

Prevention of Cardiovascular Disease in Children with Diabetes

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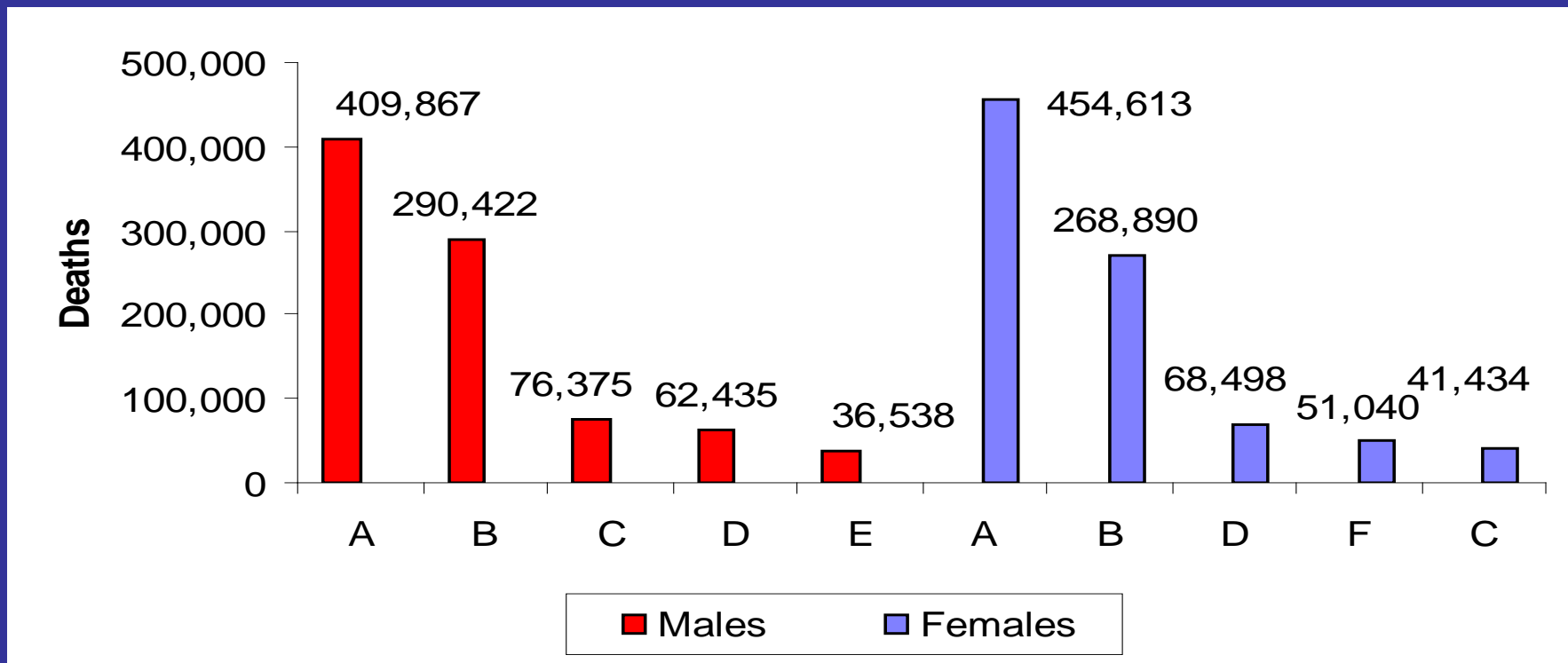
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Diabetes and Cardiovascular Disease

- **Cardiovascular disease is the leading cause of mortality in the United States.**
- **It is anticipated that this will be true worldwide in coming decades.**

Leading Causes of Death for All Males and Females

United States 2005



A. Total CVD
B. Cancer
C. Accidents

D. Chronic Lower Respiratory Diseases
E. Diabetes Mellitus
F. Alzheimer's Disease

Risk Factors for Cardiovascular Disease

Modifiable	Non Modifiable
Dyslipidemia	Age
Hypertension	Sex
Diabetes mellitus	Family history (genetic)
Cigarette smoking	
Left ventricular hypertrophy	
? Obesity	
? Inflammation	
? Hyperhomocysteinemia	

Diabetes and Cardiovascular Disease

- **Type 2 diabetes mellitus is an important risk factor for coronary heart disease in adults.**
- **Type 1 diabetes mellitus is also a CVD risk factor, but less is known about these relationships.**
- **The prevalence of type 2 diabetes is much higher than type 1 diabetes in adults.**

Diabetes and Cardiovascular Disease

Type 2 diabetes in adults is responsible for more cases of renal failure and peripheral vascular disease leading to amputations than any other disease process.

