



Welcomes You To

**THE CONVERGENCE OF
TYPE 2 DIABETES &
CARDIOVASCULAR DISEASE**

Lisa M. O'Brien, CNP
MetroHealth Medical Center

Program Overview

Cardiovascular disease and diabetes are closely related and as a result, the ACC is conducting a large initiative over the next two years to increase this awareness and to provide further education to medical professionals.

Learner Objectives

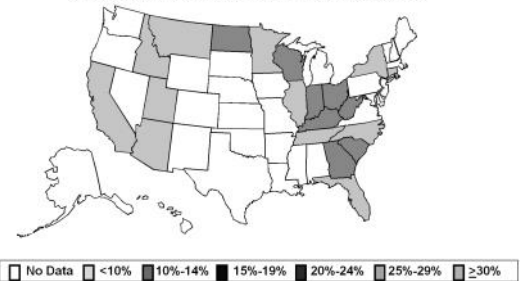
Enhance competence by providing the most up-to-date information on the correlation of type 2 diabetes and cardiovascular disease.

Upon completion of this program, attendees should be able to —

- Describe the prevalence of CV disease in patients with diabetes
- Identify patients with known diabetes and those at risk for diabetes, who are at significantly increased risk for CV disease based on the most current screening and treatment guidelines
- Apply modifiable and controllable risk factor strategies in the daily management of patients with diabetes and/or CV disease, to achieve evidence-based optimal outcomes

**Obesity Trends* Among U.S. Adults:
BRFSS - 1985**

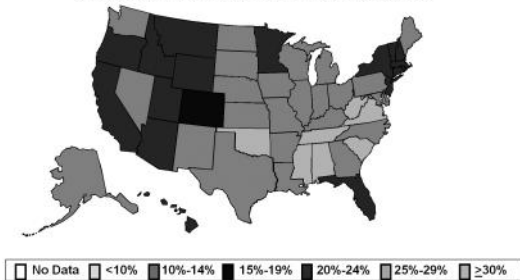
(*BMI ≥ 30 , or ~ 30 lbs overweight for 5'4" woman)



JAMA 1995;282:16. JAMA 2001;286:10

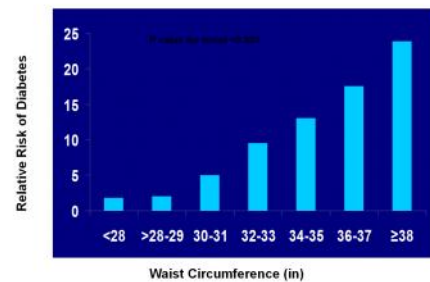
**Obesity Trends* Among U.S. Adults:
BRFSS - 2008**

(*BMI ≥ 30 , or ~ 30 lbs overweight for 5'4" woman)



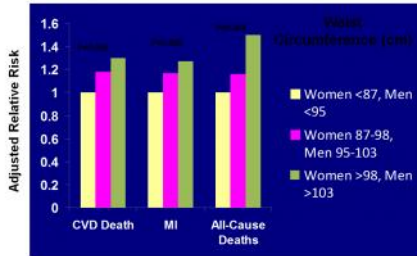
http://www.cdc.gov/obesity/downloads/obesity_trends_2008.pdf#49129 Obesity Trends* Among U.S. Adults BRFSS.

**Abdominal Adiposity Is Associated
With Increased Risk of Diabetes**



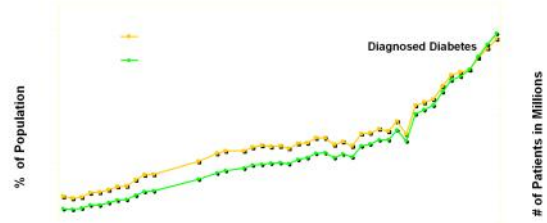
Carey VJ, et al. Am J Epidemiol. 1997;145:614-619

Abdominal Adiposity Is Associated With Increased Risk of CV Events



Dagenais GR, et al. Am Heart J. 2005; 149:54-60.

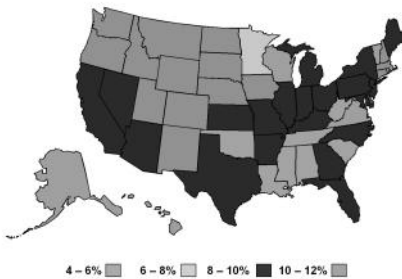
Diabetes: A Growing Challenge Prevalence in the United States



Centers for Disease Control and Prevention, Division of Diabetes Translation, National Diabetes Surveillance System. Available at <http://www.cdc.gov/diabetes/statistics>.

