Review

Epidemiology of Cardiovascular Disease in Type 2 Diabetes Mellitus

S Arulrhaj, A Kannan & A Bajpai

Abstract

Type 2 diabetes is a major and accelerating public health challenge. Type 2 diabetes is increasingly found to be a heterogeneous condition, where risk of cardiovascular disease that traditionally has been estimated at 2–4 times that of the nondiabetic population.

Cardiovascular (CV) risk factors such as obesity, hypertension and dyslipidemia are common in patients with DM, placing them at increased risk for cardiac events. In addition, many studies have found biological mechanisms associated with DM that independently increase the risk of CVD in diabetic patients. Therefore, targeting CV risk factors in patients with DM is critical to minimize the long-term CV complications of the disease.

Epidemiological studies have been powerful tools to study this phenomenon, providing data on prevalence and incidence rates in diverse populations and uncovering risk factors. This writing group has attempted to describe the scope of the problem based on current data.

This article predicts that novel insight into diabetes pathogenesis would come from biochemical and genetic epidemiology studies. It also predicts that type 2 diabetes could be prevented by healthy lifestyle change. The challenge now is for us to translate these insights into effective strategies for the prevention of the modern epidemic of diabetes and vascular disease.

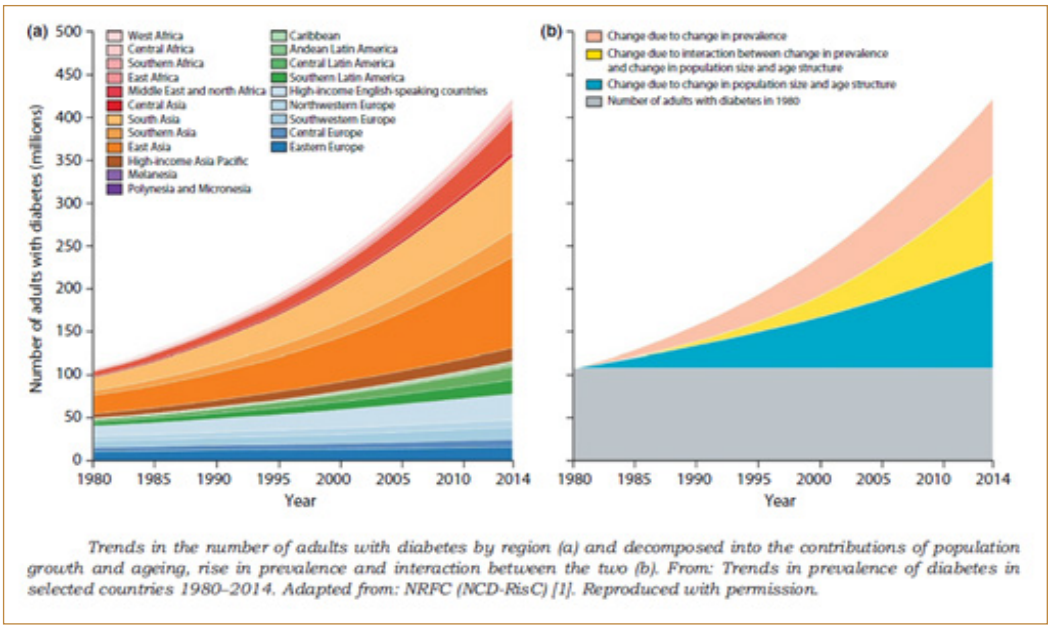
Keywords

Cardiovascular disease, Diabetes mellitus, Epidemiology, Hypertension, Dyslipidemia

Incidence of DM

The International Diabetes Federation (IDF) estimates that worldwide, 415 million people have diabetes, 91% of whom have type 2 diabetes mellitus (T2DM)[1]. People with diabetes comprise 8.8% of the world's population, and IDF predicts that the number of cases of diabetes will rise to 642 million by 2040.[1]

Using data from the Framingham Heart Study, Abraham et al.[2] noted that the overall annualized incidence rates of the disease per 1000 persons increased from 3.0 in the 1970s to 5.5 in the first decade of the 2000s. That change represented an increase in the incidence of T2DM of 83.3% and was higher in males than females by a factor of 1.61.



Trends in the number of adults with diabetes by region (a) and decomposed into the contributions of population growth and ageing, rise in prevalence and interaction between the two (b). From: Trends in prevalence of diabetes in selected countries 1980–2014. Adapted from: NRFC (NCD-RisC) [1]. Reproduced with permission.

Courtesy: Rosengren A (University of Gothenburg, Gothenburg, Sweden). Cardiovascular disease in diabetes type 2: current concepts (Review). J Intern Med 2018; 284: 240–253.

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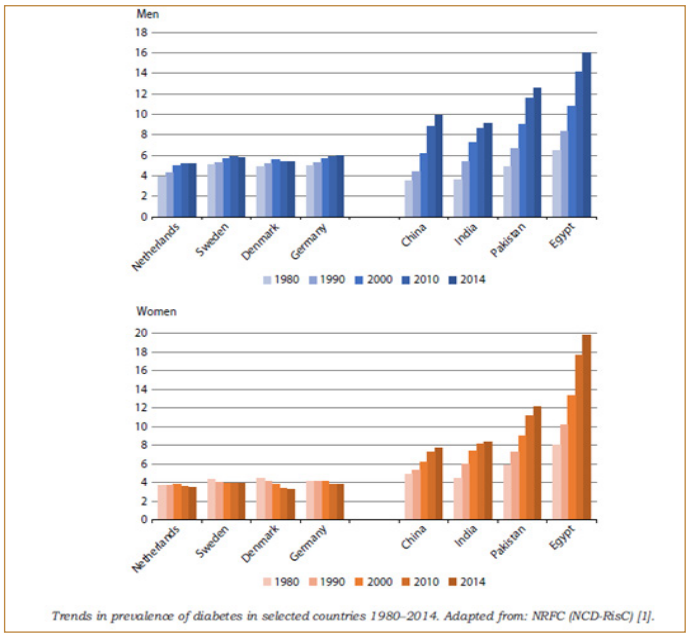

Trends in prevalence of diabetes in selected countries 1980-2014. Adapted from: NRFC (NCD-RisC) [1].