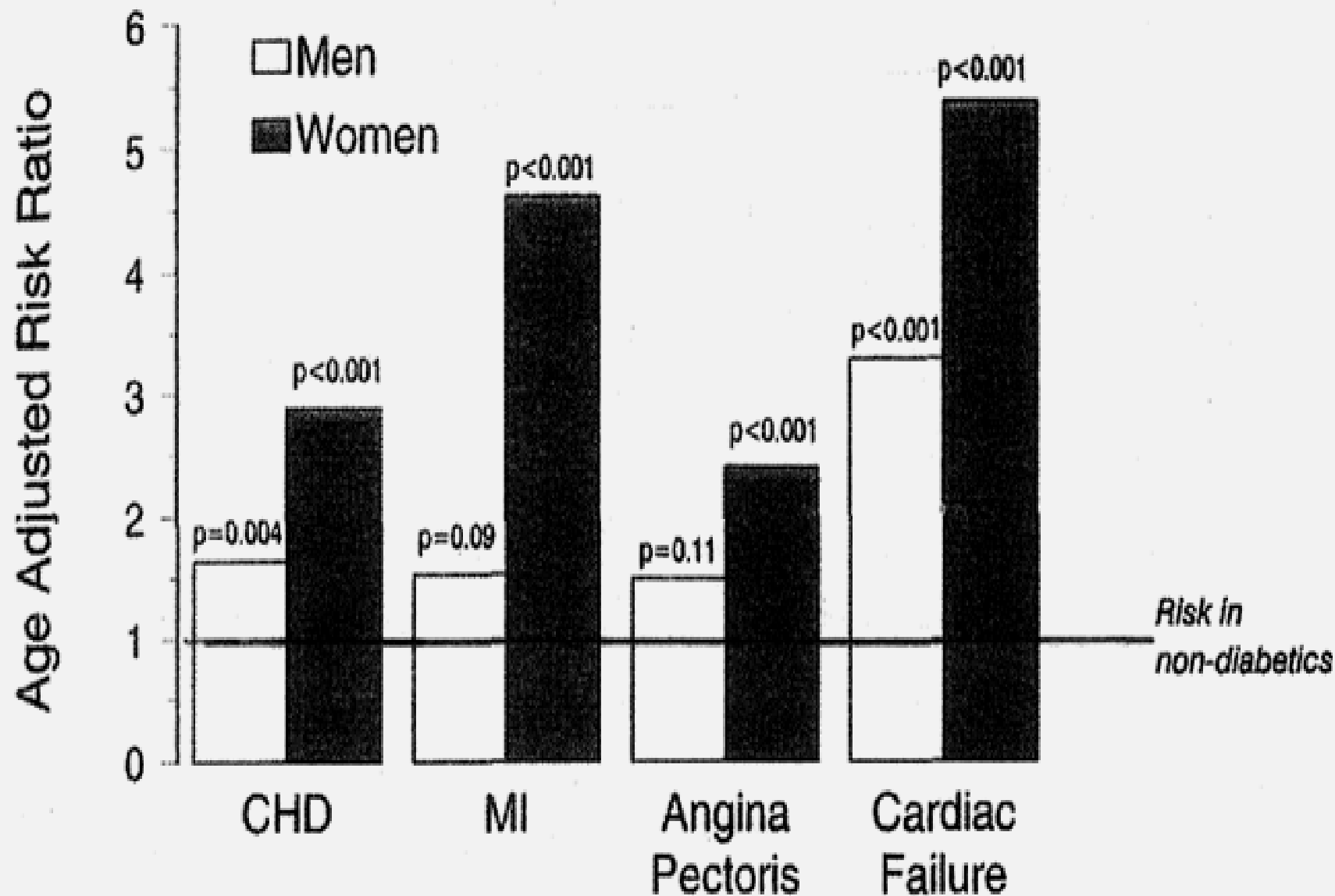


Figure 6. Diabetes and heart disease risk. Thirty-year experience of the Framingham cohort, men and women aged 35-64