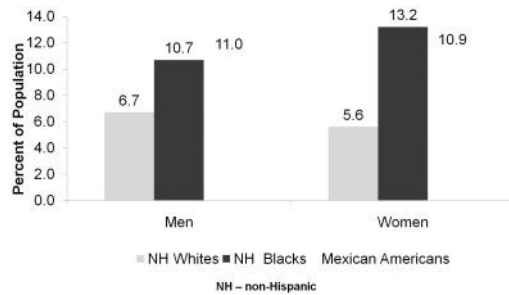
Diagnosed Diabetes in the US: 2008

CDC BRFSS: Self-Reported Diabetes: 8.2% Nationwide



<http://www.cdc.gov/diabetes/prevalence/data/tables/2008table11>

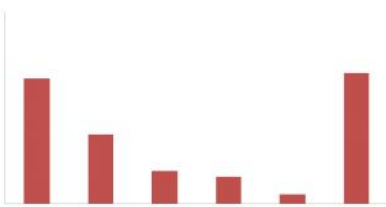
Age-Adjusted Prevalence of Physician-Diagnosed Diabetes in Adults Age 18 and Older by Race/Ethnicity and Sex



NHANES, 1999-2001. Source: NCHS and NHLBI. *Diabetes and Its Complications: A Public Health Challenge*. 2004. 24-40, 41.

Patient Beliefs About Diabetes Risks

ACC/ADA Diabetes Knowledge Survey (n=2008)



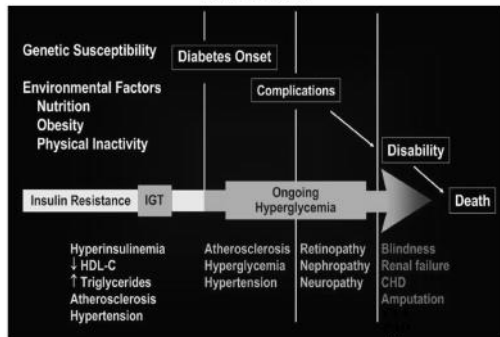
http://www.diabetes.org/education/knowledge_survey_summary.pdf

Diabetes and CVD

- Atherosclerotic complications responsible for
 - 80% of mortality among patients with diabetes
 - 75% of cases due to coronary artery disease (CAD)
 - Results in >75% of all hospitalizations for diabetic complications
- 50% of patients with type 2 diabetes have preexisting CAD. (This number may be less now that more younger people are diagnosed with diabetes.)
- 1/3 of patients presenting with myocardial infarction have undiagnosed diabetes mellitus

Lewis OF, Can J Cardiol. 1996;11(suppl C):24C-28C
 Nohammar A, et al. Lancet 2002;359:2140-2144

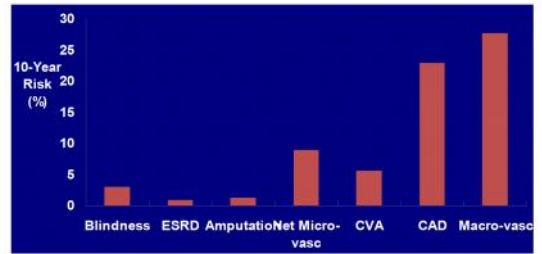
The Continuum of CV Risk in Type 2 Diabetes



Adapted from American Diabetes Association. Diabetes Care. 2005;28:3160-3167; Tsao PS, et al. Arterioscler Thromb Vasc Biol. 1998;18:947-953; Houth WA, et al. Am J Med. 1986;100(1A):45-145; American Diabetes Association. Diabetes Care. 1999;21:310-314.

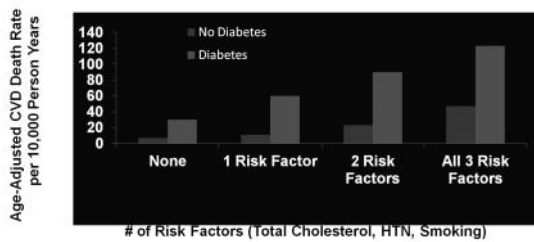
Diabetes Mellitus: A Cardiovascular Disease

United Kingdom Prospective Diabetes Study (n=3867)



UKPDS Investigators. Lancet 1998; 352: 837

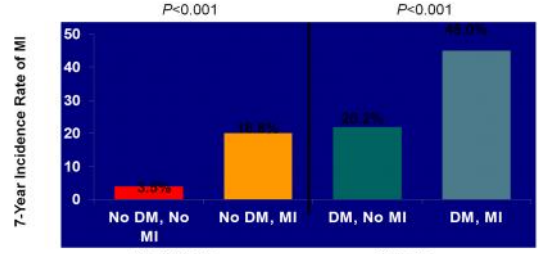
Age-Adjusted CVD Death Rates (MRFIT)



CVD=cardiovascular disease
MRFIT=multiple risk factor intervention trial

Adapted with permission from Stamler J et al. Diabetes Care. 1993;16:434-444.

