

CARDIOVASCULAR PROPHYLAXIS IN DIABETES

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Diabetes and cardiovascular risk

- DM is a condition of premature cardiovascular complications in the setting of chronic hyperglycemia



Cardiovascular Risk

- So as soon as one is diagnosed as a case of diabetes , one should be considered to have a heart attack already.

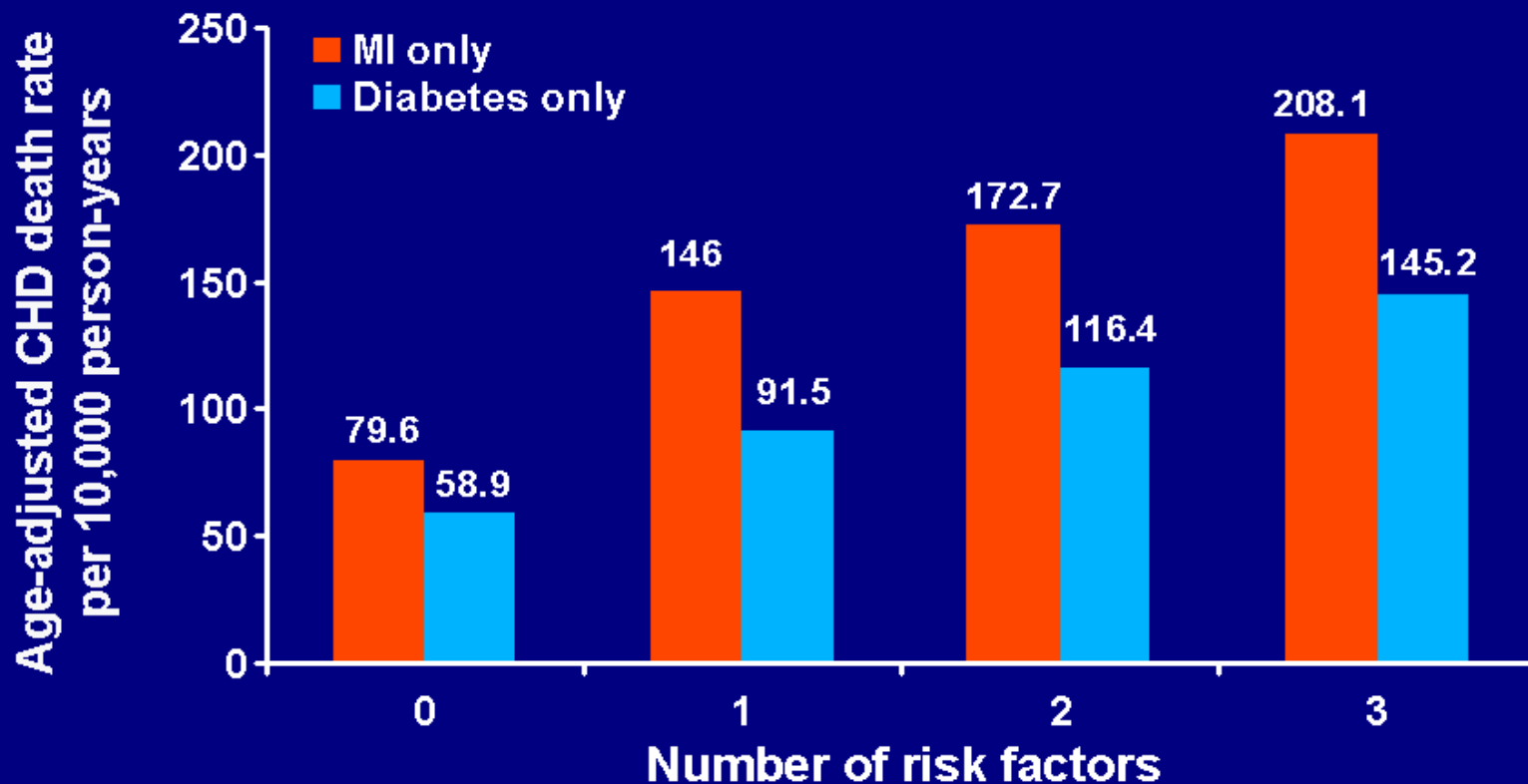
A patient with diabetes= A patient with MI



Increased Risk of Heart Disease in Diabetes

- In patients with diabetes
 - ▣ Risk of CHD increases by 3-4 fold
 - ▣ 75-80% deaths are attributed to CHD
 - ▣ High mortality rate in 1 year after first MI
 - 44 % in Diabetic men
 - 37% in Diabetic women