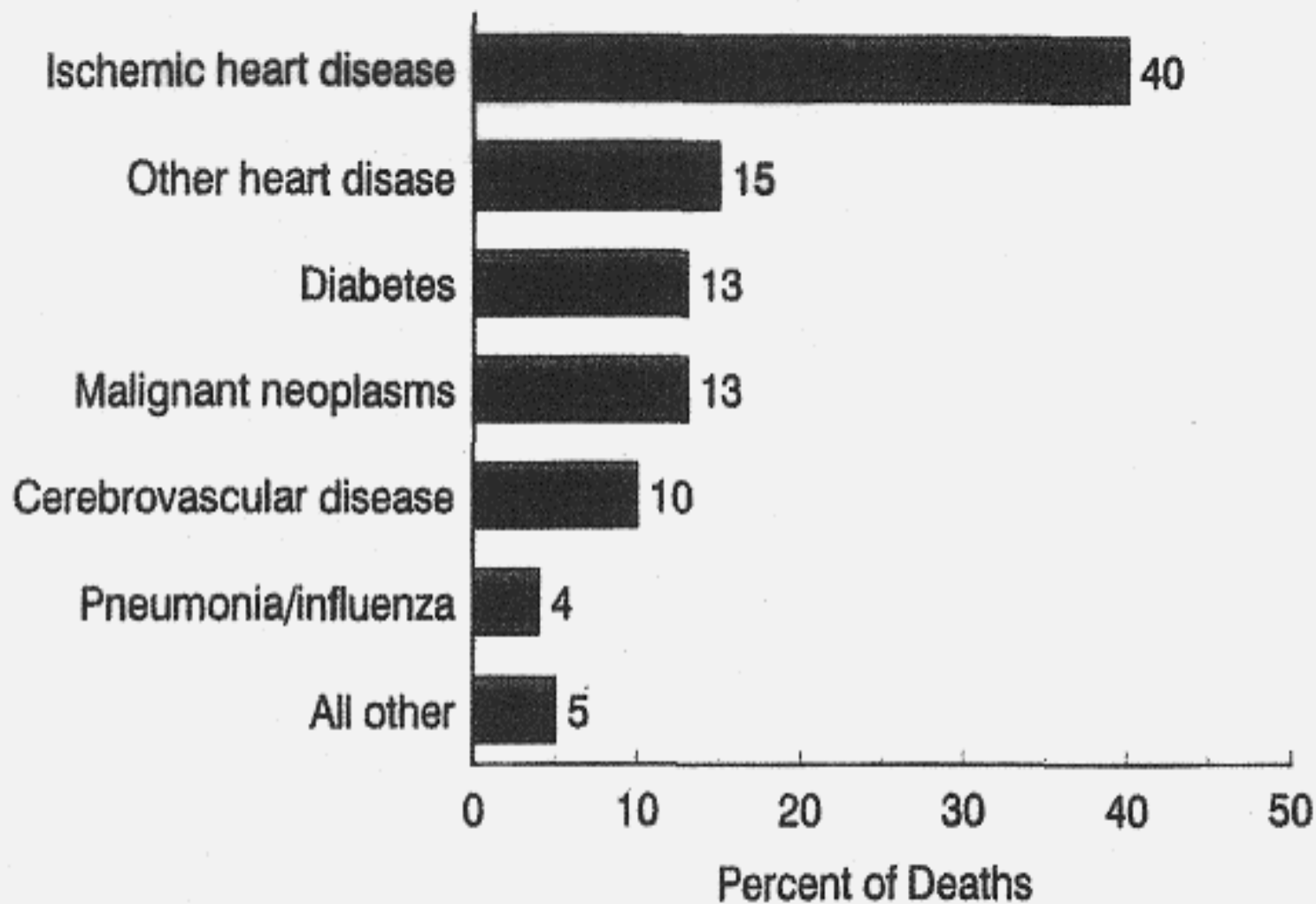


Figure 4. *Approximate distribution of causes of death in persons with diabetes, based on US studies.*

Recommendations of the American Diabetes Association (ADA) and National Cholesterol Education Program (NCEP)

A growing body of evidence reveals that people with diabetes carry an absolute risk for major coronary events similar to that of non-diabetic people with established CHD.