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

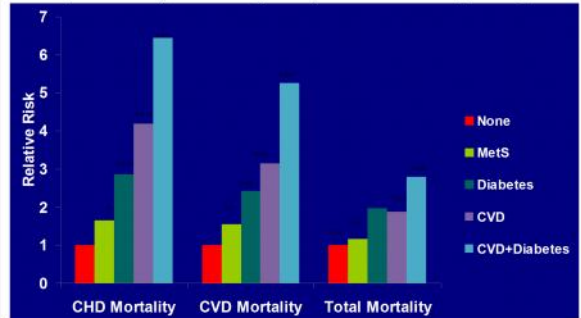


CHD=coronary heart disease; MI=myocardial infarction; DM=diabetes mellitus

Haffner SM et al. N Engl J Med. 1998;339:229-234.

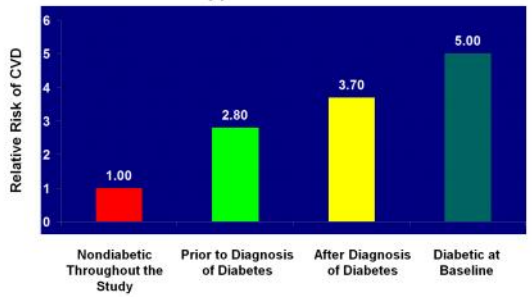
Cardiovascular Disease (CVD) and Total Mortality: U.S. Men and Women Ages 30-74

(Risk-factor Adjusted Cox Regression) NHANES II Follow-up (n=6255)



Malik and Wong, et al. Circulation 2004; 110: 1245-1250. * p<.05, ** p<.01, **** p<.0001 compared to none

Nurses' Health Study: Elevated Risk of CVD Prior to Clinical Diagnosis of Type 2 Diabetes



Adapted with permission from Hu FB et al. Diabetes Care. 2002;25:1129-1134.

Under-Treatment of Cardiovascular Risk Factors Among U.S. Adults with Diabetes



Malik S, Wong ND et al. *Diab Res Clin Pract* 2007;77:126-33

Summary

- Prevalence of obesity is increasing
- The number of patients with diabetes is increasing
- There is increased mortality and morbidity associated with diabetes
 - Primarily attributable to cardiovascular disease
- Patients with diabetes underestimate the risk of the disease

Summary of Care: ABC's for Providers



A	A1c Target Aspirin Daily
B	Blood Pressure Control
C	Cholesterol Management Cigarette Smoking Cessation
D	Diabetes and Pre-Diabetes Management
E	Exercise
F	Food Choices

A1c Target Aspirin Daily

- A1c Target: Glucose lowering to achieve normal to near normal plasma glucose, as defined by the HbA1c <7%
- Aspirin Daily: Secondary prevention or primary prevention in higher risk patients with diabetes

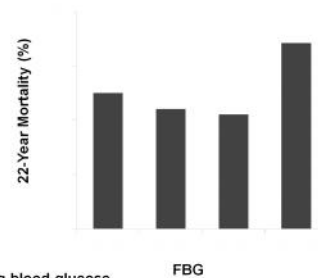
CAD Event Risk vs. Fasting Glucose (CARE)



CAD=coronary artery disease; CARE=Cholesterol and Recurrent Events trial.