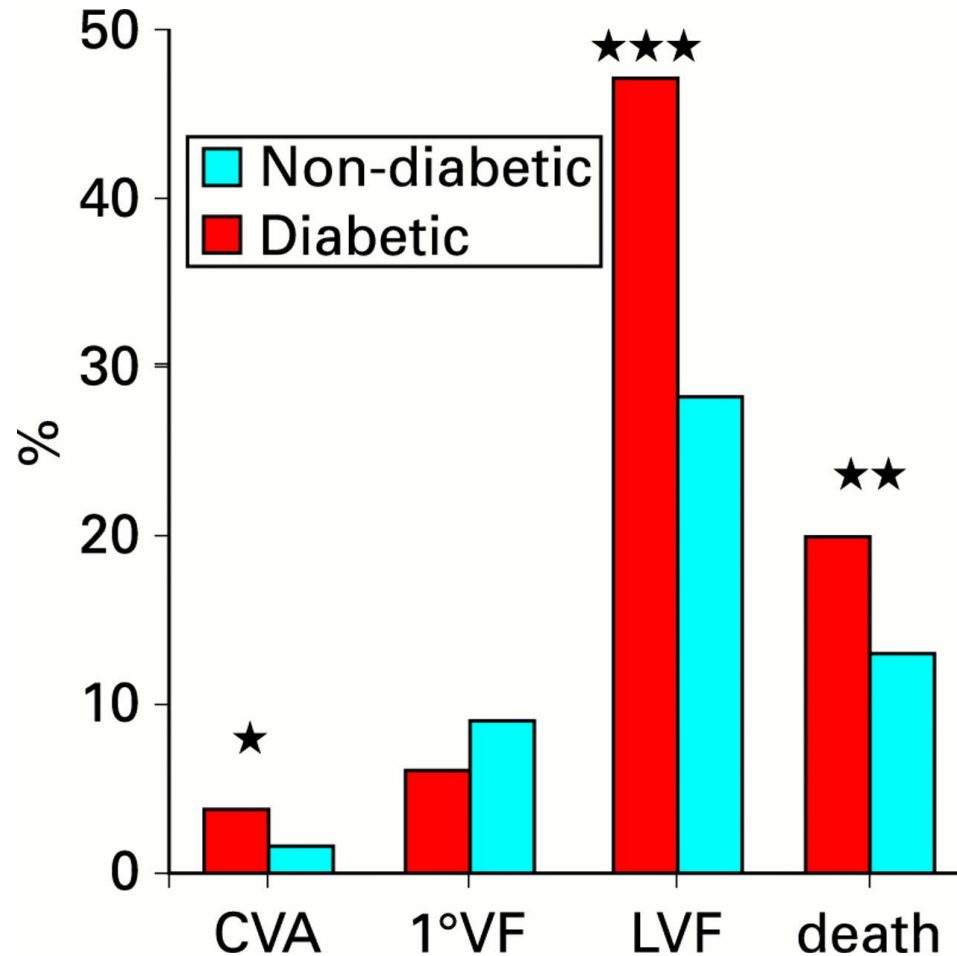
MRFIT: Impact of Diabetes on Cardiovascular Disease Mortality



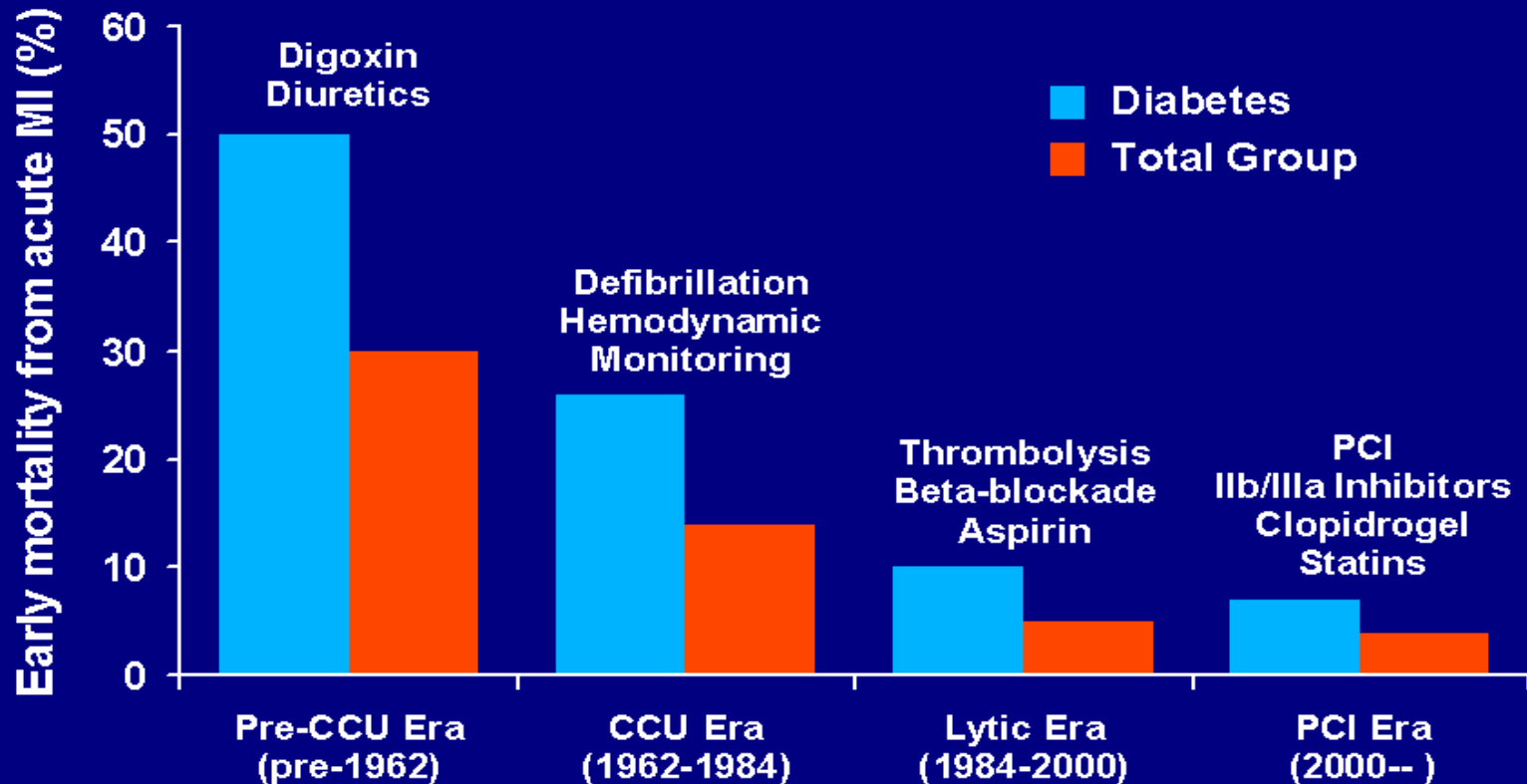
MRFIT=Multiple Risk Factor Intervention Trial.

Data from Vaccaro O et al. *Arch Intern Med.* 2004;164:1438-1443.

Complications of acute myocardial infarction in diabetic and non-diabetic patients (n = 1929).

