

# SUPPLEMENTARY DATA

**Supplementary Table 1.** Prevalence and Incidence of CVD (Coronary Heart Disease and Stroke) in T1DM. Incidence is presented as percentage over the course of follow-up or in person-years (py).

Study (Author, Year, PMID)	Study design	Population	Diabetes duration	Definition of CVD	Baseline Prevalence	Follow-up	Incidence
Roy, 2012 PMID: 22652842	Retrospective medical record review	725 African Americans with T1DM in Newark, NJ  Follow-up on 444 (62.1%)  Mean HbA1c 13.5%	10.8 years	Discharge diagnosis ICD-9 codes	Any CVD: 12.4% CHD: 9% Stroke: 4.5%	6-year	Any CVD: 15.5% CHD: 12.6% Stroke: 3.3%
Conway, 2009 PMID: 20368215	Retrospective medical record and death certificate review	Pittsburgh EDC Study 658 diagnosed with T1DM in 1950-1980 with follow-up exams in 1986 and 1988	20 years	-Fatal CHD: autopsy, coroner, or medical record  -Non-fatal CHD: medical records, Q-waves on EKG or revascularization procedures (CABG, angioplasty, coronary endarterectomy, or coronary artery stenosis $\geq 50\%$ )	None	Mean follow-up 15 years	Non-fatal MI: overall 19% men: 22% Women: 16%  Fatal CHD: 8.39% overall

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Waden, 2009 PMID: 19651819	Retrospective medical record review	Finnish Diabetic Nephropathy (Finn Diane) Study  1,845 with T1DM  HbA1c 8.5%	22 years $\pm$ $\pm$ 11.9 years	CVD includes MI, coronary artery procedure (CABG, angioplasty), stroke (ischemic, hemorrhagic), limb amputation secondary to ischemia, or peripheral artery procedure	(ND)	5.7 years	Total CVD: 8.6%
Shankar, 2007 PMID: 17526864	Retrospective death certificate review	Total cohort 996 with T1DM  Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)  ~90% White  HbA1c range 5.6% to 19.5%	>12 years	ICD-9 codes 410-459 (CHD, stroke) listed as underlying or contributory cause	Angina: 3.1% MI: 3% Stroke: 1.1%	16 years	Based on 879 without baseline CVD: CVD mortality 15%
Stettler, 2006 PMID: 16918825	Retrospective death certificate review	WHO multinational study of vascular disease in DM, Switzerland data  165 (of original 225)	23.5 years	Death due to cardiac disease and ischemic heart disease (IHD)  ICD-9 codes on death certificate: 410-414 for IHD	(ND)	14 years	CHD mortality: 17%

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Soedamah-Muthu, 2006 PMID: 16567818	Retrospective electronic medical record review	UK General Practice Research Database (GPRD) 7,479 with DM, 38,116 without DM	15 years	MI, coronary revascularizations, stroke	3% at baseline (vs. 1% in non-diabetics)	4.7 years	Absolute risk/1000 person years  Acute CHD: Men: 3.5 (2.7-4.4) Women: 2.9 (2.2-3.9)  Coronary revascularization: Men: 2.0 (1.5-2.8) Women: 1.5 (1.0 – 2.3)  Stroke (fatal and non-fatal): Men: 2.7 (2.1-3.6) Women: 2.0 (1.4-2.8)
Nathan, 2005 PMID: 16371630	RCT of intensive vs. conventional diabetes management	DCCT/EDIC Follow-up Study 1,441 with T1DM  1,422 completed DCCT and joined EDIC  -HbA1c 7.8-7.9%	23-24 years	Non-fatal MI, stroke, CVD death, confirmed angina, coronary artery revascularization, sub-clinical/silent MI via annual ECG	none	17 years	144 events in 83 participants  Intensive group: 0.38/100 person-years  Conventional group: 0.80/100 person-years
Janghorbani, M 2007	Prospective cohort	Nurses' Health Study	31.4 years	CVA	(ND)	24 years	33/303 women with T1DM had a CVA (475/100,000 person-years)

