CAPTURE: a multinational, cross-sectional study of cardiovascular disease prevalence in adults with type 2 diabetes across 13 countries

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ADDITIONAL MATERIAL

Methods S1. **List of cardiovascular (CV) medications in the CAPTURE study**

Alirocumab, amlodipine, atenolol, atorvastatin, bisoprolol, candesartan, captopril, carvedilol, clopidogrel, digoxin, dronedarone, edoxaban, enalapril, evolocumab, ezetimibe, fenofibrate, furosemide, glyceryl trinitrate, hydrochlorothiazide, indapamide, irbesartan, isosorbide mononitrate, ivabradine, lisinopril, losartan, metoprolol, nebivolol, nicotinic acid, nifedipine, perindopril, prasugrel, pravastatin, propranolol, ramipril, ranolazine, rosuvastatin, sacubitril, simvastatin, sotalol, spironolactone, telmisartan, ticagrelor, torasemide, trandolapril, valsartan and warfarin.

Methods S2. Additional methodological details for the multivariable logistic regression analyses

Candidate covariates

The candidate covariates were country, gender, age, diabetes duration, body mass index (BMI), glycated hemoglobin (HbA_{1c}), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, smoking status, hypertension, nephropathy, neuropathy, and retinopathy. Some parameters with a high proportion of missing data were not considered as candidate covariates (albuminuria, estimated glomerular filtration rate [eGFR], and physical activity; refer to Table S2). Additional sensitivity analyses were performed including eGFR as a candidate covariate.

Main analysis

Cardiovascular disease (CVD) prevalence odds ratios (PORs) were estimated in SAS PROC LOGISTIC using multivariable logistic regression models with CVD (yes/no) as dependent variable and the following covariates: model 0: country (crude bivariable model); model 1: country, gender, and age; model 2: country, gender, age, diabetes duration, BMI, HbA_{1c}, LDL cholesterol, HDL cholesterol, smoking status, hypertension, nephropathy, neuropathy, and retinopathy. The overall CAPTURE study sample was included as the reference group, with data for participants with

available covariate information merged with the dataset (i.e. doubling the number of observations). Missing data for LDL cholesterol were imputed using the following formulae (when data for non-HDL cholesterol were available):

LDL cholesterol (mg/dL) = non-HDL cholesterol (mg/dL) minus 30

LDL cholesterol (mmol/L) = LDL cholesterol (mg/dL) divided by 38.61

Other missing data were imputed by fully conditional specification. Missing data for LDL and HDL cholesterol in 110 participants from France could not be imputed. The final (reduced) model 2 (described above) was chosen via backwards selection method starting with a full (saturated) model including all clinically important demographic and clinical characteristics, which are those moderately associated with CVD prevalence in bivariable logistic regression (significance level of $p < 0.25$) and without multicollinearity (variance inflation factor ≤ 5) from the list of candidate covariates. Backwards selection was performed with a significance threshold of $p < 0.05$.

Sensitivity analyses

Sensitivity analyses were performed where the analysis (described above) was repeated (1) without imputation of missing demographic and clinical data (analyses performed for participants with complete covariate information); and (2) including eGFR as a candidate covariate with and without imputation of missing demographic and clinical data.

Table S1. Definition of CVD diagnoses in the CAPTURE study

CVD subtype	Accepted diagnoses	Further optional details
Cerebrovascular disease	Ischemic stroke	–
	Hemorrhagic stroke	–
	Unspecified stroke	–
	Transient ischemic attack	–
CHD	Myocardial infarction	–
	Stable coronary artery disease	Also referred to as angina pectoris
	Other ischemic heart disease	–
	Past revascularization procedure	–
Heart failure	Symptomatic heart failure	NYHA group II–IV or unknown; LVEF (%) < 40, 40–< 50, ≥ 50%, or unknown
	Asymptomatic heart failure	NYHA group I with LVEF (%) < 40, 40–< 50, ≥ 50%, or unknown
	Hospitalization for heart failure	–
Cardiac arrhythmia and conduction abnormalities	Atrial fibrillation	–
	Atrial flutter	–
	Ventricular tachycardia	–
	Supraventricular tachycardia	–
	Ventricular fibrillation	–
	Bradyarrhythmia	Sinus node dysfunction or atrioventricular block
Aortic disease	Aortic dissection	–
	Aortic aneurysm	–
	Thromboembolic aortic disease	–
PAD	Asymptomatic PAD	Low ankle-branchial index (< 0.90) or pulse abolition
	Claudication	–
	Limb ischemia	–
	Non-traumatic amputation	–
Carotid artery disease	Carotid artery disease	–

CHD coronary heart disease, *CVD* cardiovascular disease, *LVEF* left ventricular ejection fraction, *NYHA* New York Heart Association functional classification, *PAD* peripheral artery disease

Table S2. Distribution of missing data for demographic and clinical parameters considered as potential variables in the multivariable logistic regression analyses

Country n	Age	Sex	BMI	Hypertension	eGFR	Albuminuria	Physical activity	Smoking status	Diabetes duration	HbA_{1c}	LDL cholesterol	HDL cholesterol
Argentina (n = 834)	0	0	0	5	248	268	118	8	0	71	138	143
Australia (n = 824)	0	0	74	21	19	136	136	12	6	17	75	75
Brazil (n = 912)	0	0	5	3	238	500	73	5	0	136	202	181
China (n = 805)	0	0	17	36	512	422	282	35	0	181	275	286
Czech Republic (n = 400)	0	0	0	1	21	123	45	0	0	2	27	26
France (n = 659)	0	0	0	6	53	170	116	0	0	5	91	96
Hungary (n = 400)	0	0	0	6	17	186	114	0	0	2	148	138
Israel (n = 869)	0	0	26	15	56	97	169	27	0	23	34	36
Italy (n = 816)	0	0	0	12	129	164	365	0	0	17	123	95
Japan (n = 800)	0	0	81	16	172	302	236	11	1	6	108	124
Mexico (n = 820)	0	0	0	1	295	520	126	0	0	234	307	317
KSA (n = 883)	0	0	2	7	69	215	397	0	3	7	62	270
Turkey (n = 801)	0	0	7	51	71	238	154	0	2	18	42	71
Overall (N = 9,823)	0	0	212	180	1,900	3,341	2,331	98	12	719	1,632	1,858