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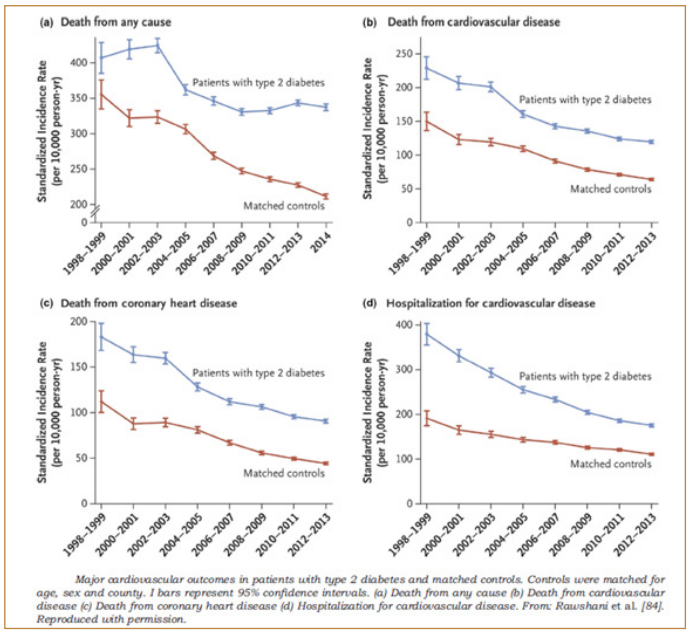

Major cardiovascular outcomes in patients with type 2 diabetes and matched controls. Controls were matched for age, sex and county. I bars represent 95% confidence intervals. (a) Death from any cause (b) Death from cardiovascular disease (c) Death from coronary heart disease (d) Hospitalization for cardiovascular disease. From: Rawshani et al. [84]. Reproduced with permission.

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Type 2 diabetes is a major and accelerating public health challenge. Between 1980 and 2014, a period of just 35 years, the number of adults with diabetes globally is estimated to have increased from 108 to422 million, due not only to sharply rising obesity rates, but also to increasing population size, longer life expectancy, and rising prevalence of diabetes worldwide. Overall, worldwide age-standardized adult diabetes prevalence doubled from 4.3% to9.0% in men and from 5.0% to 7.9% in women.[3]

The prevalence of diabetes in urban Indians has steadily increased from 2.1% in the 1970s to 8.2% in the 1980s,later climbing to 12–16%.[4,5]

Incidence of CVD in DM

Type 2 diabetes is increasingly found to be a heterogeneous condition, where risk of cardiovascular disease that traditionally has been estimated at 2–4 times that of the nondiabetic population. New research shows that excess risk varies substantially with type of outcome, age, glycaemic control, the presence of renal complications and other factors. Heart failure, previously less recognized thanother cardiovascular conditions, is increasingly coming into focus, because of strong links with poor glycaemic control and obesity.[3]

Table 1.
Prevalence of Coronary Artery Disease in South Indian Subjects With and Without Glucose Intolerance[41]

	Subjects		
	NGT	IGT	Diabetes
Documented MI (%)	0.9%	—	3.4%
Overall Q waves (%)	1.2%	1.4%	8.2%
ST-segment depression (%)	1.1%	5.4%	2.8%
T-wave abnormalities (%)	6.6%	8.1%	9.0%
Total CAD prevalence (%)	9.1%	14.9%	21.4%

Courtesy: Rosengren A (University of Gothenburg, Gothenburg, Sweden). Cardiovascular disease in diabetes type 2: current concepts (Review). J Intern Med 2018; 284: 240–253.

The Indian Scenario

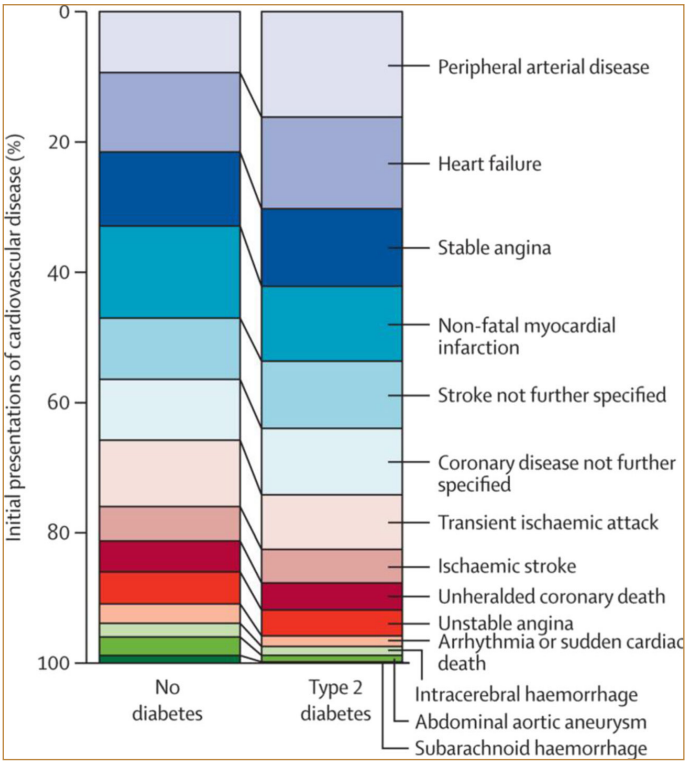
Type 2 diabetes is on the verge of becoming a pandemicin India. As type 2 diabetes shares several risk factorsin common with coronary artery disease (CAD), suchas age, hypertension, dyslipidemia, obesity, physicalinactivity, and stress, an increase in the prevalence ofdiabetes indirectly implicates an escalating risk of CADas well.[6,7]

India is predicted to bear the greatest CAD burden,according to the estimates from the Global Burden of Disease Study. Of the more than 9 million deaths dueto CAD in 1990 in developing countries, 2.4 million (25%)occurred in India.[8]