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Skrivarhaug, 2006 PMID: 16365724	Retrospective registry review	Norwegian Childhood Diabetes Registry  1,096 with T1DM (872 female, 1,034 male)	Up to 30 years	Death certificates and ICD- 10 codes (underlying cause only)  CVD death: I20-I25 and I44-I49—acute MI, fatal arrhythmia  CVA death: I60-I69— ischemic cerebral and intracranial hemorrhagic events	(ND)	Over 24.2 years with 46,147 person-years follow-up	CHD: 26.3/100,000 py in men 10.3/100,00 py in women  CVA: Men: 17.6/100,000 py Women: 0/100,000 py
Klein BEK, 2004 PMID: 15451768	Prospective cohort and death certificate review	WESRD 996 with T1DM	(ND)	Any CVD: (ICD-9 402, 404, 410-429; ICD-10 I20-I51)	angina 3.1% myocardial infarction 3.0% stroke 1.0%	20 years	Age-adjusted cumulative incidence Angina: 18.1% MI: 14.8% Stroke: 5.9%
Schram, 2003 PMID: 14597846	Prospective cohort with medical record review	EURODIAB Prospective Complications Study Europeans with T1DM  2,565 with full CVD data  -HbA1c 6.7%	13.3 years	MI, angina, CABG, stroke, and/or ischemic changes on centrally coded ECG, and/or fatal CHD, stroke, or other CVD	CVD at baseline: 9.6%	7.4 years	All CVD 6.35%  ECG abnormality: 3.74% Angina: 1.09% MI: 2.1% Stroke: 0.74% CABG: 0.43% CVD death: 0.62%

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Laing, 2003 PMID: 12774166	Death certificate and medical record review	23,751 insulin-treated diabetic individuals <30 years identified 1972-1973 in United Kingdom	(ND)	Death certificate codes for CVD: ICD-9 391-398, 402, 404-429  CHD: ICD-9 410-414, 429.2	excluded	17 years, contributing 404,073 person-years	CHD mortality: Men: 107/100,000 person-years Women: 73/100,000 person-years  All heart disease:  Men 26.4/100,000 person- years 1-39 years of age  1194.9/100,000 person-years 40-84 years of age  Women 27.4/100,000 person- years 1-39 years of age  804.5/100,000 person-years 40-84 years of age
Liang, 2003 PMID: 12574553	Death certificate and medical record review	23,751 insulin-treated DM individuals <30 years identified 1972- 1973 in United Kingdom	(ND)	Overall CVA mortality ICD- 9 codes 430-438 Hemorrhagic (430.0-432.9) Non-hemorrhagic (430.0- 437.1)	excluded	17 years	CVA Men: 18.7/100,000 person-years  Women: 21.1/100,000 person- years

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Weis, 2001 PMID: 11704692	Death certificate and medical record review	147 individuals with T1DM Portsmouth Outpatient Clinics in United Kingdom	5-20 years	CHD established by Rose questionnaire or via ECG using Minnesota-coded 12- lead ECG. Causes of death ascertained from death certificate, hospital notes, or postmortem exams	(excluded)	>14 years	CVD death: 6.8% Fatal and non-fatal CHD: 17%
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CHD – coronary heart disease, CVA - cerebrovascular disease, CVD - cardiovascular disease, Diabetes Control and Complications Trial (DCCT), EDIC - Epidemiology of Diabetes Interventions and Complications ICD - International Classification of Diseases, PAD – peripheral artery disease, GPRD - General Practice Research Database, T1DM – type 1 diabetes mellitus.

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**Supplementary Table 2.** T1DM and peripheral arterial disease (PAD). All references notated by their PMID number.

