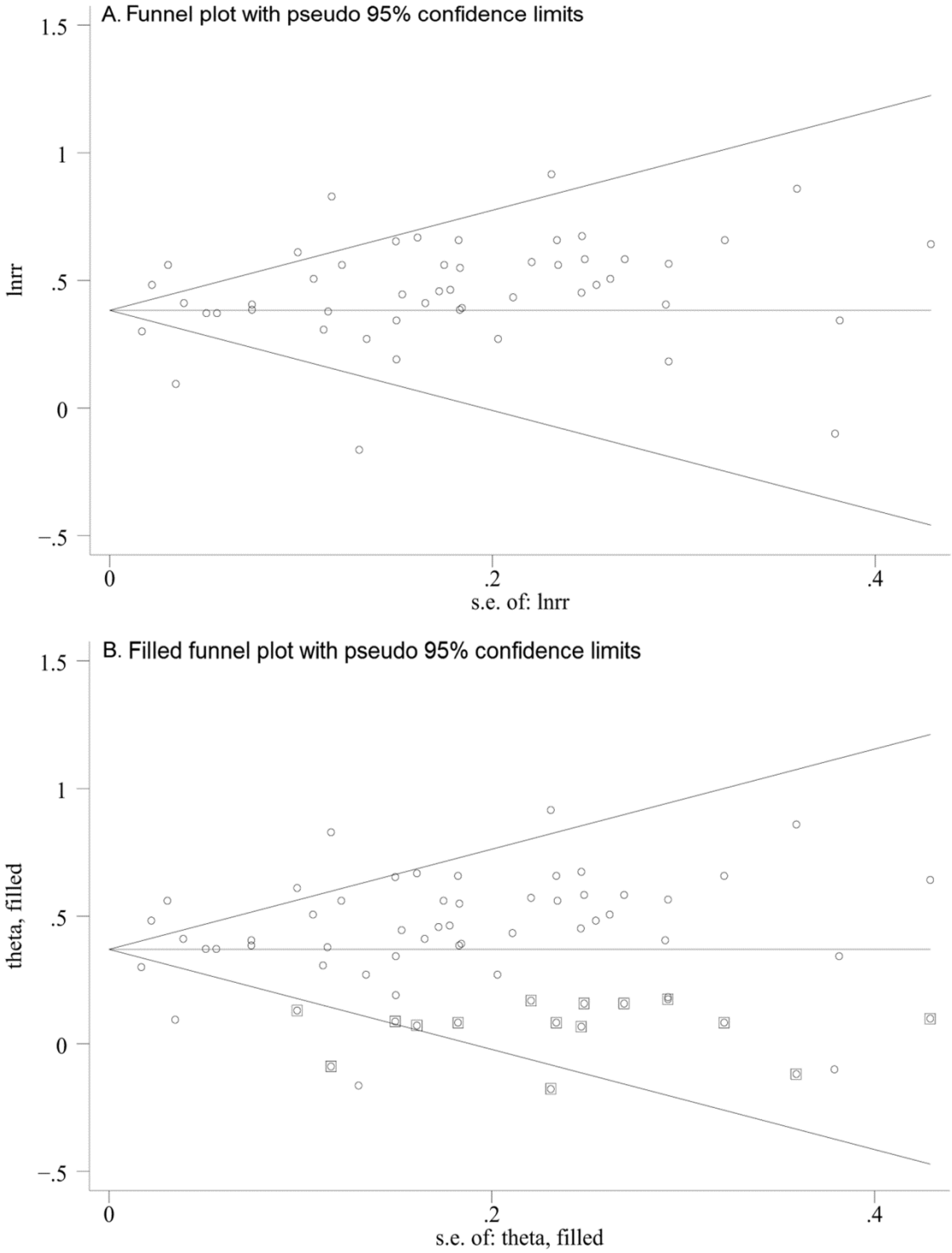

Figure legends:

The pseudo 95% confidence interval (CI) is computed as part of the analysis that produces the funnel plot, and corresponding to the expected 95% CI for a given standard error (SE). RR indicates relative risk.

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