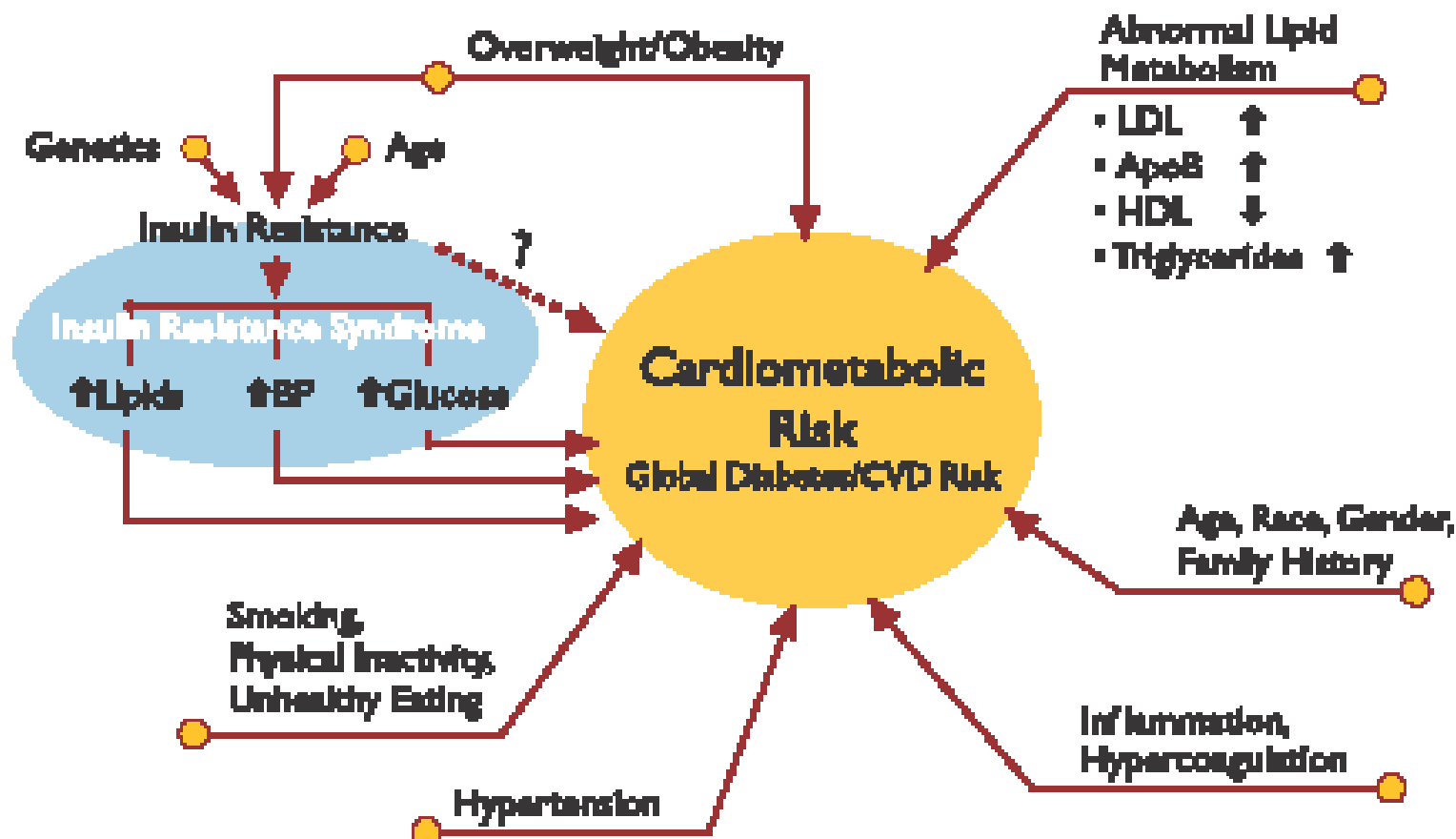


Diabetes Doubles Risk for MI Mortality Despite Advances in Cardiac Care



Adapted from Braunwald E. *N Engl J Med.* 1997;337:1360-1369.

Factors Contributing to Cardiometabolic Risk



Visceral Obesity

Insulin Resistance
↑ Free Fatty Acids

Glycemic disorders

Dyslipidemia
- Low HDL
- Small, dense LDL
- Hypertriglyceridemia
- Postprandial lipemia

Hypertension

Impaired thrombolysis
- ↑ PAI-1, fibrinogen




Endothelial dysfunction/ inflammation
- ↑ CRP, MMP-9,
↓ adiponectin

Microalbuminuria

Atherosclerosis

Brunzell J, Hokanson J. *Diabetes Care*. 1999;22(Suppl 3):C10-C13.
McFarlane S, et al. *J Clin Endocrinol Metab*. 2001;86(2):713-718.
Frohlich M, et al. *Diabetes Care*. 2000;23(12):1835-1839.
Kuusisto J, et al. *Circulation*. 1995;91:831-837.
Parulkar AA, et al. *Ann Intern Med*. 2001;134:61-71.
Hseuh WA, et al. *Diabetes Care*. 2001;24(2):392-397.
Lebovitz H. *Clin Chem*. 1999;45(8B):1339-1345.

Type 2 DM and cardiovascular risk

- Endothelial dysfunction
- Hypertension
- Advanced Glycation products
- Prothrombosis -  Fibrinogen/PAI 1 increased
- Dyslipidemia -  Total C/TG/LDL/Apo B
 HDL-C

Cardiovascular Risk factors specific for Diabetes

- Serum Insulin
- Microalbuminuria
- Massive proteinuria
- PAI-1
- Abnormal Platelet function
- Fibrinogen level

Cardiovascular Risk Factors In Diabetes

- Fasting/postprandial hyperglycemia
- Overweight/obesity
- Elevated systolic and diastolic blood pressure,
- Dyslipidemia.
- Smoking

**Risk factors- Hypertension,
Obesity, Diabetes, Cholesterol,
Smoking**

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graph TD; A[Risk factors- Hypertension, Obesity, Diabetes, Cholesterol, Smoking] --> B[Preclinical disease- Hypertrophy : LVH, Vascular Atherosclerosis : Carotid, Cardiac]; B --> C[Morbid Events- MI, Stroke, Arrhythmia, SCD];
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Preclinical disease-
Hypertrophy : LVH, Vascular
Atherosclerosis : Carotid, Cardiac