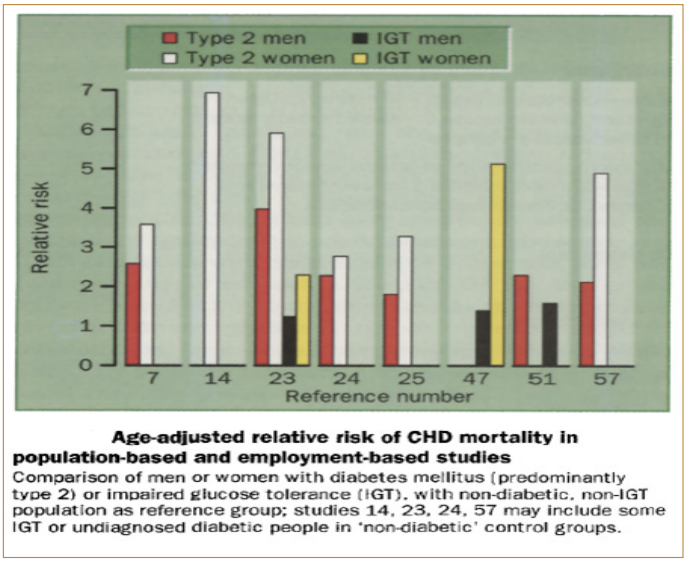
The Chennai Urban Population Study,[9] a population-based study in Chennai, in South India, showed aprevalence of CAD of 11%, which is 10 times more than what it was in 1970. Clustering of risk factors for CADsuch as hyperglycemia, central body obesity, dyslipidemia, and hypertension tends to occur, and interplay of theserisk factors could explain the enhanced CAD risk in Indians. Additionally, low-grade inflammation and apossible inherent genetic susceptibility are other contributing factors. Preventive measures such as lifestylemodification with healthy diet, adequate physical activity, and decrease in stress could help prevent the twinepidemics of Diabetes and CAD.

Morbidity and Mortality of Cardiovascular Disease in Diabetes Mellitus

Cardiovascular deaths account for 44% of death in those with type 1 DM and 52% of deaths in type 2 DM [10]. Type 2 DM carries



Distribution of initial presentations of cardiovascular disease in participants with and without type 2 diabetes and no history of cardiovascular disease. (with permission from Shah et al. Lancet Diabetes Endocrinol. 2015;3:105–13)



Age-adjusted relative risk of CHD mortality in population-based and employment-based studies
Comparison of men or women with diabetes mellitus (predominantly type 2) or impaired glucose tolerance (IGT), with non-diabetic, non-IGT population as reference group; studies 14, 23, 24, 57 may include some IGT or undiagnosed diabetic people in 'non-diabetic' control groups.

Ref.: Lancet 1997; 350 (SUPPl I): 4-9

a two to six times risk of death from cardiovascular etiologies, such that age-adjusted prevalence of white Americans for coronary heart disease is double in those with type 2 DM than those without[11]. Initial presentations of CVD in DM most commonly manifest as peripheral arterial disease (16.2% or three times greater) and heart failure (14.7%) followed by angina and non-fatal MI. This suggests the need for earlier screening of subclinical PAD and HF.[12]

In the San Antonio Heart Study, 4875 patients followed over 7–8 years demonstrated that DM was significantly associated with increased all-cause mortality (RR 2.1, 95% CI 1.3–3.5 in men; RR 8.5 95% CI, 2.8–25.2 in women). Heart failure risk rose to 40% in DM patients compared to non-diabetics with age-adjusted odd ratio of 2.8 (95% CI, 2.2–3.6), and had a two to three times greater risk of development.[13]

In the National Health and Nutrition Examination Survey cohort (NHANES), 26.3% of strokes were associated with diabetes, with a 2-fold greater risk in those with diabetes for ischemic strokes and 50% increase for hemorrhagic strokes.[14]

Mortality rates post-MI are also higher in Diabetics than non-diabetic patients, and the cardiovascular death rate is 4.4-fold increased in diabetes alone without other traditional cardiovascular risk factors in comparison to nondiabetics in the same age groups.[15]

Gender Differences in DM and CVD Risk

Several studies have also shown different CVD risks across gender among those with DM.

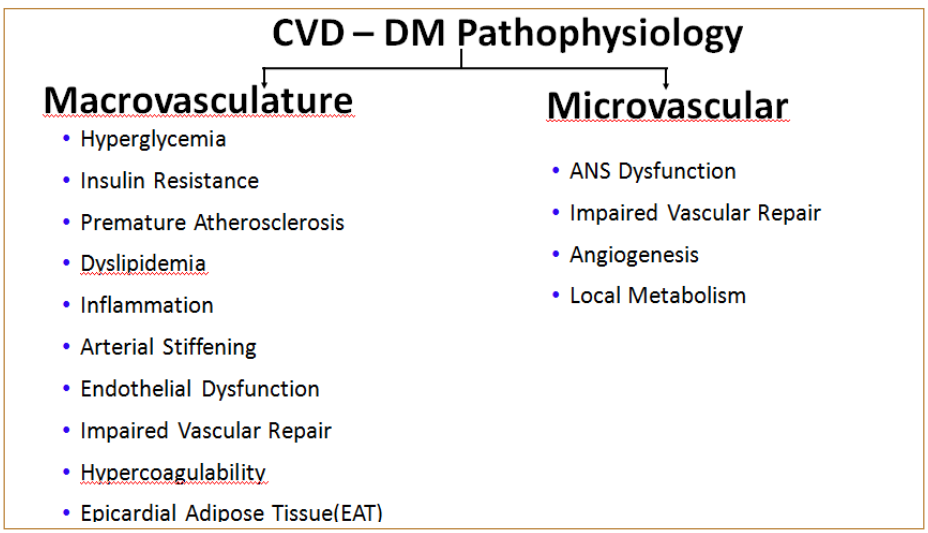
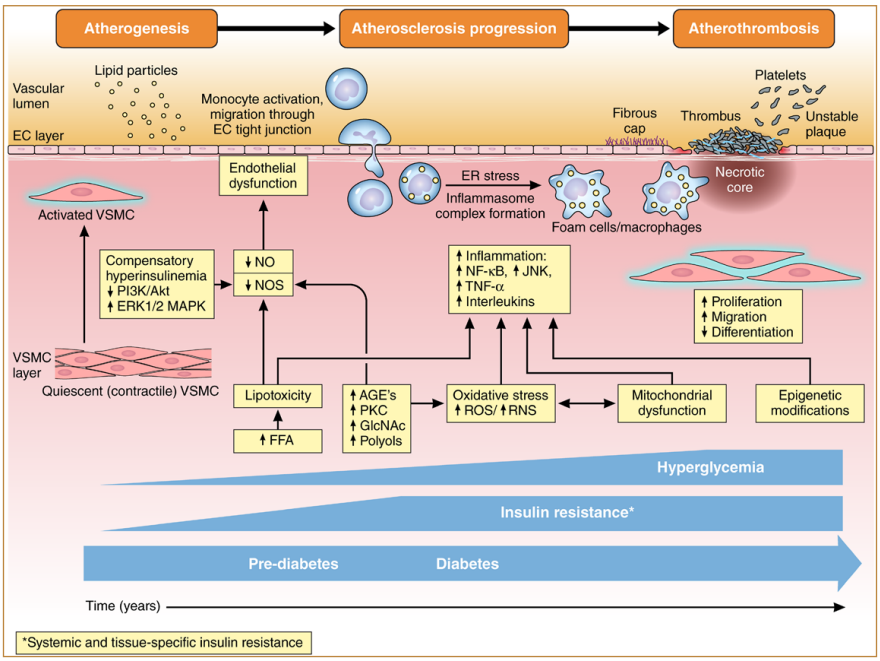