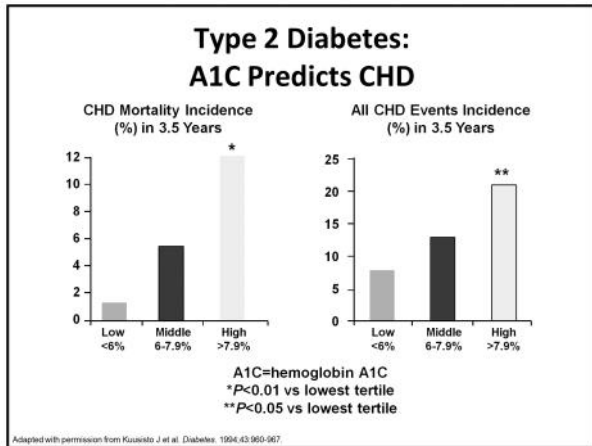
Adapted with permission from Ostberg RB et al. *Circulation* 1998;98:2513-2519

CV Mortality vs. FBG: 22-Year Follow-Up



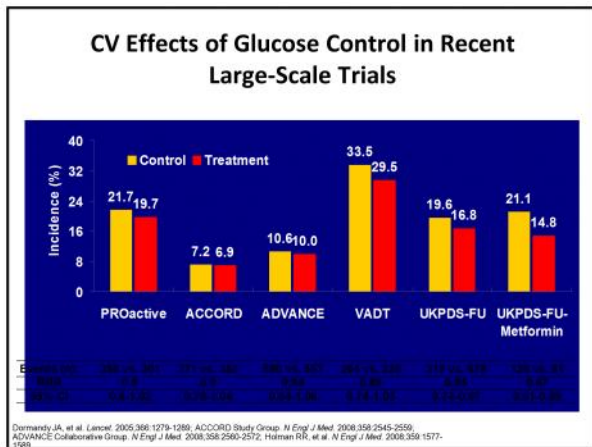
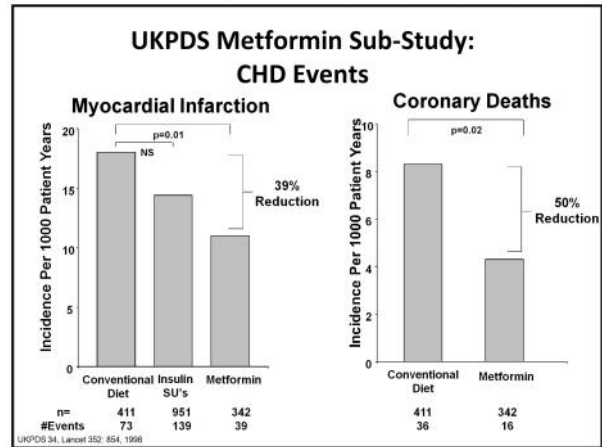
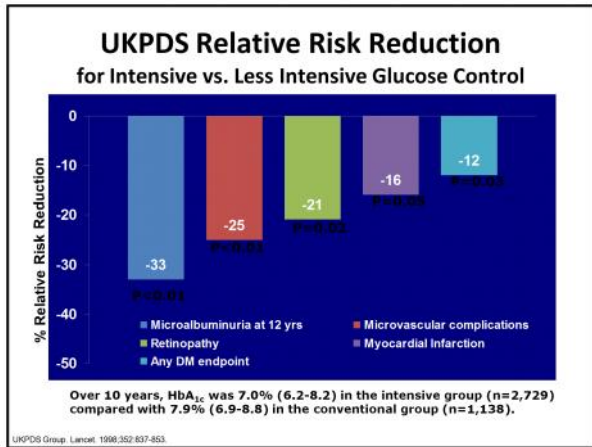
FBG=fasting blood glucose

Adapted with permission from Bjornholt JV et al. *Diabetes Care* 1999;22:45-49



Impact of Glycemic Control on Clinical Outcomes

- Proven efficacy for microvascular complications
- Uncertain effects on cardiovascular outcomes
 - Most trials to date not designed nor powered to assess CVD effects



2009 ADA/AHA/ACC Statement Recommendations

- Goal of A1c<7% For uncomplicated patients and for those with macrovascular disease
- Incremental microvascular benefit may be obtained from even lower goals
- Less stringent goals may be appropriate for those with labile glucose control or with advanced micro- or macrovascular disease

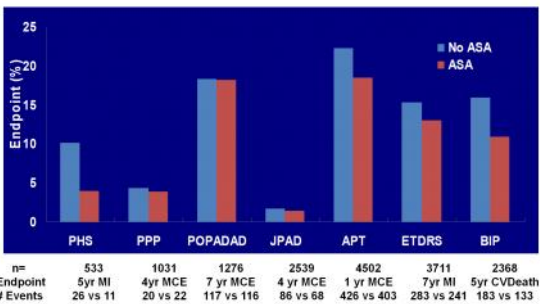
A1c Target Aspirin Daily

- A1c Target: Glucose lowering to achieve normal to near normal plasma glucose, as defined by the HbA1c <7%
- Aspirin Daily: Secondary prevention or primary prevention in higher risk patients with diabetes