Morbid Events-
MI, Stroke, Arrhythmia, SCD



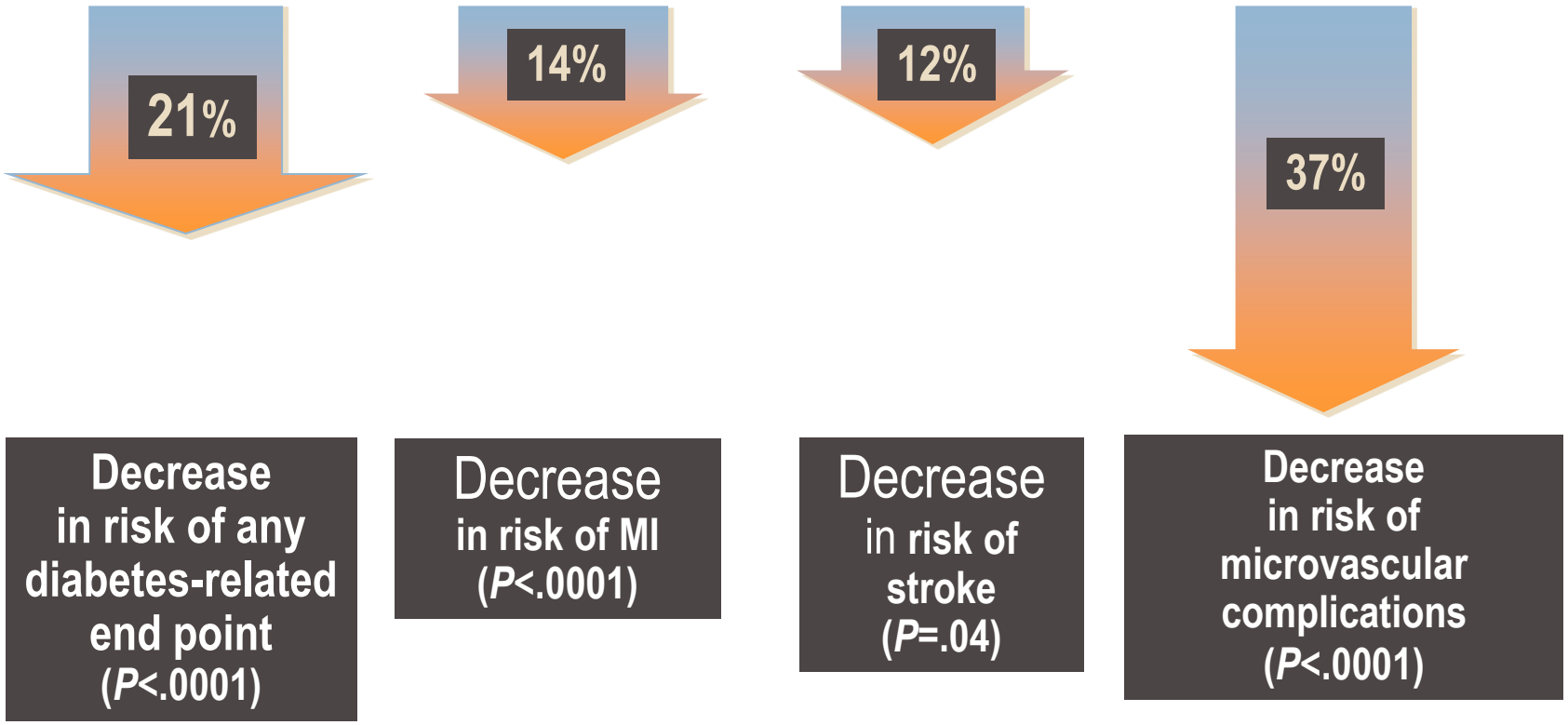
So, how to keep the CV risk at bay in diabetics?

- 
- First step is to keep a good glycemic control.