Study (Author, Year, PMID)	Study design	Population	Diabetes duration	Definition of PAD	Baseline prevalence	Follow-up	Incidence
McAlpine 2005 PMID 15717888	population-based registry	942 T1DM patients from Tayside, Scotland obtained from the Diabetes Audit and Research in Tayside, Scotland (DARTS) registry who were free of LEA	(ND)	LEA	(excluded)	(ND)	per 1000 patients with T1DM  PAD: 5.5 (2.4-12.8) LEA: 3.2 (1.2-9.4)
Moss 1999 PMID 10372248, PMID 1546925	Population-based study	-906 T1DM patients from the WESDR (defined as age of onset of <30 years).  -mean A1c 10.8%	13.5 years	LEA	2.4%	14 years	LEA 7.2%
Jonasson et al, 2008 (PMID 18443192)	National health registry data	-31,354 patients with T1DM from the Swedish Inpatient Registry identified from 1975-2004 compared to the Swedish population -incident non-traumatic LEA	(ND)	LEA	(ND)	12.5 years	by age 65 years, cumulative probability of LEA was 11% (women) and 20.7% (men)
Olson 2002 PMID 11833057	Prospective cohort	586 T1DM patients from the Pittsburgh Epidemiology Complications Study  mean HbA1c 10.3-10.9	19 years	claudication, ischemia, ulceration, gangrene, amputation, infection, necrobiosis diabeticorum	(excluded)	10 years	incidence 1.3/100 person-years
Roy et al, 2008 (PMID 18346155)	Prospective cohort	457 African Americans with T1DM  -mean HbA1c 13.5%	10.4 years	history of amputation or leg angioplasty	(excluded)	6 years	5.7% of patients developed LEAD

ABI- ankle-brachial index, DCCI -, DM- diabetes mellitus, EDIC- LEAD- lower extremity arterial disease, T1DM- type I diabetes mellitus, WESDR- Wisconsin Epidemiologic Study of Diabetic Retinopathy.

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**Supplementary Table 3.** T1DM, cIMT and CAC. All references notated by their PMID number.

Study	Population	Epidemiology Data
<b>cIMT</b>		
Margeirsdottir 2010 PMID 20530748	-314 T1DM children and adolescents from Norway compared to 118 age-matched healthy controls -mean age 13.7 years -mean DM duration 5.5 years -mean A1c 8.4%	-mean cIMT higher in boys with T1DM (0.46 mm) vs controls (0.44 mm, $p=0.04$ ); no difference observed in girls -no carotid plaques were observed
Yamasaki 1996 PMID 8168638	-105 patients with T1DM (4-25 years of age), 529 patients with type 2 DM (31-86 years of age), 104 non-DM controls (7-76 years of age) -DM duration 0.5-49 years	-cIMT values in T1DM patients (10-19 years of age, 0.525 mm) or 20-25 years of age (0.696 mm) were greater than age-matched non-DM patients (0.444, $p=0.01$ to $p<0.001$ )
Jarvisalo 2002 PMID 11812760	-50 T1DM patients, 35 age-sex-body size matched controls -mean age 11 years -DM duration 4.4 years -mean HbA1c 8.9%	-mean cIMT higher in T1DM patients (0.47 mm) vs controls (0.42 mm, $p<0.001$ )
Dalla Pozza 2007 PMID 17374703	-150 T1DM patients -mean HbA1c 7.8% -mean age 13.9 years	-mean cIMT higher in T1DM (0.46 mm) vs controls (0.42 mm, $p=0.002$ ) in multivariable models adjusted for age, sex, DM duration, BMI, systolic blood pressure
DCCT/EDIC, 2003 (PMID 12788993)	-1229 T1DM patients (611 conventional Rx; 618 intensive Rx) from the DCCT trial followed longer term as part of the EDIC study and 222 healthy controls (mean age 39 years) -carotid ultrasound in 1994-1996 and 1998-2000 -mean age 34-36 years -mean DM duration 13.3-14.2 years -mean HbA1c during DCCT: 7.2-9.1% -mean HbA1c year 1 EDIC: 7.8-8.3%	-by year 6 of EDIC, T1DM cIMT greater than non-DM controls ( $p<0.003$ ) -less progression of IMT in the intensive arm of DCCT (0.032 mm) vs the conventional arm (0.023 mm, $p=0.01$ )