Aspirin Therapy

- Aspirin therapy 75-162 mg for secondary prevention in patients with diabetes with CVD
- Aspirin therapy 75-162 mg for type 1 or type 2 at increased CV risk (10 year risk > 10%)
 - Men > 50 or women > 60 and
 - Family History
 - Hypertension
 - Smoker
 - Dyslipidemia
 - Albuminuria

Therapeutic Efficacy in Diabetes: ASA



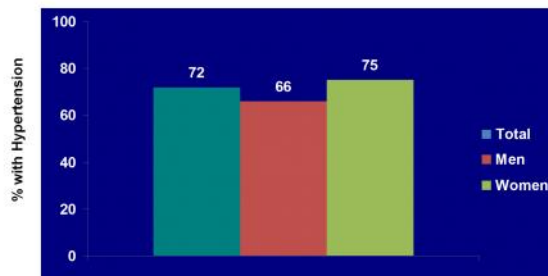
NEJM 1989; 321: 129; Diabetes Care 2003; 26: 3264; BMJ 2008; 337: a1840; JAMA 2008; 300: 2134; BMJ 1994; 308: 81; JAMA 1992; 268: 1292; Am J Med 1998; 105: 494

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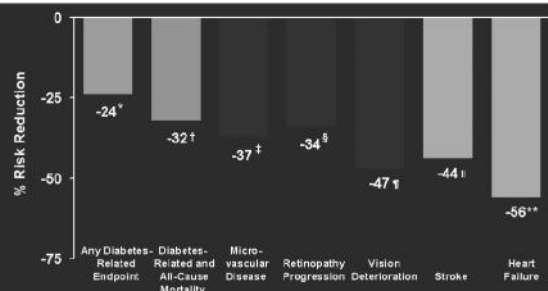
Prevalence of Hypertension* in Adults with Diabetes: NHANES III 1988-1994



*BP ≥130/85 or therapy for hypertension

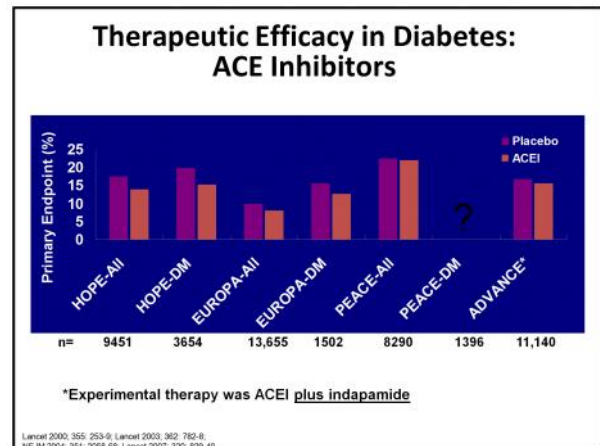
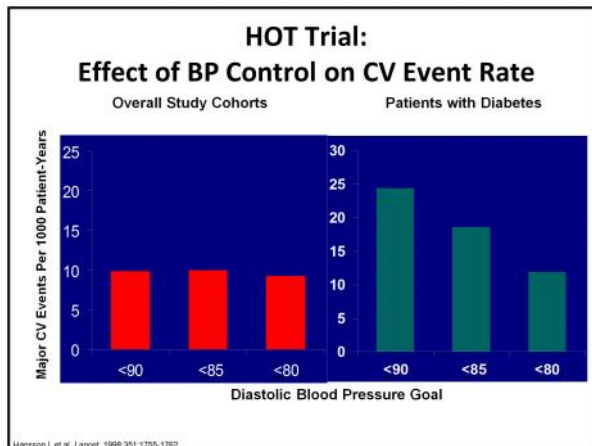
Goss LS, et al. Am J Prev Med. 2002;22:42-48.

UKPDS: Effects of Tight vs. Less-Tight Blood Pressure Control



*P=0.0046; †P=0.019; ‡P=0.0092; §P=0.0038; ¶P=0.0036; **P=0.013; ***P=0.0043

UK Prospective Diabetes Study Group. BMJ. 1998; 317:703-713.