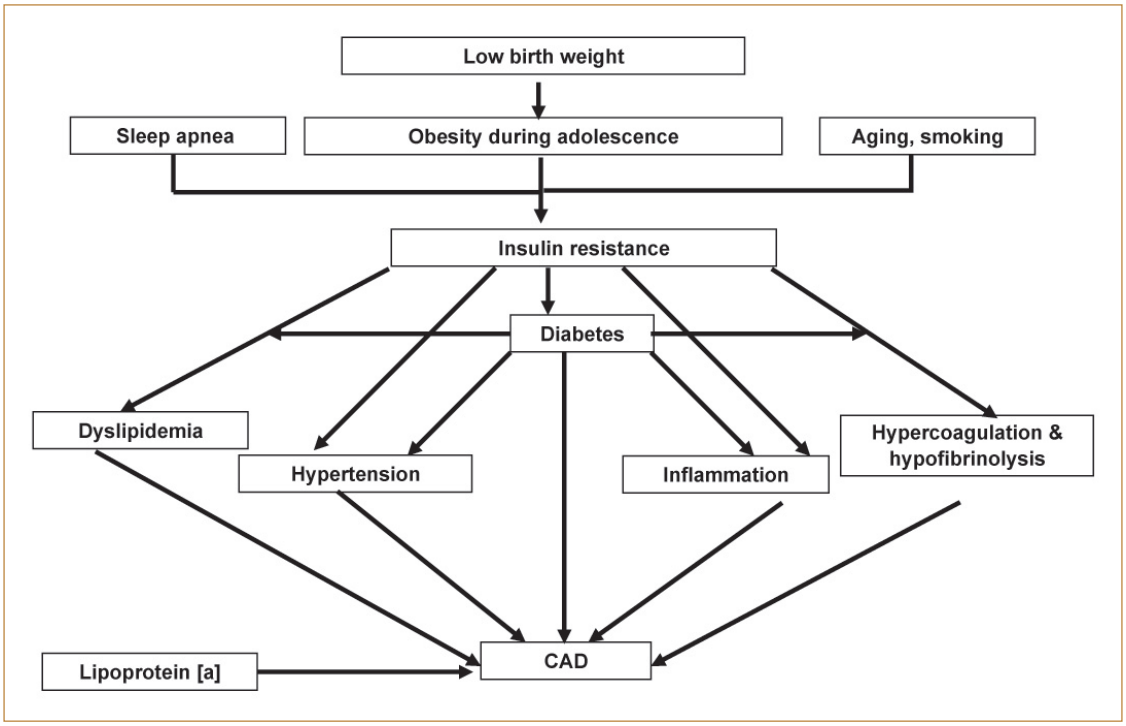
Figure 6.

Epidemiology of Cardiovascular Disease in Type 2 Diabetes Mellitus

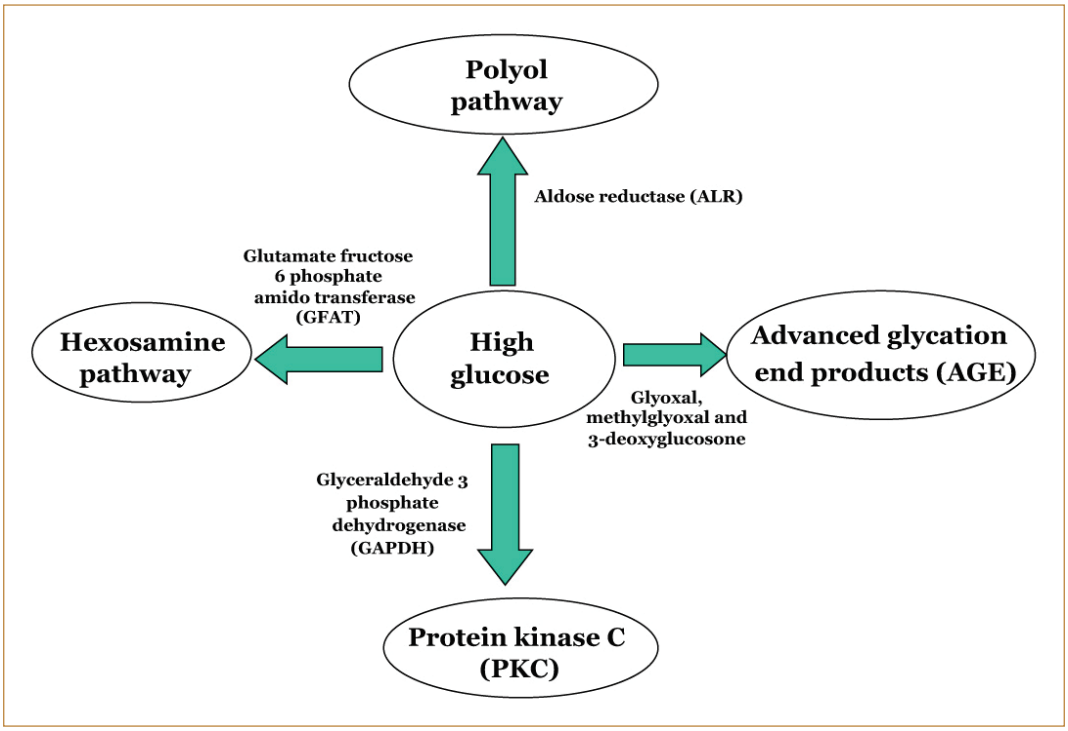


Ref. - Circulation. 2016;133:2459–2502. DOI: 10.1161/CIRCULATIONAHA.116.022194.