Studies have shown that control of diabetes can reduce the CV complications

- DCCT 1984-1992
- UKPDS 1978-1998
- KUMAMOTO 1992-2000
- EDIC 1996
- ACCORD 2002-2007
- ADVANCE

Improved Glycemic Control Reduces Risk of Complications

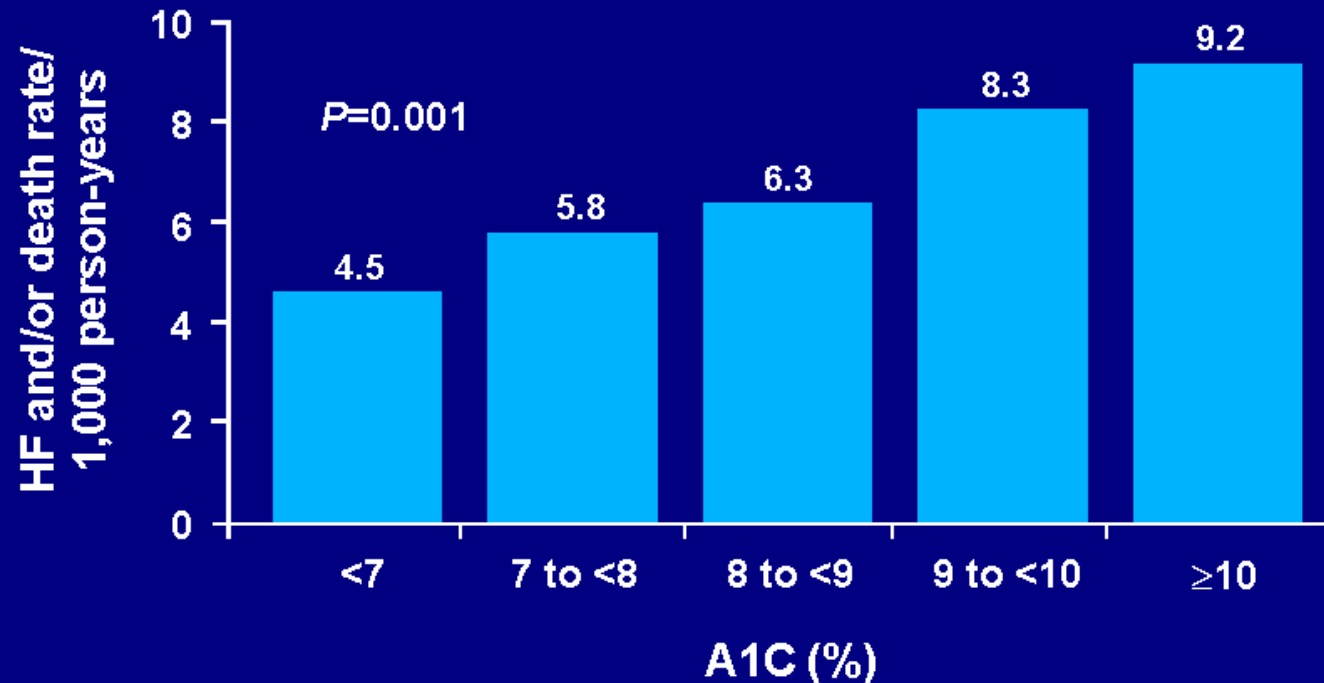


Stratton IM et al. *BMJ*. 2000;321:405-412.

UKPDS Follow-up

- UKPDS 66 Patients with fatal MI had higher HbA(1c) than those with nonfatal MI (odds ratio 1.17 per 1% HbA(1c), $P = 0.014$).
- Patients with fatal stroke had higher HbA(1c) than those with nonfatal stroke (odds ratio 1.37 per 1% HbA(1c), $P = 0.007$)

Glycemic Control and Risk of Development of HF in Diabetes



HF=heart failure.

Data from Iribarren C et al. *Circulation*. 2001;103:2668-2673.

ADA Standards of Care 2011

- ADA recommends a general A1C target of $<7\%$
- The goal of therapy for the individual patient is to achieve an A1C as close to normal as possible without hypoglycemia
- More stringent glycemic goals may reduce the risk of serious diabetes-related complications
- Less stringent treatment goals may be appropriate for certain patient populations and patients with severe or more frequent hypoglycemia

Life style modification

- Diet
- Weight loss
- Physical activity/Exercise
- Cessation of smoking

Diet and diabetes

- Individualised
- Realistic
- Flexible
- Suitable to patient's life style



What not eat

Sweets

Chocolates

Beef fry

Pastry

Mutton

Cola

Chips

Sugar





Weight Loss



Benefits of 10% weight loss

- 20% fall in mortality
- 30% fall in diabetes related death
- 40 % fall in obesity related death
- 20% fall in SBP
- 10% fall in DBP
- 15% fall in LDL-C
- 30% fall in TG
- 8% increase in HDL-C



Exercise



Exercise

□ Benefits

- Good glycemic control
- Improves insulin sensitivity
- Optimizes body weight
- Gives psychological well being
- Decreases cardiovascular mortality



Exercise

- ❑ **Disadvantages of unplanned exercise**
 - ❑ Strain the compromised CVS
 - ❑ Predisposes hypoglycemia
 - ❑ Injures musculoskeletal system



Calorie expenditure

□ Lying down/sleeping/sitting	1
□ Standing/ desk work/ driving	2
□ Level walking level bi cycling	3
□ Social double badminton	4
□ Social singles badminton	5
□ Gardening , swimming	6
□ Competetive badminton	7
□ Jogging	8
□ Basketball	9
□ Running 1 km/hour	10

Calories spent in various activities

- Walking 3 miles/hour 275/hr
- Walking 5 miles/hour 420/hr
- Cycling 8 miles/hour 325/hr
- Mopping/vacuuming 240/hr
- Scrubbing floors 300/hr
- Gardening 220/hr
- Vigorous dancing 400/hr




Exercise guidelines

- ❑ Medical evaluation for CVD, PVD and PN
- ❑ Choose enjoyable activities
- ❑ Walking at least 20 min/day
- ❑ 5 min warm up
- ❑ 5 min calm down
- ❑ Education on hypoglycemia
- ❑ Proper foot care and footwear
- ❑ Pre and post RBS monitoring
- ❑ Insulin and carbohydrate adjustments
- ❑ Should carry snacks along with





Smoking

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- Cessation of smoking reduces 50% risk of MI in first year after quitting