Data are number of participants with missing information

BMI body mass index, *eGFR* estimated glomerular filtration rate, *HbA_{1c}* glycated hemoglobin, *HDL* high-density lipoprotein, *KSA* Kingdom of Saudi Arabia, *LDL* low-density lipoprotein

Table S3. Additional descriptive statistics summarizing the demographic and clinical characteristics of the CAPTURE study sample overall and stratified by CVD status

Characteristic minimum; maximum mean ± standard deviation	**Overall** **N = 9,823**		**By CVD status**			
			CVD **n = 3,582**		**Non-CVD** **n = 6,241**	
	n	**Data**	**n**	**Data**	**n**	**Data**
Age, years	9,823	18.0; 97.0 63.4 ± 11.4	3,582	29.0; 97.0 67.4 ± 10.0	6,241	18.0; 96.0 61.2 ± 11.5
Diabetes duration, years	9,811	0.5; 60.0 12.4 ± 8.6	3,577	0.5; 60.0 14.5 ± 9.2	6,234	0.5; 52.6 11.2 ± 8.1
HbA_{1c}, %	9,104	3.10; 29.00 7.68 ± 1.65	3,289	4.00; 18.90 7.73 ± 1.61	5,815	3.10; 29.00 7.65 ± 1.67
HbA_{1c}, mmol/mol	9,104	10; 293 60 ± 18	3,289	20; 183 61 ± 18	5,815	10; 293 60 ± 18
FPG, mmol/L	8,204	1.80; 33.80 8.32 ± 3.14	2,924	2.28; 33.57 8.31 ± 3.15	5,280	1.80; 33.80 8.33 ± 3.13
Body weight, kg	9,742	33.0; 190.0 81.3 ± 18.3	3,550	33.0; 178.0 81.5 ± 18.2	6,192	36.0; 190.0 81.2 ± 18.5
BMI, kg/m^2	9,611	14.5; 66.1 29.9 ± 5.9	3,514	14.5; 64.2 29.8 ± 5.8	6,097	16.2; 66.1 29.9 ± 6.0
Systolic blood pressure, mmHg	9,618	76.0; 251.0 132.2 ± 16.3	3,531	76.0; 251.0 132.5 ± 17.2	6,087	80.0; 226.0 132.1 ± 15.8
Diastolic blood pressure, mmHg	9,616	10.0; 133.0 76.9 ± 10.2	3,529	39.0; 129.0 75.5 ± 10.6	6,087	10.0; 133.0 77.7 ± 9.9
Total cholesterol, mmol/L	8,272	1.03; 14.80 4.48 ± 1.18	3,001	1.03; 12.76 4.21 ± 1.19	5,271	1.20; 14.80 4.63 ± 1.14
LDL cholesterol, mmol/L	8,090	0.20; 10.39 2.51 ± 0.95	2,924	0.20; 10.39 2.27 ± 0.94	5,166	0.39; 7.67 2.64 ± 0.94
HDL cholesterol, mmol/L	7,965	0.24; 5.54 1.21 ± 0.35	2,907	0.36; 5.54 1.16 ± 0.34	5,058	0.24; 3.65 1.24 ± 0.35
Triglyceride, mmol/L	8,466	0.25; 36.90 1.89 ± 1.36	3,082	0.25; 36.90 1.91 ± 1.42	5,384	0.30; 24.45 1.88 ± 1.33
Duration of smoking[a], years	3,733	0.0; 70.0 26.9 ± 14.4	1,646	0.0; 70.0 29.0 ± 14.9	2,087	0.0; 62.0 25.3 ± 13.8

To convert the values for glucose to mg/dL, divide by 0.0555. To convert the values for cholesterol to mg/dL, divide by 0.0259. To convert the values for triglycerides to mg/dL, divide by 0.0113. Data were not weighted

[a]Only applies to participants categorized as current or previous smokers

BMI body mass index, *CVD* cardiovascular disease, *FPG* fasting plasma glucose, HbA_{1c} glycated hemoglobin, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein

Table S4. Overall weighted prevalence of CVD in people with type 2 diabetes by CVD subtype and diagnosis

CVD diagnosis	n	Prevalence estimate [95% CI]
Cerebrovascular disease	672	7.2 [5.9; 8.4]
Ischemic stroke	403	5.0 [3.9; 6.0]
Hemorrhagic stroke	45	0.3 [0.1; 0.4]
Stroke, unspecified	117	1.2 [0.7; 1.8]
Transient ischemic attack	141	0.8 [0.4; 1.3]
Carotid artery disease	627	8.4 [7.0; 9.7]
Coronary heart disease	2,078	17.7 [16.2; 19.3]
Myocardial infarction	930	4.6 [4.0; 5.2]
Stable coronary artery disease	639	10.9 [9.5; 12.4]
Other ischemic heart disease	524	1.8 [1.3; 2.3]
Past revascularization procedures	972	4.5 [3.8; 5.2]
Heart failure	579	2.4 [2.1; 2.7]
Symptomatic heart failure	397	1.8 [1.5; 2.1]
NYHA group II	176	1.0 [0.8; 1.2]
NYHA group III	91	0.3 [0.2; 0.4]
NYHA group IV	23	0.2 [0.0; 0.3]
NYHA unknown	104	0.3 [0.2; 0.3]
LVEF ≥ 50%	105	0.5 [0.4; 0.6]
LVEF 40–< 50%	67	0.3 [0.2; 0.4]
LVEF < 40%	106	0.4 [0.3; 0.5]
LVEF unknown	116	0.6 [0.3; 0.8]
Asymptomatic heart failure (NYHA group I)	195	0.6 [0.5; 0.7]
LVEF ≥ 50%	81	0.2 [0.1; 0.3]
LVEF 40–< 50%	36	0.1 [0.1; 0.2]