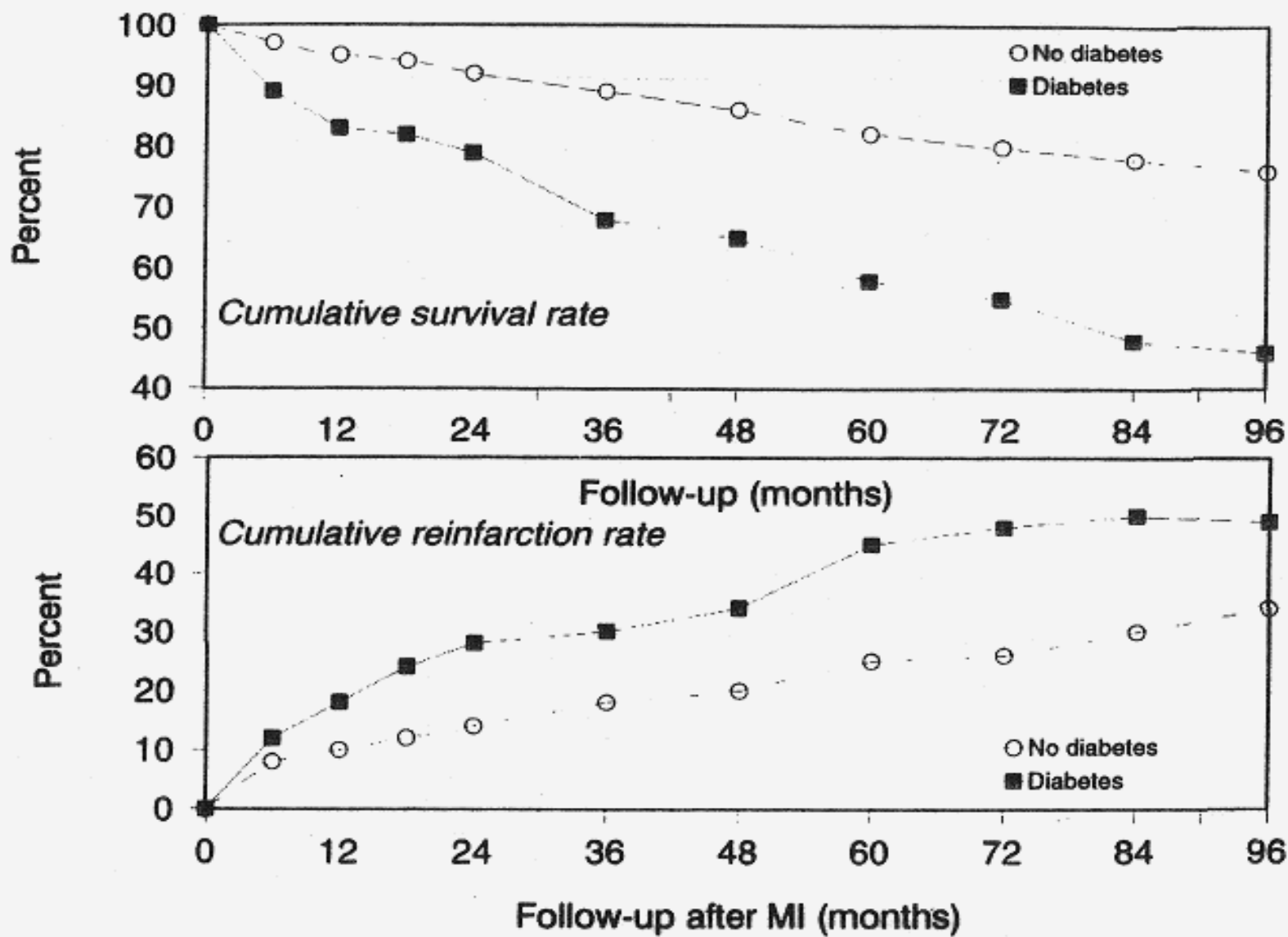


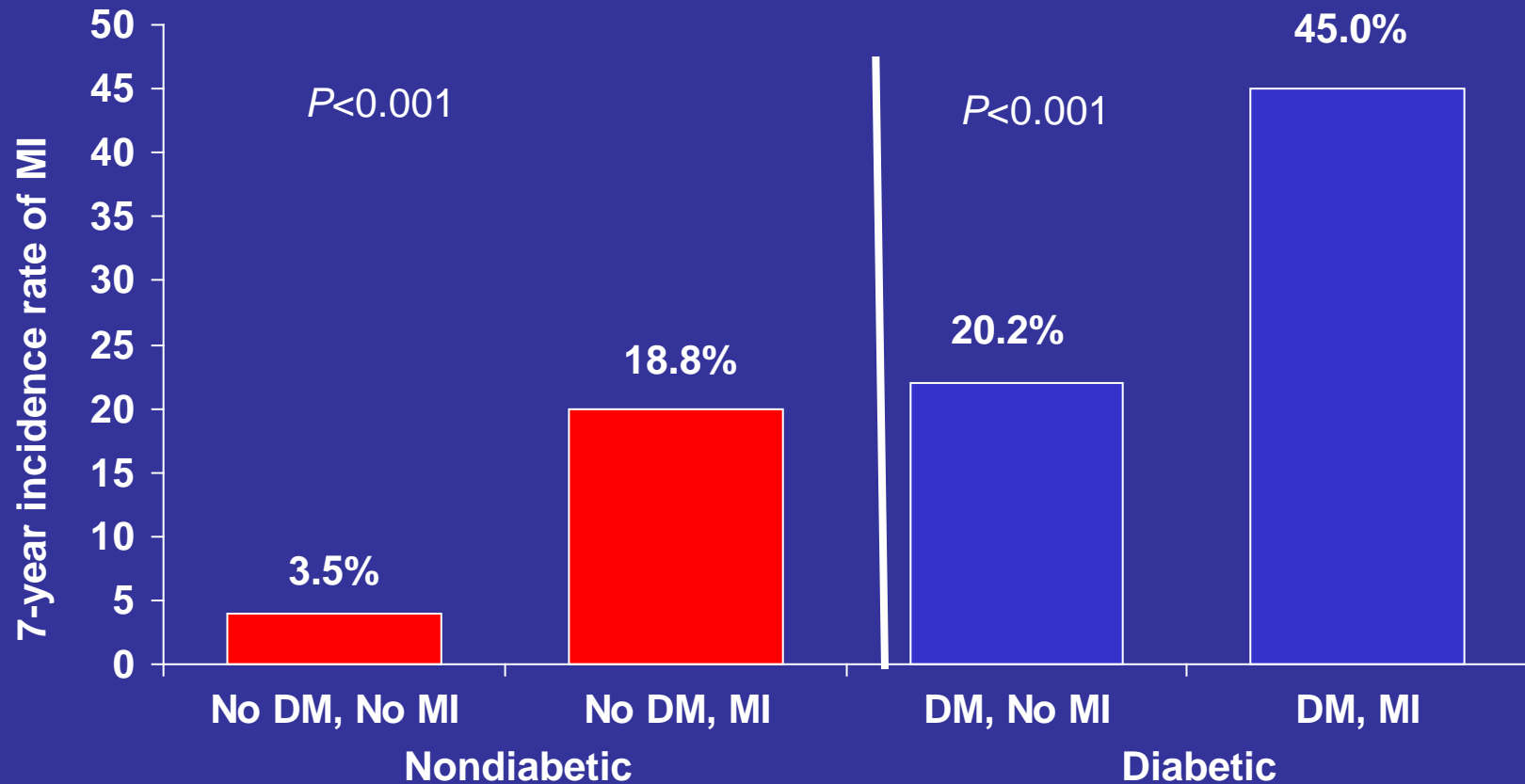
Figure 7. Cumulative survival and reinfarction post-MI in diabetics and nondiabetics.

Diabetes and Cardiovascular Disease

- Oasis Study – high CHD rate for diabetics
- Hope Study – annual event rate 2.5%

Both studies support the concept that individuals with type 2 diabetes have high risk of CHD.

Type 2 Diabetes and CHD 7-Year Incidence of Fatal/Nonfatal MI (East West Study)



CHD=coronary heart disease; MI=myocardial infarction; DM=diabetes mellitus

Diabetes and Cardiovascular Disease

- The time from diagnosis of diabetes to CVD event is approximately 10-15 years in adults. There is often a pre-diagnosis period of hyperglycemia (5-10 years).
- Total time from onset to CVD = 25 years

Diabetes and Cardiovascular Disease

If the time course of CVD related to diabetes is the same for adolescents as adults, it is anticipated that adolescents with type 2 diabetes will begin having substantial CVD morbidity and mortality in their 30's or 40's.