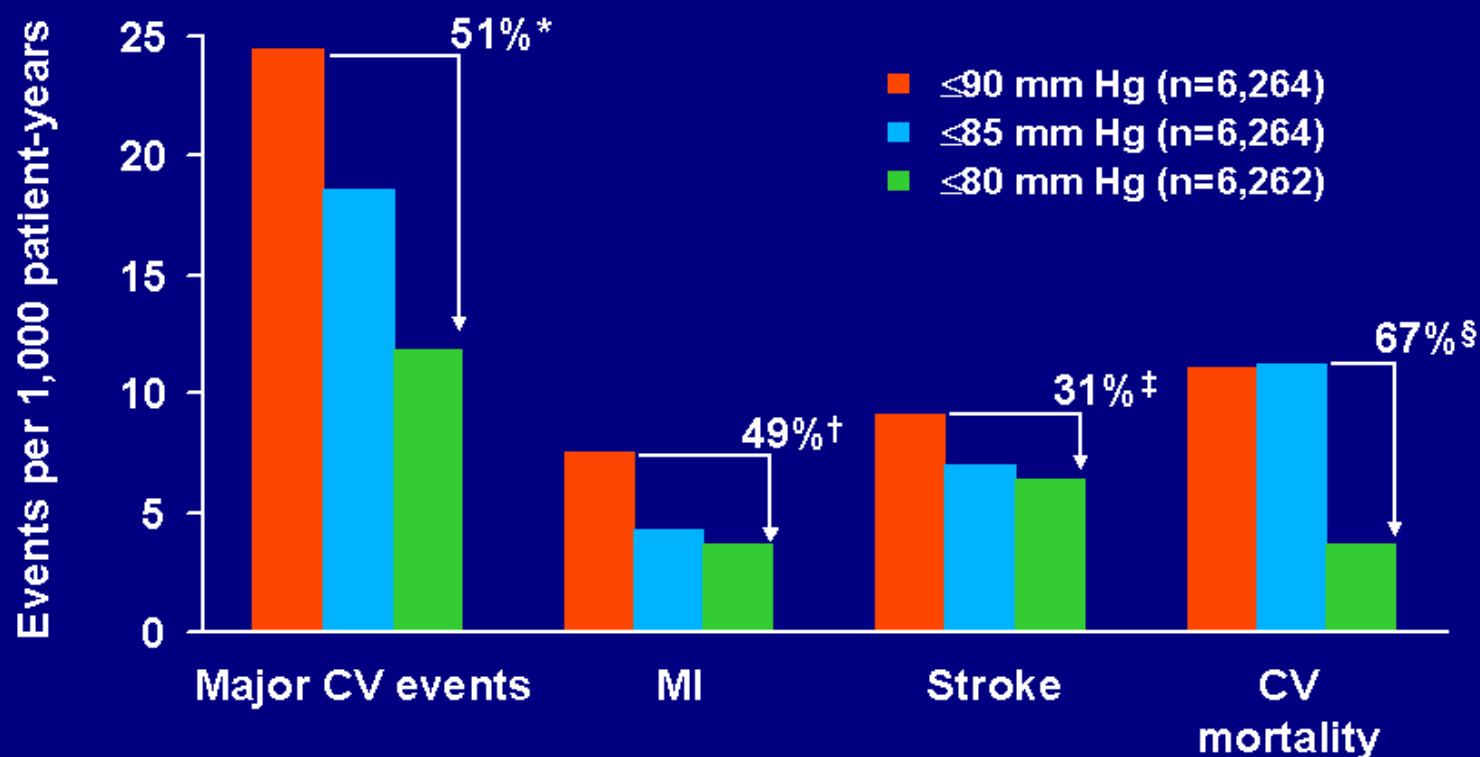
Control of Hypertension

Treatment of hypertension

- Target blood pressure
- How to treat ?
- What is the preferred one?



HOT: Cardiovascular Events by Target DBP in Diabetes Subgroup

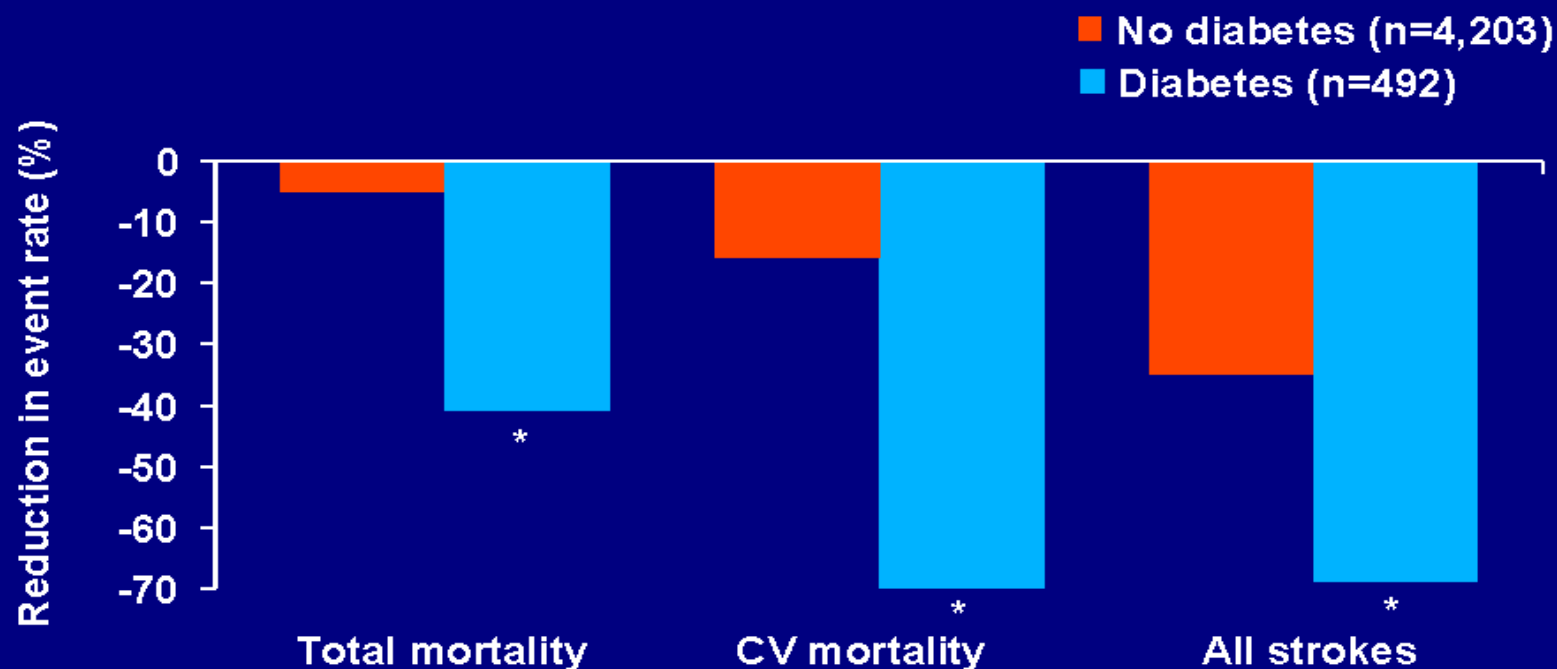


P for trend = *0.005; †0.11; ‡0.34; §0.016.

DBP=diastolic blood pressure.

Hansson L et al. *Lancet*. 1998;351:1755-1762.