LVEF < 40%	25	0.1 [0.0; 0.1]
LVEF unknown	52	0.2 [0.1; 0.3]
Hospitalization for heart failure	170	0.5 [0.4; 0.6]
Cardiac arrhythmia and conduction abnormalities	685	4.2 [3.4; 5.1]
Atrial fibrillation	417	2.0 [1.4; 2.5]
Atrial flutter	27	0.2 [0.0; 0.3]
Supraventricular tachycardia	102	0.9 [0.4; 1.3]
Ventricular tachycardia	47	0.1 [0.1; 0.2]
Ventricular fibrillation	16	0.0 [0.0; 0.1]
Bradyarrhythmia sinus node dysfunction	34	0.4 [0.1; 0.7]
Bradyarrhythmia AV block	93	0.8 [0.4; 1.2]
Aortic disease	96	0.4 [0.2; 0.6]
Aortic dissection	14	0.1 [0.0; 0.3]
Aortic aneurysms	45	0.1 [0.1; 0.2]
Thromboembolic aortic disease	38	0.2 [0.0; 0.3]
Peripheral artery disease	489	2.6 [2.0; 3.1]
Asymptomatic peripheral artery disease	169	1.3 [0.8; 1.7]
Claudication	225	0.7 [0.6; 0.9]
Limb ischemia	84	0.4 [0.2; 0.7]
Non-traumatic amputation	75	0.2 [0.2; 0.3]

Data are overall prevalence estimates (95% CI), which were calculated as weighted estimates to account for the size of the diabetes population of each country [ref 1] and the sampling of participants by healthcare setting, if it was different from as planned. n numbers are the crude data (i.e. they were not weighted). Diagnoses are not mutually exclusive; one participant may have multiple diagnoses

AV atrioventricular, *CI* confidence interval, *CVD* cardiovascular disease, *LVEF* left ventricular ejection fraction, *n* number of participants with diagnosis, *NYHA* New York Heart Association Functional Classification