Diabetes and Cardiovascular Disease

Reasons To Be Concerned About Type 2 Diabetes

1. Hyperglycemia may itself be deleterious for the heart and vasculature.
2. Type 2 diabetes is generally accompanied by a constellation of metabolic risk factors.

Metabolic syndrome

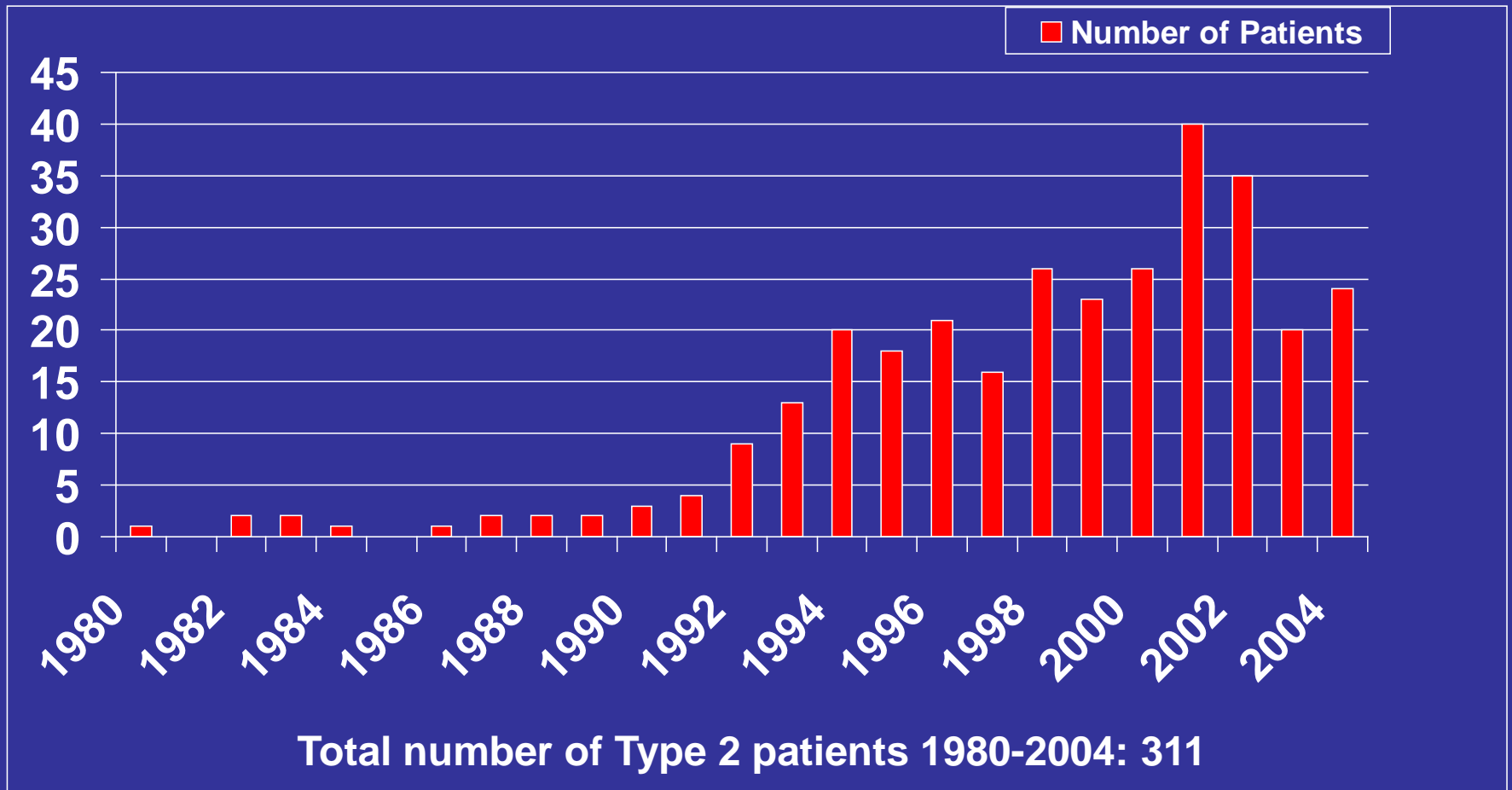
obesity (central)
insulin resistance
hypertension
atherogenic dyslipidemia
(↑TG, ↓HDL-C)

3. High risk in adults may translate to high risk in adolescents.

Diabetes and Cardiovascular Disease

As the prevalence and severity of obesity have increased in childhood, the prevalence of type 2 diabetes has also increased.

CCHMC Type 2 Diabetes 1980-2004



Time Course of Development of Atherosclerosis

Numerous studies now show that atherosclerosis begins early in life and that the risk factors for this early development are similar compared to adults.

Early Development of Atherosclerosis

McNamara et al – War in Viet Nam

Of 105 soldiers examined:

- 45% - some evidence of coronary atherosclerosis
- 5% - evidence of severe coronary atherosclerosis with plaque formation

Early Development of CVD in Transplanted Hearts

262 heart transplant recipients 1 month after transplant had intracoronary ultrasound.