Syst-Eur: Reduction in Event Rate in Adults (≥ 60 Years) With Diabetes



* $P < 0.01$ compared with no diabetes.
Syst-Eur=Systolic Hypertension in Europe.

Tuomilehto J et al. *N Engl J Med.* 1999;340:677-684.

ADA 2011

- Target blood pressure
 - ▣ Systolic less than 130 mm Hg
 - ▣ Diastolic less than 80 mm Hg

- ACEi/ARB - Decrease IR, LDL , Increase HDL slightly
- HCTZ – Increase IR, LDL , Decrease HDL slightly
- B Blockers-Increase IR, LDL,Decrease HDL slightly
- Alpha Blockers - Decrease IR, LDL , Increase HDL slightly
- Ca channel blocker - neutral



Cholesterol

Name	N	Agent	Baseline LDL-C	Reduction LDL-C %	Reduction in cardiovascular events %	P
CARE	586	Pravastatin	3.5	28	25	0.05
4S	202	Simvastatin	4.6	36	55	0.0002
LIPID	782	Pravastatin	3.8	25	19	Ns
Heart Protection Study	269	Simvastatin	2.3	43	24	<0.0001

Target level of Cholesterol ADA 2011

□ LDL -C

- Less than 100 mg/dl (2.6mmol/L)if patient has no overt CVD
- Less than 70 mg / dl (1.8 mmol/L) in diabetic pateints with CVD
- 30-40 % reduction from baseline

□ HDL –C

- More than 40 mg/ dl (1 mmol/L) in male
- More than 50 mg /dl (1.3 mmol/L)

□ Triglyceride

- Less than 150 mg/ dl (1.7 mmol/L)

What to do reduce Cholesterol ?

- Lifestyle modification
- Statin therapy
- Fibrates

When to start statin in diabetes ?

- All diabetic patients
 - With a history of overt CVD
 - Over 40 years of age with one or more risk factors
 - If LDL-C is more than 100 mg/dl in absence of risk other factor

Modifications of lipoprotein levels :

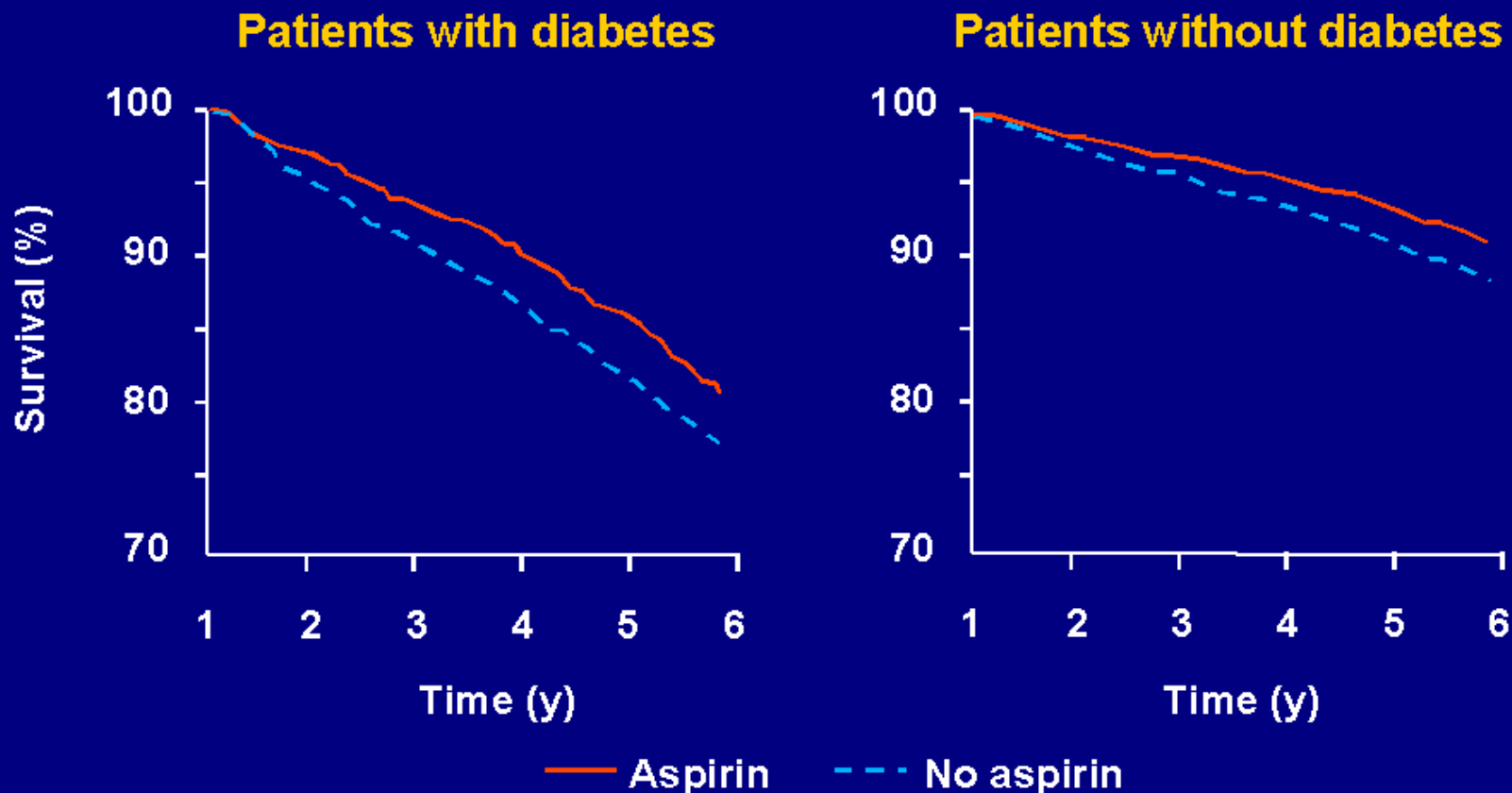
Glucose lowering medications

- Improved control of hyperglycemia can reduce some degree of dyslipidemia
- Glucose lowering medication can decrease triglyceride level
- Thiazolidiones increase HDL-C level but can also decrease LDL-C level
- Optimal glycemc control may result in less atherogenic LDL paricle
- Complete reversal of dyslipidemia by improved glycemc control is usually unacheivable



Role of Aspirin

Effect of Aspirin Use on Survival in Patients With CAD



CAD=coronary artery disease.