Figure S1. Participant flow through the CAPTURE study

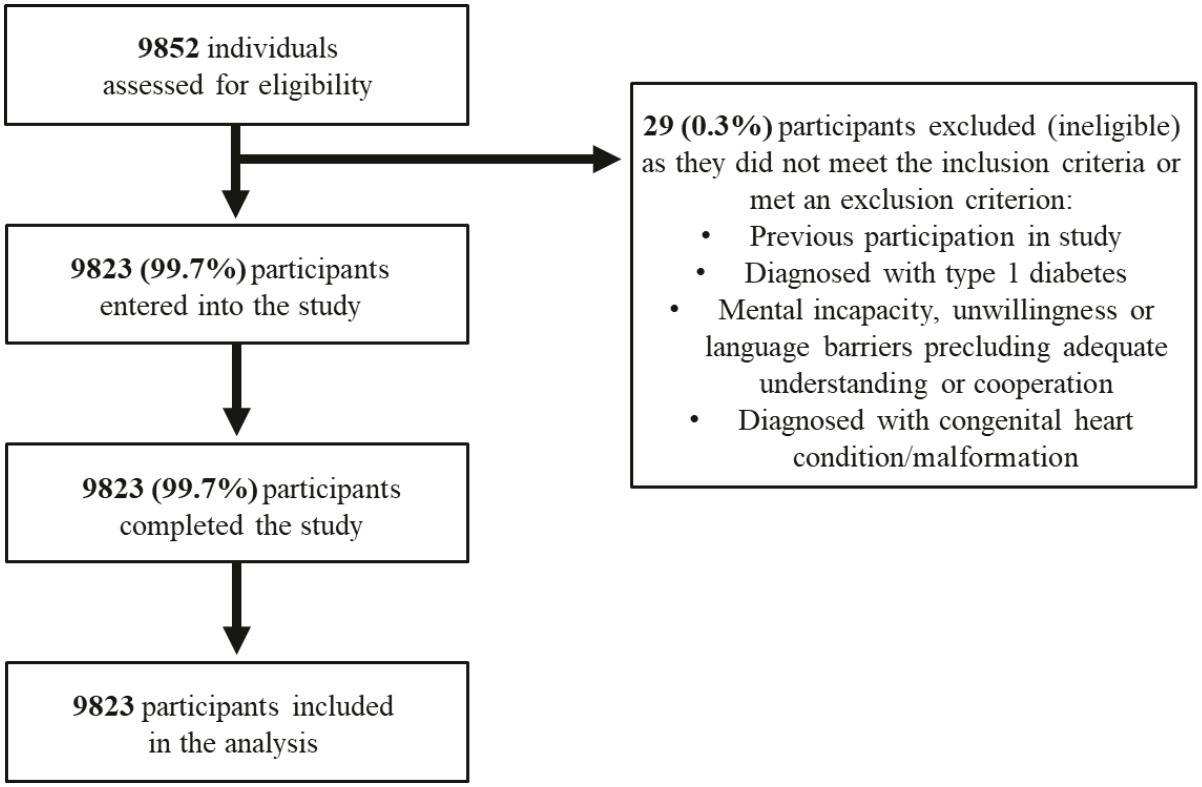
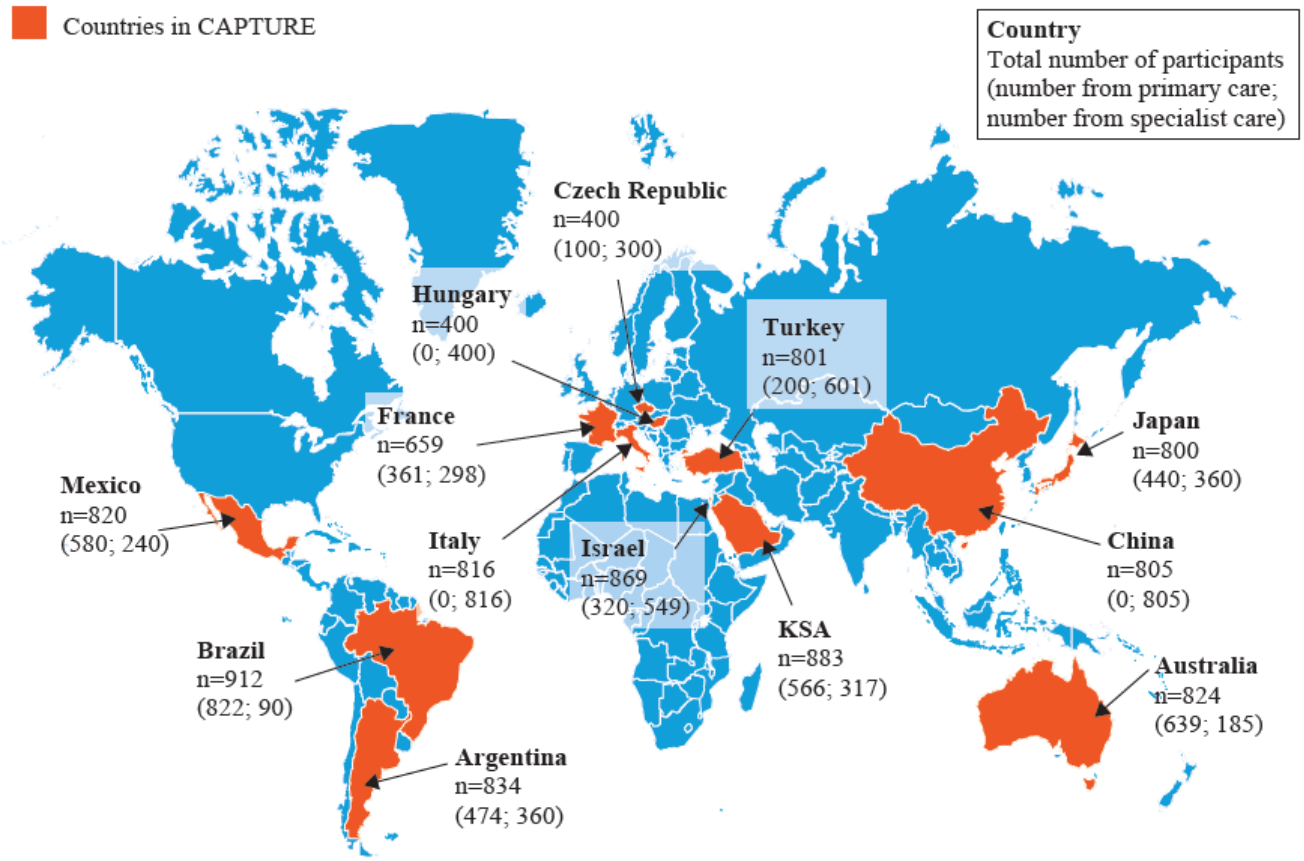
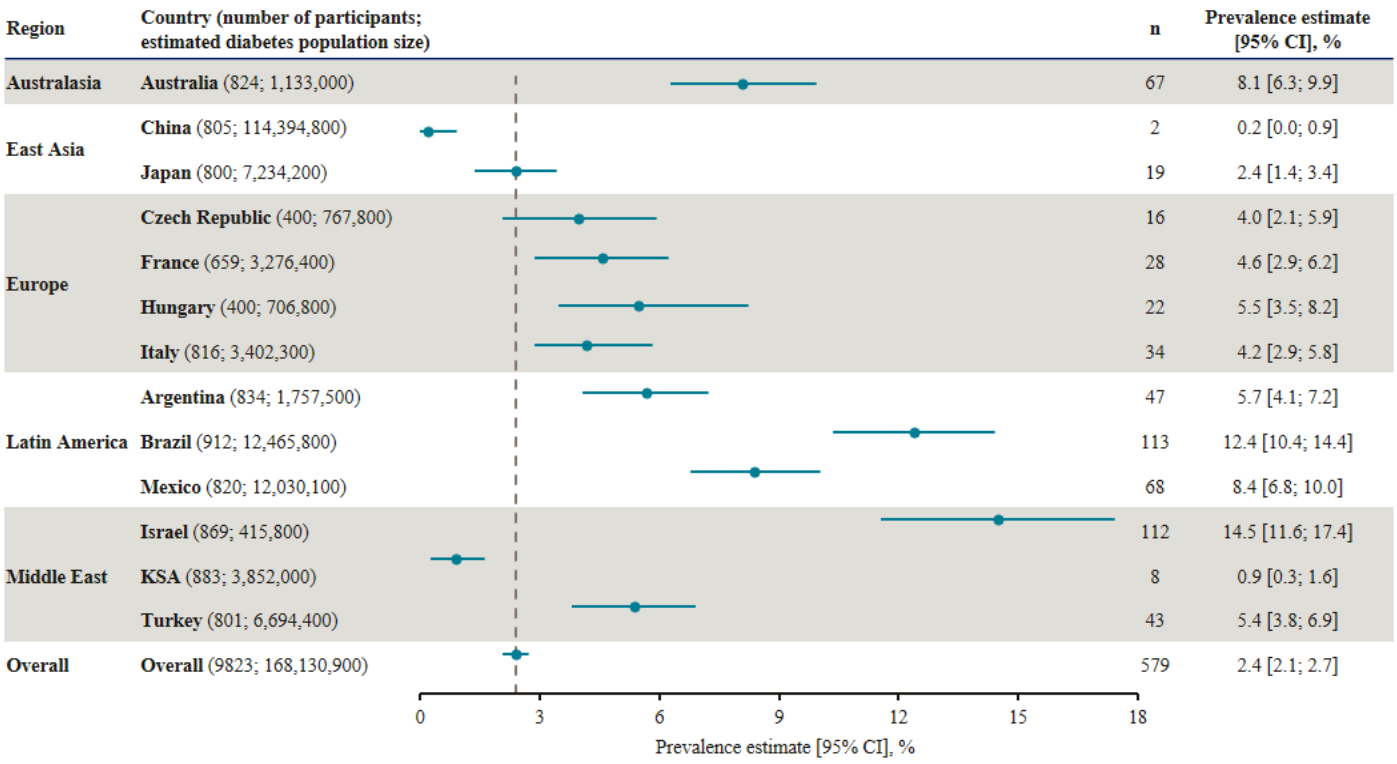