Donor age – 33 ± 13 years

Atherosclerotic lesions 51.9%

<20 years of age 17%

>50 years of age 85%

Diabetes and Cardiovascular Disease

The Bogalusa Study examined the relationship of antemortem risk factors to the extent of atherosclerosis at autopsy in young persons.

TABLE 1. CORRELATION BETWEEN THE EXTENT OF LESIONS IN THE AORTA AND CORONARY ARTERIES AND ANTEMORTEM RISK-FACTOR VARIABLES.*

RISK-FACTOR VARIABLE	AORTA		CORONARY ARTERIES	
	FATTY STREAKS	FIBROUS PLAQUES	FATTY STREAKS	FIBROUS PLAQUES
Body-mass index	0.33†	0.24‡	0.41§	0.29†
Systolic blood pressure	0.31†	0.17	0.47§	0.41§
Diastolic blood pressure	0.14	0.10	0.18	0.24‡
Total cholesterol	0.54§	0.15	0.26‡	0.23
LDL cholesterol	0.54§	0.16	0.29‡	0.32†
HDL cholesterol	-0.03	0.05	-0.14	-0.12
Triglycerides	0.23	0.26‡	0.32†	0.37†

*Values shown are Spearman correlation coefficients. In this analysis, we used average z scores for risk factors in subgroups, defined by age, race, and sex, of all participants in the cross-sectional surveys. Although there was a total of 93 participants, because of missing data, the numbers used varied from 65 to 86, depending on the variables.

†P<0.01.

‡P<0.05.

§P<0.001.

Diabetes and Cardiovascular Disease

Clustering of Risk Factors

The presence of multiple risk factors is associated with increased risk of atherosclerosis.

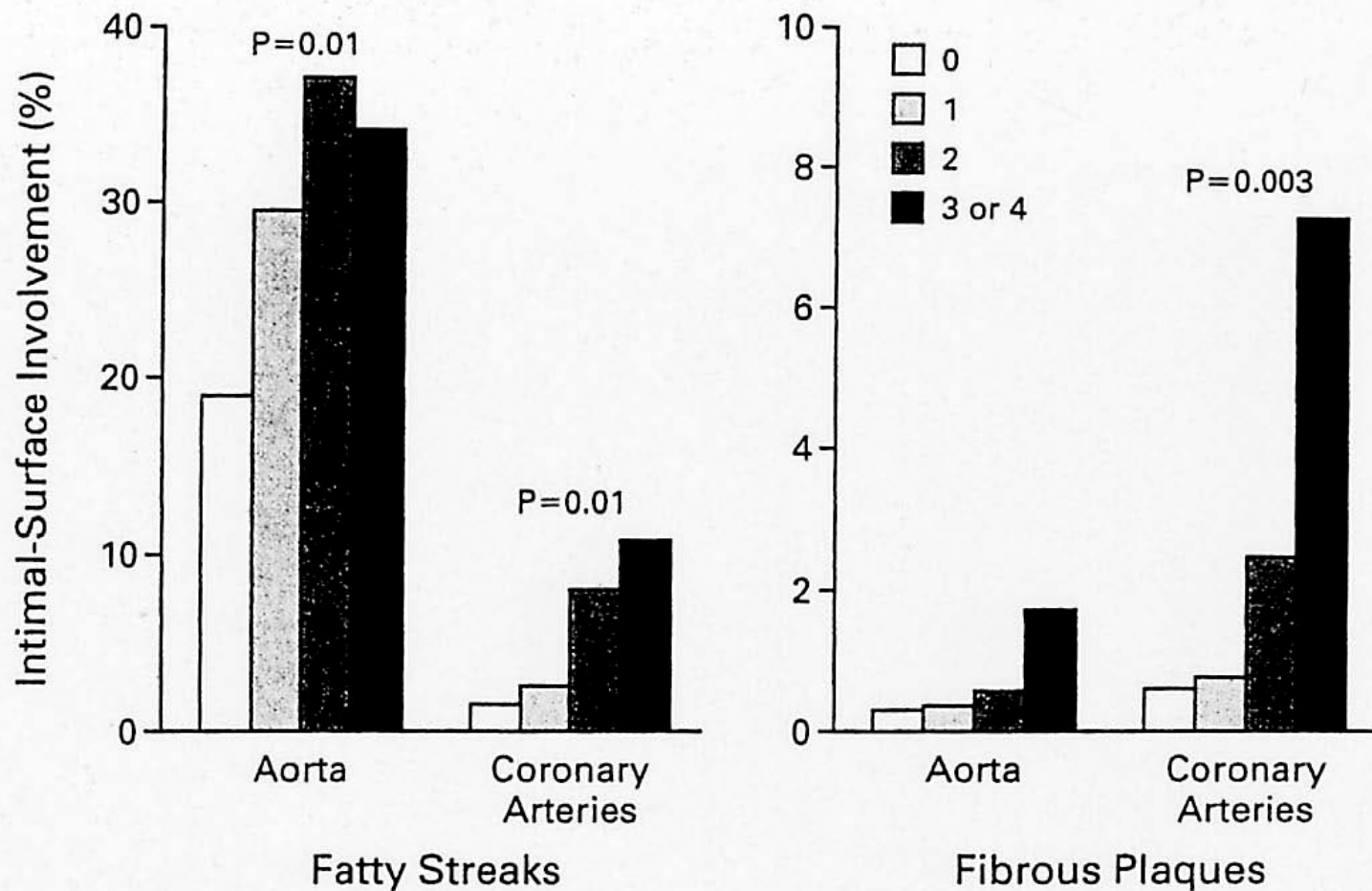


Figure 3. The Effect of Multiple Risk Factors on the Extent of Atherosclerosis in the Aorta and Coronary Arteries in Children and Young Adults.