- The Early Rancho Bernando Study demonstrated that men with DM had a 2.4-fold increased risk of ischemic heart disease compared to men without,while diabetic women had a 3.5 increased risk.[16]
- Additionally, there was a 3-fold excess fatal CHD risk in type2 DM females, with a hazard ratio of 14.74 (95% CI 6.16–35.27) compared to men (HR 3.77; 95% CI, 2.52–5.65).[17]
- Not only was there a higher mortality for MI in diabetic womencompared to men, myocardial infarction also occurred earlier in women.[18]
- For stroke analysis, a comprehensive systematic review and meta-analysis from 64 cohorts with12,000 strokes, the adjusted RR for stroke and DM was 2.28(95% CI, 1.93–2.69) for women vs. 1.83 (95% CI, 1.60–2.08)in men.[19]



The interaction of cardiovascular risk factors.
Ref. : J Diabetes Sci Technol Vol 4, Issue 1, January 2010



Multiple biochemical aberrations based on high glucose.
Ref. J Diabetes Sci Technol Vol 4, Issue 1, January 2010

- In addition, in the Framingham Study with36 years of follow-up data, diabetic women were also notedto have greater age-adjusted risks of PAD (risk ratio 6.4 vs. 2.9in men), heart failure (7.8 vs. 4.4), as well as overall CVDevents (3.7 vs. 2.2) when compared to Diabetic men.[20]

Pathogenesis of CVD in DM

Macrovascular events in diabetes remain the leading cause of mortality, and the burden of cardiovascular disease attributable to diabetes has increased over the past two decades (Stratton et al.2000; Morrish et al. 2001).

Insulin resistance is the underlying factor for all the features of metabolic syndrome and is considered crucial in the pathophysiology of vascular damage (Stout 1969; DeFronzo 2010; Reddy et al.2010; Kanwar et al. 2008a).

The **two key metabolic abnormalities** that characterize type 2 diabetes (T2DM) are **hyperglycemia** and **insulin-resistance**, and the **two main pathological processes** in vascular wall that can elicit CV events are **atherosclerosis** and **arterial stiffening**.

Indeed, patients with diabetes mellitus show both premature atherosclerotic changes and accelerated arterial stiffening.

Patho Physiology mechanisms

- **Insulin resistance** has been shown to be associated with decreased synthesis/release of NO and enhanced generation of reactive oxygen species, as well as with an excessive free fatty acids release from adipose tissue.
- **Obesity** - Impaired nutrition contributes to hyperlipidemia and insulin resistance causing hyperglycemia. Obesity is associated with increased levels of a number of adipokines
- **Premature Atherosclerosis** - Multiple mechanisms associated with insulin resistance may promote diabetic atherosclerosis in type 2 diabetes like - Secretion of adipokines from adipose tissue , Fatty acid binding protein (FABP), C peptide as a decomposition product of proinsulin, and Diabetic hyperlipidemia.
- **Diabetic Dyslipidemia** - Diabetic blood is more likely to be high in triglycerides, Low HDL, moderate high LDL which promotes atherosclerosis.
- **Inflammation** - Diabetes is a state of chronic, low-level inflammation, some immune activation may precede insulin resistance in diabetic and pre-diabetic states and ultimately may be the factor that initially increases cardiovascular risk in these disease processes.
- **Arterial Stiffness** - Diabetes accelerate the natural aging process of the arterial tree.
- **Carotid Plaque** - CIMT and Plaque Presence are surrogate markers of atherosclerosis. Plaque presence indicates more advanced atherosclerotic process.
- **Endothelial Dysfunction** - Healthy endothelium is vasodilatory, anti-atherogenic, and anti-inflammatory- When defective, the process of atherosclerosis is accelerated.
- **Impaired Vascular Repair in Diabetes** - Diabetes also impairs response to vascular damage by reducing endothelial repair processes.
- Hypercoagulability -Up to 80% of patients with diabetes die a thrombotic death. 75% of these deaths are the result of

an MI, and the remainder are the result of cerebrovascular events and complications related to PVD.

Clinical Presentation

- **Hypertension** is very common among patients with T1DM and T2DM, with prevalence rates of 30% and 60%, respectively. Hypertension among diabetic patients is closely tied to the development of diabetic nephropathy (DN).
- DM appears to contribute directly to the development of **Diabetic cardiomyopathy(CMP)**. Annual mortality rates up to 20%
- **Myocardial infarction** - Patients with DM are in a prothrombotic and procoagulant state, which may account for the higher rates of MI. The prevalence of diabetes in patients with CAD is up to 40% in many countries.
- **Silent CAD** is far more prevalent in patients with DM (10%-20%) than those without DM (1%-4%). Diabetic neuropathy is one factor that may explain the increased incidence of silent ischemia in patients with DM
- Risk for **heart failure** increases 2.4-fold in men and 5-fold in women in comparison with those without diabetes mellitus. Microvascular disease, characterized by arterial thickening and fibrosis, as well as endothelial and vasomotor dysfunction, can increase risk of heart failure in diabetes mellitus.
- **Cerebrovascular Disease** - Diabetes is a major risk factor for development of carotid atherosclerosis and stroke, both ischemic and hemorrhagic Data from the Emerging Risk Factors Collaboration found that diabetes was associated with a 2.27 fold increase in the risk of ischemic stroke and a 1.56 fold increase in the risk of hemorrhagic stroke. Diabetes is actually considered an established risk factor for cognitive impairment, dementia, and Alzheimer disease. (Gorelick 2012; Ott et al. 1999; Peila et al. 2002; Biessels et al. 2006)
- **Peripheral Artery Disease** - Diabetes is also associated with a twofold increase in the risk of lower limb ischemia, and an estimated 21% of patients have signs of peripheral artery disease (PAD).
- **Diabetic Reno-Vascular Disease** - Efferent arteriolar hyalinosis is an important lesion seen in DN .Nonspecific arteriosclerosis may be present, which is associated with more severe glomerular disease. "Matrix to Media ratio" is increased. Significant medial thickness may be associated with Hypertension. Neovascularisation is seen. Diabetic kidney disease includes glomerular hyper filtration, progressive albuminuria, declining GFR, and ultimately, ESRD
- **Cardiovascular autonomic neuropathy (CAN)** - Common among patients with DM and is correlated with an increased 5-year mortality ratefrom CVD. The development and progression of CAN is likely related to dysregulation of the autonomic nervous system (ANS) with increased sympathetic activity and elevated inflammatory markers. Incidence of CAN increases with age and inadequate glycemic control, which places patients with DM at higher risk of developing both CAN and CVD.