Figure S2. Global distribution of the CAPTURE study participants



KSA Kingdom of Saudi Arabia

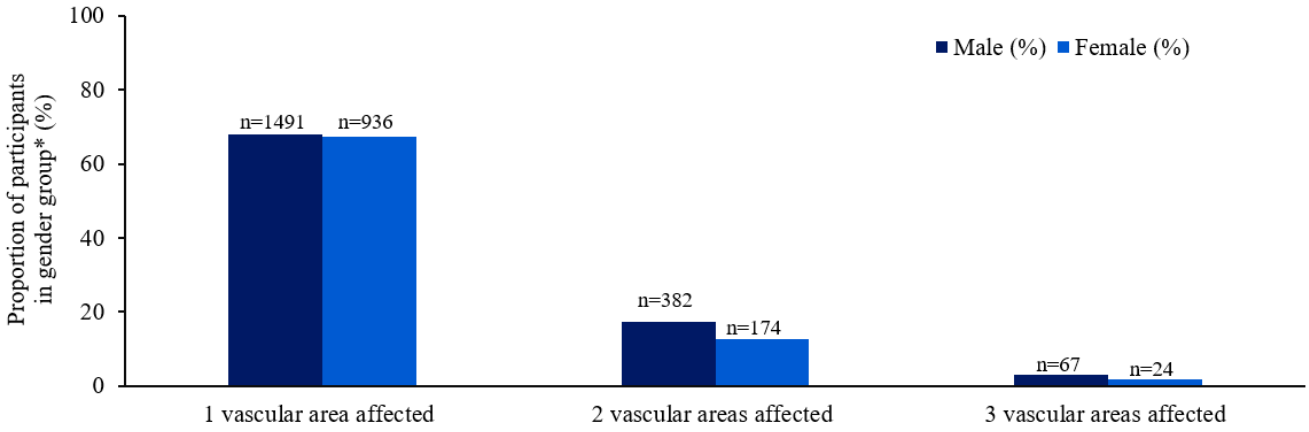
Figure S3. Weighted prevalence of heart failure in people with type 2 diabetes across the 13 countries (by country and overall)



The overall prevalence estimate (across the 13 countries) was calculated as a weighted estimate to account for the size of the diabetes population of each country [ref 1] and is represented by the grey dotted line. Both the overall and country-level prevalence estimates were weighted by the sampling of participants by healthcare setting, if it was different from as planned. n numbers are the crude number of participants with heart failure (i.e. they were not weighted)

CI confidence interval, *KSA* Kingdom of Saudi Arabia, *n* number of participants with heart failure