Values shown are the percentages of the intimal surface covered with lesions in subjects with 0, 1, 2, and 3 or 4 risk factors. Risk factors were elevated values for body-mass index, systolic blood pressure, and serum triglyceride and LDL cholesterol concentrations, defined as values above the 75th percentile for the study group (specific for study period, race, sex, and age). There were 52 subjects with no risk factors, 20 with one, 14 with two, and 7 with three or four. The P value is based on the analysis of trend. A marked increase in the percentage of the intimal surface covered by fibrous plaques is evident in the coronary vessels of subjects with multiple risk factors.

Knowledge About the Relationship of Diabetes and CVD in Adolescents

- 1. Know that atherosclerosis begins in childhood and is progressive.**
- 2. Know that the traditional risk factors are operative.**
- 3. Do not know the extent to which diabetes increases risk for CVD in young individuals.**

Diabetes and Cardiovascular Disease

Factor	Type 1	Type 2
Age of Onset	11 years	Adulthood
Glucose Variability	↑↑↑	↑
Insulin Resistance	↑	↑↑↑
Inflammation	?	↑
Other Risk Factors	?	?
Microvascular Complications	↑↑↑	↑
Macrovascular Complications	↑ ?	↑↑↑

Diabetes and Cardiovascular Disease

Type 1 Diabetes

- **Glycemic control is important for both microvascular and macrovascular outcomes.**
- **Higher HbA1c is associated with greater risk of CVD outcomes.**

Diabetes and Cardiovascular Disease

Odds of calcification was
7 times higher (OR=7.11)
for subjects with HbA1c over 7.5%.

Non Invasive Methods to Study Cardiovascular Abnormalities

- **Carotid ultrasound**
 - **Carotid intimal medial thickness**
- **Carotid IMT has been shown to correlate with coronary artery abnormalities.**
- **Greater carotid IMT is a risk factor for stroke and CAD.**

Diabetes and Cardiovascular Disease

Type 1 Diabetes

- Pediatric studies using carotid intimal medial thickness or arterial stiffness have not shown associations with glycemic control.
- Studies are smaller and shorter-term.