Summary of prevalence rates of cardiovascular comorbidities in persons with type 2 diabetes

Sex	Cardiovascular outcome	Studies	N	Rate[a] (%)	95% confidence interval (%)
Both	Stroke	39	3,901,505	7.6	6.6–8.6
	Myocardial infarction	13	3,518,833	10.0	7.5–12.5
	Angina pectoris	4	354,743	14.6	12.0–17.3
	Heart failure	14	601,154	14.9	13.0–16.7
	Atherosclerosis	4	1153	29.1	21.7–36.4
	Coronary artery disease	42	3,833,200	21.2	20.3–22.2
	Cardiovascular disease (any)	53	4,289,140	32.2	30.0–34.4
Males[b]	Stroke	10	232,525	6.7	6.0–7.3
	Myocardial infarction	2	1170	11.9	4.3–19.5
	Angina pectoris	1	454	21.1	16.3–26.9
	Heart failure	4	73,361	25.3	11.4–39.2
	Coronary artery disease	9	237,367	18.7	16.5–20.8
	Cardiovascular disease	16	241,406	27.6	25.3–29.9
Females[b]	Stroke	10	202,348	5.9	5.1–6.7
	Myocardial infarction	2	1812	9.8	3.5–16.0
	Angina pectoris	1	803	17.4	15.0–20.2
	Heart failure	4	62,690	24.0	11.2–36.8
	Coronary artery disease	10	205,493	14.3	12.4–16.1
	Cardiovascular disease	16	209,153	27.2	22.7–31.7

[a] Weighted by inverse variance

[b] No studies reported atherosclerosis for males or females; only in the aggregate. Rates for males and females do not sum to the total as not all studies reported all outcomes

Ref. : Einarson et al. Cardiovasc Diabetol (2018) 17:83

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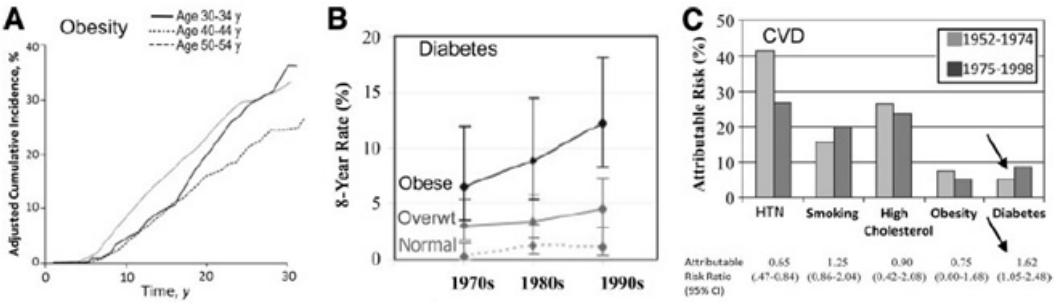


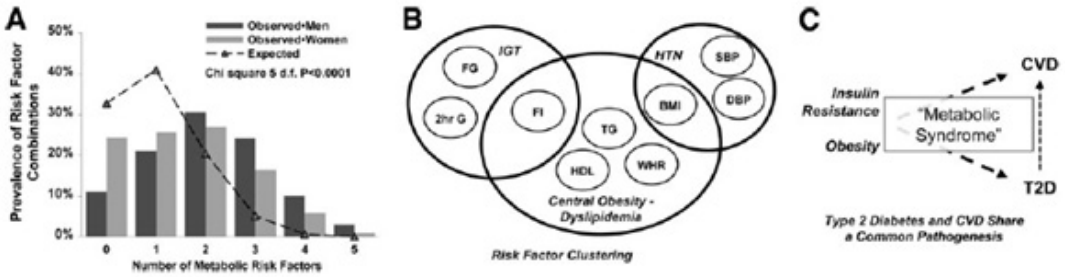
Increasing rates of obesity are associated with increasing rates of diabetes, which in turn are associated with increasing rates of CVD in FHS. A: Shows the dramatically rising 30-year mortality-adjusted cumulative incidence rate of obesity (BMI ≥30 kg/m^2) for men in different age-groups; the experience was similar among women (adapted from Vasan et al. [2]). B: Shows that the 8-year incidence rate of diabetes increased primarily in those with obesity (among both men and women) (adapted from Fox et al. [3]). C: Shows a 1.6-fold increase over time in the attributable risk percent for CVD associated with diabetes (arrows); among common CVD risk factors, only diabetes contributed significantly to increased rates of CVD (adapted from Fox et al. [5]). HTN, hypertension.

Ref.: Diabetes Care, Volume 33, Number 8, August 2010

Novel risk factors and possible mechanisms of the excess risk of CHD in type 2 diabetes mellitus

Risk factor	Possible mechanisms
Hyperglycaemia	Glycation/oxidation—lipoproteins; vessel wall matrix/collagen Increased diacylglycerol/protein kinase C—altered growth factors, permeability, and other vascular changes
Hyperinsulinaemia, hyperproinsulinaemia, and insulin resistance	Increased vascular matrix; proliferation of arterial smooth muscle; increased plasminogen-activator inhibitor-1 concentrations; and increased small, dense LDL-cholesterol concentrations
Dyslipidaemia	
High triglyceride concentrations	Lower serum HDL cholesterol
Low serum HDL cholesterol	Atherogenesis
Small, dense LDL cholesterol	Atherogenesis
Increased central adiposity	Insulin resistance; dyslipidaemia
Increased plasminogen-activator inhibitor 1	Decreased fibrinolysis
Increased platelet aggregation/adhesiveness	Increased thrombosis
Increased fibrinogen concentrations	Thrombogenesis, atherogenesis
Increased plasma oxidative state	Endothelial damage; lipoprotein oxidation/atherogenesis
Renal dysfunction	Atherogenesis, hypertension, oxidation
Cardiovascular autonomic neuropathy	Sudden death
Abnormal vascular reactivity	Vasoconstriction, ischaemia, hypertension