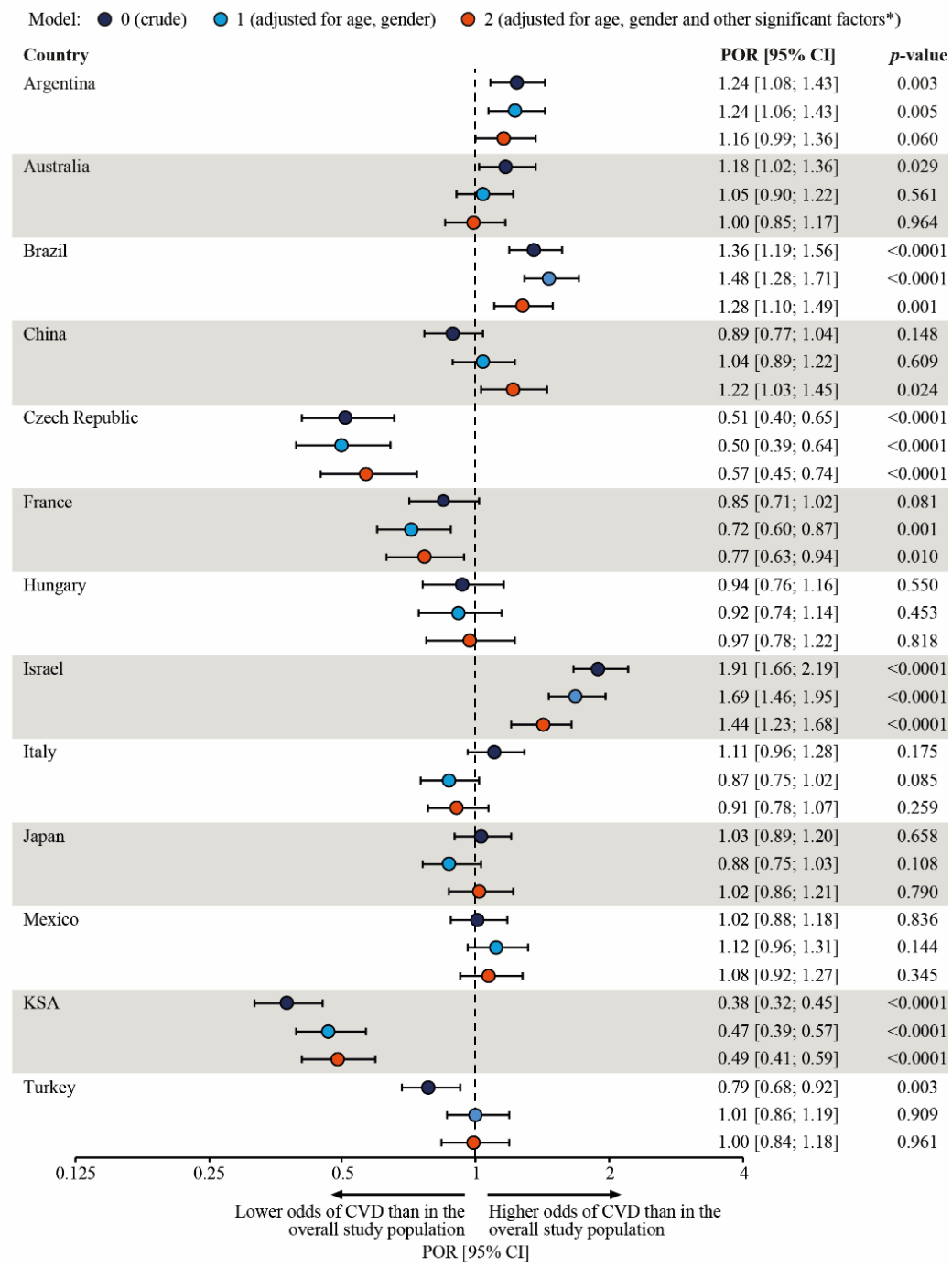
Figure S4. Number of vascular areas affected among participants with CVD, stratified by gender



Vascular areas were defined as coronary, cerebrovascular or peripheral. *Information on vascular beds was available for 1134 females and 1940 males

CVD cardiovascular disease

Figure S5. Adjusted associations between country and CVD prevalence (prevalence odds ratios) – covariates identified via logistic regression