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Distiller et al, 2006 (PMID 16949514)	-148 patients with T1DM of relatively-long duration (>18 years) -mean age 48 years -mean DM duration 26 years -median HbA1c 7.8% -examined carotid plaque (defined as irregular thickening of at least 1.5 mm) in addition to cIMT	-multivariable predictors of IMT are age, DM duration, BMI, hypertension, HDL -multivariable predictors of carotid plaque are age, HTN, smoking, retinopathy
Larsen et al, 2004 (PMID 15759107)	-39 T1DM patients followed prospectively for 18 years compared to a healthy reference population -mean age 42-44 years -mean DM duration 30-31 years -mean HbA1c 8.1-8.3% -examined cIMT and iVUS	-IMT consistently higher in T1DM compared to a healthy population across age groups (35-45 and 45-55 years) - IMT associated with percent coronary vessel area stenosis by IVUS (r=0.43, p=0.034)
Ogawa et al, 2009 (PMID 19763015)	-73 T1DM patients with long DM duration (at least 20 years) -mean age 37.2-38.4 years -mean duration 26.4-27.8 years -mean A1c 7.7-8.1% -examined cIMT and plaque, defined as IMT $\geq$ 1.1 mm	-multivariable correlates of cIMT include age and dyslipidemia -age, age at DM diagnosis, and HbA1c during adolescence associated with plaque presence
<b>CAC</b>		
Lopes-Virella et al. 2011 DCCT (PMID:21156319)	476 T1DM patients from DCCT	Oxidized LDL from baseline samples correlates with subsequent development of CAC 11-20 years later
Snell-Bergeon JK et al. 2010 (PMID: 21059097) Schauer et al. 2011 (PMID: 20978091)	CACTI study of T1DM patients.	Measures of mean glucose and glucose variability were associated with CAC in men. Higher non-esterified fatty acid levels were associated with CAC
Rodrigues TC et al. 2010 (PMID: 21088805)	100 patients with T1DM but without CAD or end-stage renal disease	Insulin resistance, measured using the estimated glucose disposal rate (eGDR), was worse in those with worse CAC

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Rodrigues TC et al. 2011 (PMID: 20855932)	261 patients with T1DM, 100 of them had CAC measured; cross sectional study	Hypertension is associated with CAC more strongly than metabolic syndrome
Salem M et al. 2011 (PMID: 20706852)	60 adolescents (ages 12-18 years) with T1DM for 10 to 15 years duration	Twelve patients with diabetes (20%) had positive CAC. CAC was associated with smoking, age, duration of diabetes, severe retinopathy, nephropathy and higher A1C
Maurovich-Horvat P et al. 2010 (PMID: 20581785)	21 patients with T1DM, cross-sectional study	CAC was associated with measures of glucose disposal, age, disease duration, waist circumference, LDL but not A1C.
Conway B et al. 2010 (PMID: 20388043)	105 patients from the Pittsburgh EDC study.	CAC was associated with skin fluorescence, an indicator of accumulation of advanced glycation end products (AGEs), particularly in those with severe CAC.
Colhoun HM et al. 2008 (PMID: 18230111)	199 patients with T1DM	Serum IgG to bacteria involved in periodontal disease <i>P. gingivalis</i> and <i>A. actinomycetemcomitans</i> are associated with coronary artery atherosclerosis
Conway B et al. 2007 (PMID: 18158704)	315 individuals with T1DM. Mean age and diabetes duration were 42 and 34 years.	Adiposity was measured by CT (visceral and subcutaneous). Adiposity was associated with the presence but not the degree of CAC.

CAC- coronary artery calcification, DM- diabetes mellitus, T1DM- type I diabetes mellitus, WESDR- Wisconsin Epidemiologic Study of Diabetic Retinopathy.