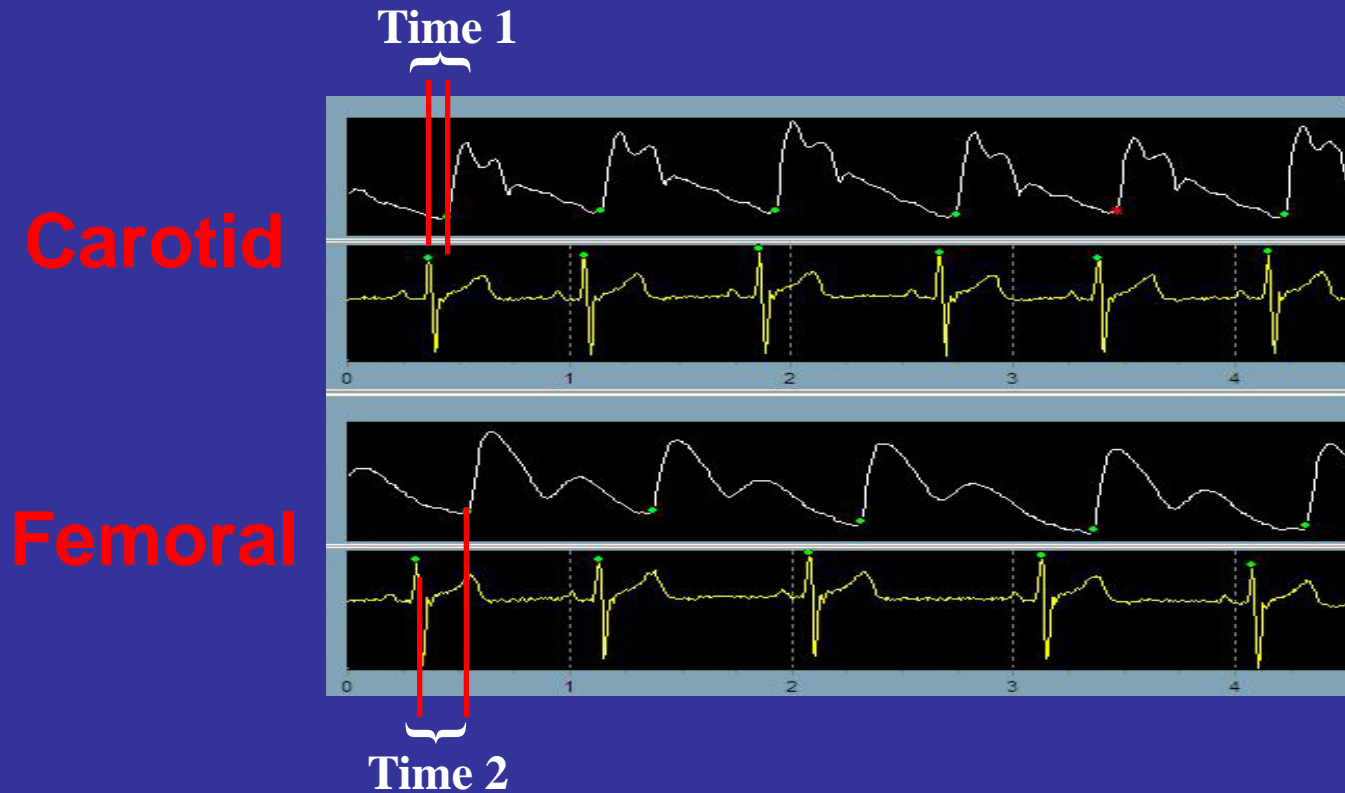
Diabetes and Cardiovascular Disease

- A meta-analysis of randomized controlled studies compared outcomes in T1DM and T2DM.
- Results: Glycemic control improves CVD risk in both type 1 and type 2, but greater improvement in type 1.

Diabetes and Cardiovascular Disease

- **Pulse wave velocity is a measure of arterial stiffness.**
- **Pulse wave velocity is a predictor of mortality in both type 1 and type 2 diabetic patients.**

Pulse Wave Velocity



- Tonometers (pressure sensors) used to measure Pressure waves at Carotid & Distal Site (radial, femoral or foot)
- Distance measured directly in cm
- Time measured from R on ECG to foot of pressure wave
- Calculate PWV = $\frac{\text{distance}}{\Delta t}$

Diabetes and Cardiovascular Disease

In children and adolescents, those with type 2 diabetes had higher pulse wave velocity than those with type 1 diabetes after controlling for age and sex.

Diabetes and Cardiovascular Disease

**These results may be due to
increased obesity in young
patients with type 2 diabetes.**

Diabetes and Cardiovascular Disease

Risk Factors for CVD

Other risk factors such as blood pressure elevation and dyslipidemia are important for patients with type 1 and type 2 diabetes.

Diabetes and Cardiovascular Disease

Blood Pressure

Prevalence of hypertension
(*BP > 90th percentile*)

Type 1 DM

22%

Type 2 DM

73%

Diabetes and Cardiovascular Disease

Blood Pressure - ADA Guidelines

- Measurement of BP at each visit
- 90th-95th percentile =
Prehypertension
- >95th percentile = Hypertension
 - If hypertension is present, perform echocardiogram for left ventricular hypertrophy.

Diabetes and Cardiovascular Disease

Blood Pressure - ADA Guidelines

- **Intervention**
 - first, non-pharmacologic
 - second, pharmacologic (ACE inhibitor)
- **Goal is reduction of BP < 90th percentile**

Diabetes and Cardiovascular Disease

Dyslipidemia

	<u>Type 1</u>	<u>Type 2</u>
LDL > 160 mg/dL	3%	9%
LDL > 130 mg/dL	14%	24%
LDL > 100 mg/dL	48%	54%

Diabetes and Cardiovascular Disease

Dyslipidemia

	<u>Type 1</u>	<u>Type 2</u>
HDL < 40 mg/dL	12%	44%
Triglycerides > 150 mg/dL	10%	39%

ADA Recommendations for Lipid Abnormalities

	Type 1	Type 2
Initial screening	≥ 2 yr at diagnosis if other CVD risk factors; otherwise at 12 yr (puberty)	At diagnosis, regardless of age
Rescreening, if lipid profile is normal	5 yr	2 yr
Test – Fasting Lipid Profile		

ADA Recommendations for Lipid Abnormalities

Initial management of dyslipidemia:

- **Glycemic control**
- **Diet**
- **Physical activity**

Diabetes and Cardiovascular Disease

LDL-C concentration for pharmacological treatment if initial management fails (age 10+ yr)

**LDL-C >160 mg/dL:
Begin medication**

**LDL-C 130-159 mg/dL:
“Consider” medication based on other adult risk factors**

- Hypertension
- Obesity (95th percentile for age and sex)
- Parental TC >240 mg/dL or family history of cardiovascular event in a parent before 55 yr of age
- HDL-C <35 mg/dL

Diabetes and Cardiovascular Disease

Optimal concentration:

- LDL-C <100 mg/dL
- HDL-C >35 mg/dL
- Triglyceride <130 mg/dL

Summary

- **Diabetes has been established as a particularly potent risk factor for CVD in adults.**
- **This has led to the concept that diabetic adults be treated in an equivalent fashion with persons who have established CAD.**

Summary

- **The prevalence of type 2 diabetes is increasing in adolescents.**
- **It is not known if adolescents with type 2 diabetes have an equally high risk for CVD as adults.**

Summary

- It is known that adolescents have many of the elements of the metabolic syndrome when they develop type 2 diabetes.
- Type 1 diabetes is also associated with increased risk of CVD in adults.

Summary

- **Glucose control appears to be more of a clinical issue in type 1 diabetes.**
- **Abnormal risk factors for CVD are common in type 1 and type 2 diabetes (more common in type 2).**

Summary

- **Aggressive management of risk factors for cardiovascular disease is indicated in adolescents and young adults with type 1 and type 2 diabetes mellitus.**