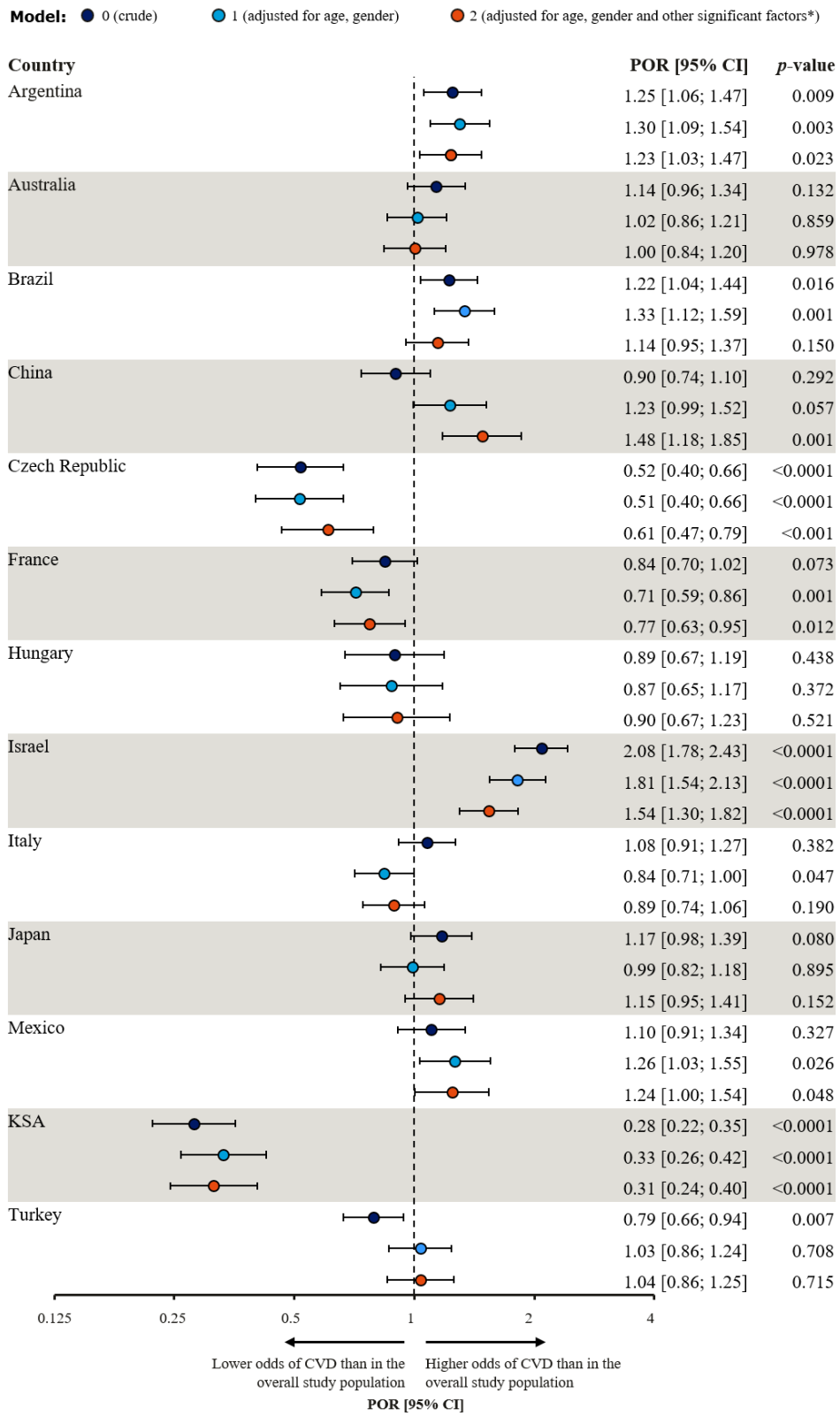


Analysis set (n = 9,713). Data are POR [95% CI] from logistic regression models with CVD (yes/no) as dependent variable and the following covariates: model 0, country; model 1, country, gender and age; *model 2, country, gender, age, diabetes duration, body mass index, HbA_{1c}, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, smoking status, hypertension,

nephropathy, neuropathy, and retinopathy. Missing data were imputed by fully conditional specification. The x-axis uses a log (base 2) scale

CI confidence interval, *CVD* cardiovascular disease, *HbA*$_{1c}$ glycated hemoglobin, *KSA* Kingdom of Saudi Arabia, *POR* prevalence odds ratio

Figure S6. Sensitivity analysis. Adjusted associations between country and CVD prevalence (prevalence odds ratios) – covariates identified via logistic regression without imputation of missing data

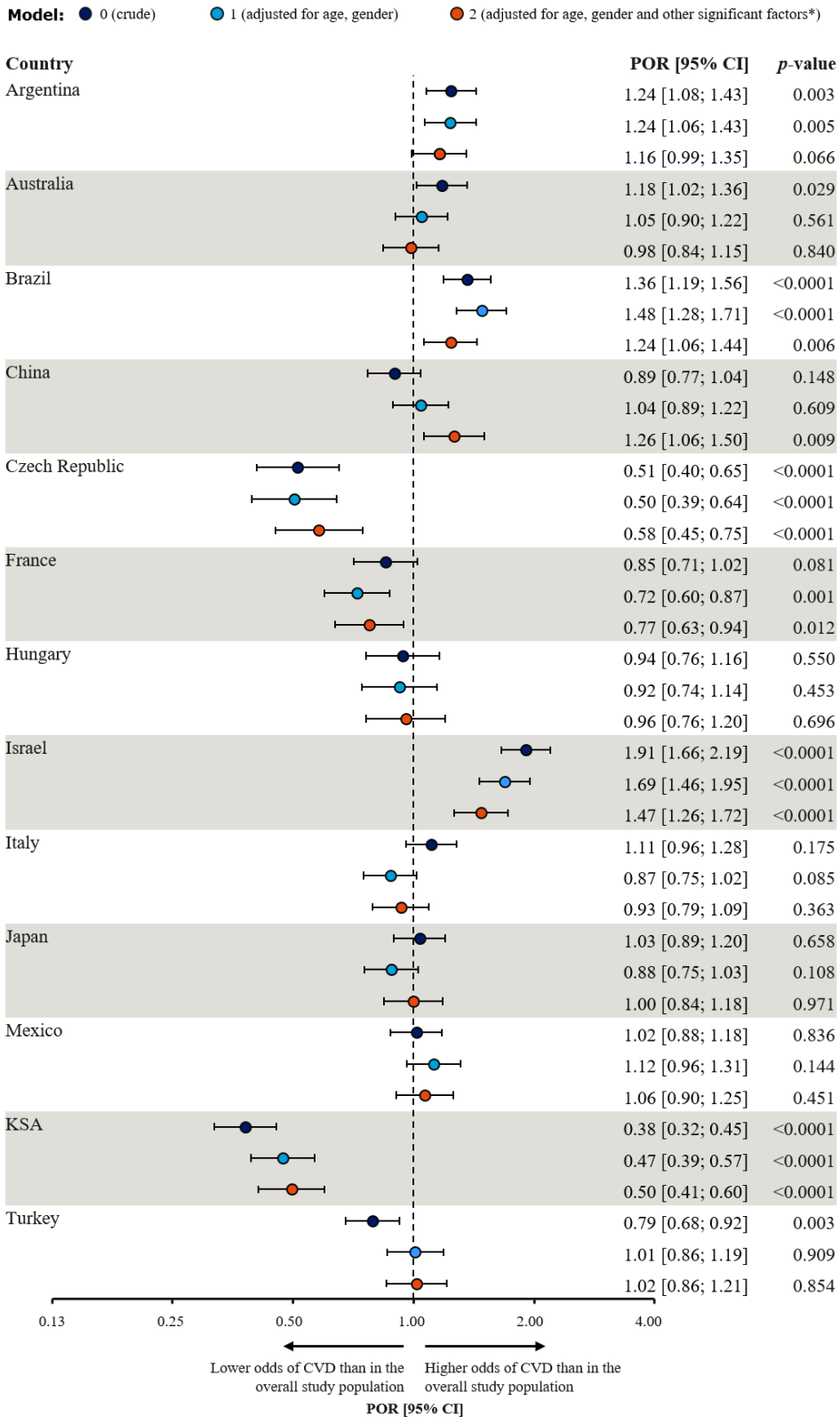


Analysis set (n = 7,163) with complete covariate information. Data are POR [95% CI] from logistic regression models with CVD (yes/no) as dependent variable and the following covariates: model 0: country; model 1: country, gender, and age; *model 2: country, gender, age, diabetes duration, body mass index, HbA_{1c}, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, smoking status, hypertension, nephropathy, neuropathy, and retinopathy. Missing data were not imputed. The x-axis uses a log (base 2) scale