Harpaz D et al. *Am J Med.* 1998;105:494-499.

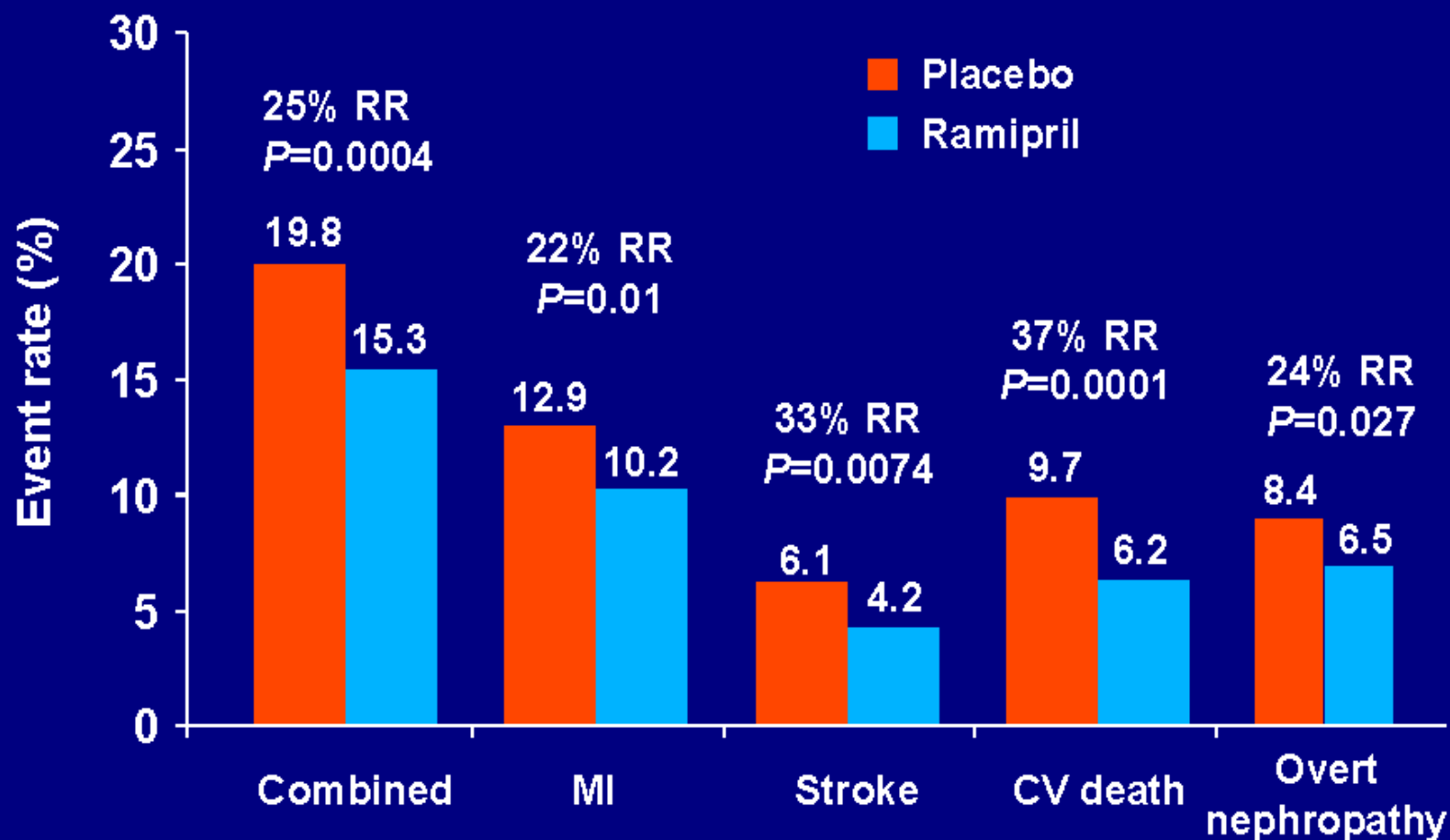
Use of aspirin

- HOT trial : 36 % risk reduction of MI & 15 % reduction in major CV events
- Physicians Health study: 44 % risk reduction of MI & 18% reduction in major CV events
- APT trial :33 % reduction in MI/Stroke
- ETDRS :18% risk reduction of fatal/non fatal MI

Aspirin : When to use?

- **For primary prevention this should be used**
 - ▣ 10 year cardiovascular risk $> 10\%$
 - ▣ In male > 50 years and in female > 60 years with with at least one additional risk factor eg. HTN, Smoking, F/H of CVD, Dyslipidemia, Albuminuria
- **For secondary prevention**
 - ▣ All diabetic patients with a history of CVD

HOPE: Outcomes in Patients With Diabetes



RR = risk reduction.

HOPE Study Investigators. *Lancet*. 2000;355:253-259.

ACE inhibitor therapy for Patients With Diabetes

- Microalbuminuria is a significant risk factor for cardiovascular events
- ACE-I inhibits the progression from microalbuminuria to macroalbuminuria
- ACE-I is recommended to all patients of diabetes with hypertension
- Patients with Type 2 Diabetes and hypertension treated with ACE-I have a significantly lower risk of major vascular events than those treated with B blockers or calcium channel blocker

Take Home Messages

- Having Diabetes is as bad as having an AMI
- Death in DM patients is majority from acute coronary events
- IR plays major role in atherosclerosis
- Coronary events are more extensive and more fatal in DM patients
- Dietary and life style modification are vital
- Anti hypertensives should be judiciously selected
- Lipid lowering therapy should be aggressive
- Aspirin is also an important tool for CV prophylaxis



THANK YOU