Ref.: Lancet 1997; 350 (SUPPL I): 4-9



Type 2 diabetes and CVD risk factor clustering is called metabolic syndrome. A: Shows that the observed co-occurrence of two or more of elevated fasting glucose (FG), fasting insulin (FI), triglycerides (TG), blood pressure (BP), BMI, or low HDL cholesterol (all defined in A as the extreme 20th percentile, light gray bars for women and dark gray bars for men) co-occur to a far greater degree than would be expected by change alone (compared with a binomial distribution, dashed line, P < 0.0001). B: Shows that the pattern of risk factor clustering for these risk factors (including, as well, glucose levels 2 h after an oral glucose tolerance test [2-h G] and waist-to-hip ratio [WHR]) represent three clinically identifiable phenotypes: impaired glucose tolerance (IGT), hypertension (HTN), and central obesity-dyslipidemia, linked together by obesity (in this figure, BMI) and fasting hyperinsulinemia (reflecting, in part, insulin resistance). C: Illustrates that obesity and insulin resistance constitute the common physiological antecedents leading to increased risk for the development of both type 2 diabetes (T2D) and CVD; the name currently applied to this phenomenon is metabolic syndrome. A and B are adapted from Wilson et al. (7) and Meigs et al. (8). DBP, diastolic blood pressure; SBP, systolic blood pressure.

Ref.: Diabetes Care, Volume 33, Number 8, August 2010

		n (%)				
		1970–79	1980–89	1990–99	2000–05	P-trend
Hypertension†						
Prevalence	No Diabetes	306 (36.3)	387 (30.0)	259 (21.6)	164 (25.4)	<0.001
	Diabetes	27 (81.8)	48 (81.4)	63 (80.8)	27 (77.1)	0.64
Treatment	No Diabetes	65 (21.2)	142 (36.7)	124 (47.9)	87 (53.1)	<0.001
	Diabetes	7 (25.9)	20 (41.7)	30 (47.6)	17 (63.0)	0.006
Controlled	No Diabetes	24 (7.8)	70 (18.1)	93 (35.9)	59 (36.0)	<0.001
	Diabetes	0 (0.0)	4 (8.3)	6 (9.5)	4 (14.8)	0.06
High LDL cholesterol‡						
Prevalence	No Diabetes	481 (61.8)	730 (59.9)	534 (45.2)	261 (41.2)	<0.001
	Diabetes	26 (86.7)	41 (80.4)	59 (88.1)	26 (74.3)	0.44
Treatment	No Diabetes	12 (2.5)	11 (1.5)	65 (12.2)	61 (23.4)	<0.001
	Diabetes	1 (3.9)	4 (9.8)	6 (10.2)	8 (30.8)	0.009
Controlled	No Diabetes	2 (0.4)	2 (0.3)	42 (7.9)	52 (19.9)	<0.001
	Diabetes	0 (0.0)	1 (2.4)	5 (8.5)	6 (23.1)	0.001
Cigarette smoking	No Diabetes	315 (43.8)	401 (31.1)	251 (20.9)	124 (19.2)	<0.001
	Diabetes	18 (58.1)	21 (35.6)	23 (29.5)	6 (17.1)	<0.001
Obesity§	No Diabetes	141 (16.7)	242 (18.8)	288 (24.0)	152 (23.5)	<0.001
	Diabetes	12 (36.4)	24 (40.7)	54 (69.2)	21 (61.8)	<0.001
Age 60		(N=1,000)	(N=986)	(N=1,231)	(N=278)	
Hypertension†						
Prevalence	No Diabetes	474 (50.9)	421 (46.6)	463 (42.0)	99 (42.9)	<0.001
	Diabetes	58 (90.6)	73 (91.3)	102 (81.0)	41 (87.2)	0.14
Treatment	No Diabetes	157 (33.1)	197 (46.8)	300 (64.8)	63 (63.6)	<0.001

†Hypertension is defined as >140/90 mm Hg or treatment for individuals without diabetes and >130/80 mm Hg or treatment for individuals with diabetes. Hypertension treatment was calculated by dividing the number of participants receiving antihypertensive medication by the total number of individuals with hypertension. Hypertension control was calculated by dividing the number of participants with SBP <140/90 mm Hg (<130/80 mm Hg for individuals with diabetes12) by the total number of individuals with hypertension.

‡High LDL cholesterol is defined as ≥130 mg/dL or treatment for individuals without diabetes and ≥100 mg/dL or treatment for individuals with diabetes. LDL treatment was calculated by dividing the number of participants receiving lipid lowering medication by the total number of individuals with high LDL. LDL control was calculated by dividing the number of participants with LDL <130 mg/dL (<100 mg/dL for individuals with diabetes12) by the total number of individuals with high LDL cholesterol.§Obesity is defined as a body mass index of ≥30 kg/m2.

Prevalence, treatment, and control of cardiovascular disease risk factors by time among participants with and without diabetes in the Framingham Heart Study (1970–2005).

New Concepts in Evaluating CVD in Persons With Diabetes

The development of non-invasive methods of measuring atherosclerosis and vascular disease provides the opportunity to test hypotheses related to the development of atherosclerosis in persons with diabetes. These new methods can evaluate the following:

- The extent of atherosclerosis and its progression over time (electron beam computed tomography, spiral computed tomography, carotid ultrasound [intima-media thickness])
- Large-vessel vascular function, such as vascular stiffness and compliance (ie, pulse-wave velocity, tonometry)
- Endothelial function (brachial artery flow-mediated vasodilatation plethysmography)
- Cardiac function (echocardiography and magnetic resonance imaging)

- Peripheral vascular disease (ankle-brachial blood pressure)
- Brain imaging (magnetic resonance imaging–detected silent infarct, brain structure, and white matter characteristics)
- Characteristics of atherosclerosis plaque (magnetic resonance imaging of carotid, aortic, and coronary arteries)
- EAT(Epicardial adipose tissue) - An imaging biomarker(ECHO & CTA) has gained attention due to its intimate location to the coronary vessels and the myocardium. It is associated withprevalent subclinical atherosclerosis, ischemia, and future major adverse cardiac events.