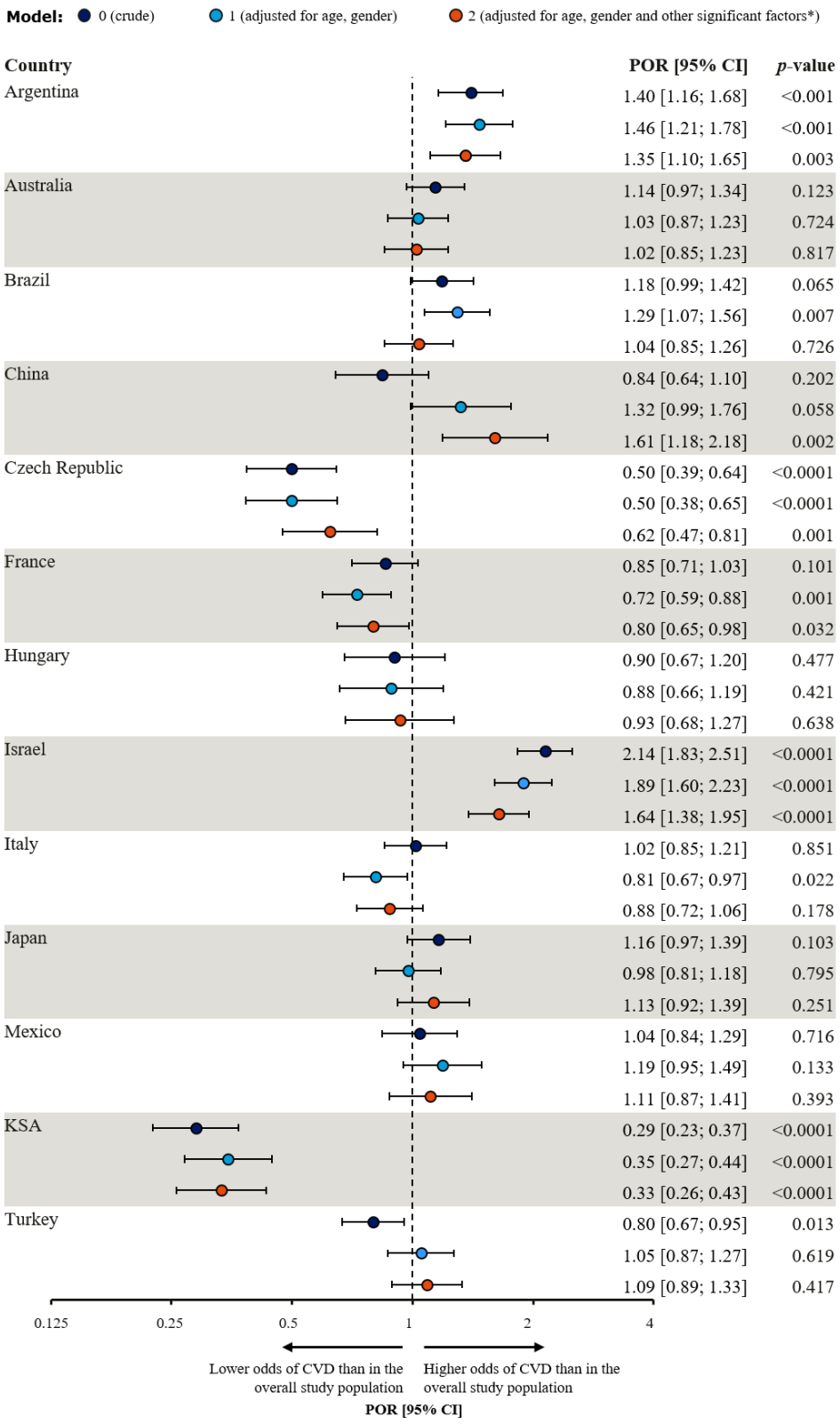
CI confidence interval, *CVD* cardiovascular disease, *HbA_{1c}* glycated hemoglobin, *KSA* Kingdom of Saudi Arabia, *POR* prevalence odds ratio

Figure S7. Sensitivity analyses. Adjusted associations between country and CVD prevalence (prevalence odds ratios) – covariates identified via logistic regression (including eGFR)

A) With imputation of missing data



B) Without imputation of missing data



Analysis set (A: n = 9,713; B: n = 6,369 with complete covariate information). Data are POR [95% CI] from logistic regression models with CVD (yes/no) as dependent variable and the following

covariates: model 0: country; model 1: country, gender, and age; *model 2: country, gender, age, diabetes duration, body mass index, HbA_{1c}, eGFR, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, smoking status, hypertension, nephropathy, neuropathy, and retinopathy. In A: missing data were imputed by fully conditional specification; in B: missing data were not imputed. The x-axis uses a log (base 2) scale

CI confidence interval, *CVD* cardiovascular disease, *eGFR* estimated glomerular filtration rate, HbA_{1c} glycated hemoglobin, *KSA* Kingdom of Saudi Arabia, *POR* prevalence odds ratio

Additional reference

1. International Diabetes Federation. IDF Diabetes Atlas, 8th edn. Brussels, Belgium: International Diabetes Federation; 2017.

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