These new non-invasive methods, in combination with measures of thrombogenesis, fibrinogenolysis, and inflammation, will enhance our ability to predict clinical CVD.

Recommendations and Prevention (AHA Programs)

Given the magnitude of the current role that diabetes plays in CVD and the strong likelihood that the impact of diabetes on CVD will increase greatly in the near future, aggressive programs will be needed to further reduce the CVDmortality and morbidity. The magnitude and scope of the problem are so great that it will be imperative to collaborate with other organizations such as the American Diabetes Association, National Institutes of Health, and Centers for Disease Control and Prevention, which are also concerned with this issue.Following are some recommendations for futureAHA programs:

- Monitor the extent of the increasing burden of CVD attributable to diabetes to assess its public health and clinical importance forthe general US population. This can be achieved by CV event and mortality follow-up on the National Health and Nutrition Examination Survey (NHANES) II, NHANES III, and Hispanic Health and Nutrition Examination Survey populations in a similar way to that performed in theNHANES I study.
- Establish large cohorts of youth with type 1 and type 2 diabetes to define CVD risk factors and clinical outcomes so that preventive strategies can be tested. Clinical trials of proven therapies in adults should also be initiated in youth to determine their efficacy.
- Identify children who already have type 2 diabetes, IGT, or high risk for developing these (ie,obese with strong family history or exposure to a diabetic in utero environment). Demonstrate the effects of incorporating nutrition education and physical activity into school programs in reducing CVD risk for these children.
- Develop, implement, and evaluate public education programs to increase understanding of the role diabetes plays in CVD and how individuals can recognize and address risk factors forCVD if they have diabetes.
- Develop, implement, and evaluate education programs for both the public and healthcare providers on dietary and physical activity programs appropriate for preventing or reducing CVDand its risk factors in patients with diabetes.
- Develop and evaluate programs to ensure that every person with newly diagnosed diabetes has aggressive control of all CVD risk factors. Develop effective programs to ensure that every patient with diabetes, regardless of ethnicity and economic status, receives adequate preventive therapies aimed at smoking cessation, dyslipidemia correction, blood pressure lowering, and blood glucose level reduction.
- Stimulate research to better understand risk factors for CVD in those with diabetes. This should include research into both lifestyle and biochemical markers. Research should include appropriate intervention studies.

Conclusion:

- T2DM Coronary Equivalent 50 % of DM have CVD More in women
- Hyperglycemia & Insulin Resistance-Metabolic
- Atherosclerosis & Arterial stiffness-Pathology
- Macro- Lipid dependant&Endothelial Dysfunction
- Micro- ANS dependant

Recommendations Primary Prevention CVD in PWD

- Lifestyle management
  - Weight Reduction
  - Medical nutrition therapy
  - To achieve reductions in LDL-C
  - Physical activity
  - Tobacco cessation
- Glycemic targets
- Blood pressure targets
- Lipids regulation
- Antiplatelets

References

1. International Diabetes Federation. idf diabetes atlas. 7th ed. Brussels: International Diabetes Federation; 2015.
2. Abraham TM, Pencina KM, Pencina MJ, et al. Trends in diabetes incidence: the Framingham heart study. Diab Care. 2015;38:482–7.
3. Rosengren A (University of Gothenburg, Gothenburg, Sweden). Cardiovascular disease in diabetes type 2: current concepts (Review). J Intern Med 2018; 284: 240–253.
4. Ramachandran A, Snehalatha C, Kapur A, et al. Diabetes Epidemiology Study Group in India (DESI). High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. Diabetologia. 2001;44(9):1094–101.
5. Mohan V, Deepa M, Deepa R, et al. Secular trends in the prevalence of diabetes and impaired glucose tolerance in urban South India— the Chennai Urban Rural Epidemiology Study (CURES-17). Diabetologia. 2006;49(6):1175–8.
6. Haffner SM, Lehto S, Rönnemaa T, et al. Mortality from coronary heart disease in subjects with Type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998;339(4):229–34.
7. Kannel WB. Metabolic risk factors for coronary heart disease in women: perspective from the Framingham Study. Am Heart J. 1987;114(2):413–9.
8. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. Lancet. 1997;349(9064):1498–504.
9. Shanthi Rani CS, Rema M, Deepa R, et al. The Chennai Urban Population Study (CUPS)— methodological details—(CUPS Paper No. 1). Int J Diab DevCountries. 1999;19:149–57.
10. Morrish NJ, Wang SL, Stevens LK, et al. WHO multinational study group. Mortality and causes of death in the WHO multinational study of vascular disease in diabetes. Diabetologia. 2001;44(Suppl 2):S14–21.
11. Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. JAMA. 1999;281:1291–7.
12. Shah AD, Langenberg C, Rapsomaniki E, et al. Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1.9 million people. Lancet Diabetes Endocrinol. 2015;3:105–13.
13. Wei M, Gaskill SP, Haffner SM, et al. Effects of diabetes and level of glycemia on all-cause and cardiovascular mortality: the San Antonio heart study. Diabetes Care. 1998;21:1167–72.
14. Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative metaanalysis of 102 prospective studies. Lancet. 2010;375: 2215–22.
15. Abbud ZA, Shindler DM, Wilson AC, et al. Myocardial infarction data acquisition system study group. Effect of diabetes mellitus on short-and long-term mortality rates of patients with acute myocardial infarction: a statewide study. Am Heart J. 1995;130:51–8.
16. Wenger NK. You've come a long way, baby cardiovascular health and disease in women: problems and prospects. Circulation. 2004;109:558–60.
17. Manson JE, Colditz GA, Stampfer MJ, et al. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. Arch Intern Med. 1991;151:1141–7.
18. Huxley R, Barzi F, Woodward M. Excess risk of fatal coronary heart disease associated with diabetes in men and women: metaanalysis of 37 prospective cohort studies. BMJ. 2006;332:73–8.
19. Peters SA, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775 385 individuals and 12 539 strokes. Lancet. 2014;383:1973–80.
20. Fox CS. Cardiovascular disease risk factors, type 2 diabetes mellitus, and the Framingham heart study. Trends Cardiovasc Med. 2010;20(3):90–5.

Review