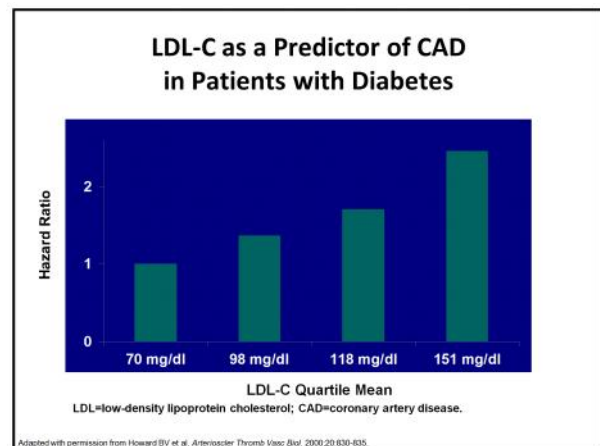


- ### Scientific Statements: Diabetes, CV Disease and Hypertension
- JNC VII Report on Diabetic Hypertension
 - BP goal (<130/80 mm Hg)
 - Commonly requiring combinations of ≥2 drugs
 - ACEIs, CCBs, Thiazide-diuretics, β-blockers, and ARBs shown to reduce CVD/CVA risk
 - ACEIs/ARBs reduce progression of diabetic nephropathy and reduce albuminuria
 - ARBs reduce progression of macroalbuminuria
- Grundy BM et al. Circulation. 1999;100:1134-1148; Chobanian AV, et al. JAMA. 2003;289:2560-2572.

- ### ADA Standards of Medical Care in Diabetes – 2010
- Treatment of hypertension
 - Target SBP<130 and DBP<80 mmHg
 - In patients with BP 130-139/80-89 may try three months of diet, weight management and exercise
 - ACEI or ARB for initial drug therapy
 - Especially with micro or macroalbuminuria, given benefit in both type 1 diabetes and type 2 diabetes
 - Multiple drug therapy is generally required to achieve BP control
- American Diabetes Association. Diabetes Care. 2010;33 (suppl 1) pgS12-S61

Summary of Care: ABC's for Providers

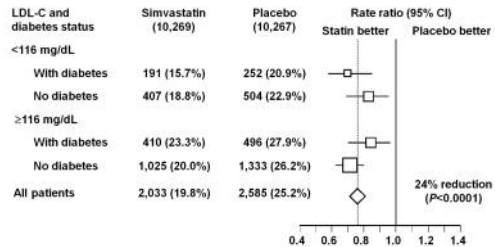
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Lipid Treatment Goals for Patients with Type 2 Diabetes

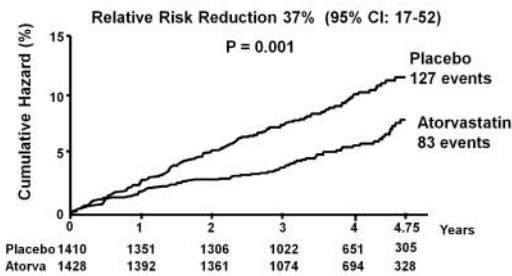
	ADA 2010 ¹	ATP III ⁴
LDL (mg/dL)	<100 <70 highest risk	<100
TG (mg/dL)	<150	<150
HDL (mg/dL)	>50	*
Non HDL (mg/dL)	<130	<130

HPS Substudy: First Major Vascular Event by LDL-C and Prior Diabetes Status



HPS Collaborative Group. *Lancet*. 2003;361:2005-2016.

CARDS: Primary Endpoint



CARDS: Treatment Effect on the Primary Endpoint

Event	Placebo*	Atorva*	Hazard Ratio	Risk Reduction (CI)
Primary endpoint	127 (9.0%)	83 (5.8%)	0.63 (0.47-0.85)	37% (17-52) p=0.001
Acute coronary events	77 (5.5%)	51 (3.6%)	0.64 (0.47-0.86)	36% (9-55)
Coronary revascularization	34 (2.4%)	24 (1.7%)	0.64 (0.47-0.86)	31% (-16-59)
Stroke	39 (2.8%)	21 (1.5%)	0.51 (0.34-0.76)	48% (11-69)

* N (% randomized)

Favors Atorvastatin | Favors Placebo

ADA 2010 Guidelines

- Statin therapy should be added to lifestyle therapy, regardless of baseline lipid levels, for diabetic patients:
 - With overt CAD
 - Without CVD >40 and have ≥ 1 CVD risk factor

American Diabetes Association. *Diabetes Care*. 2010;33(suppl 1):e63-112.

Specific Dyslipidemias: Elevated Triglycerides

Non-HDL: Secondary Target


- Non-HDL = TC – HDL
- Non-HDL: secondary target of therapy when serum triglycerides are ≥200 mg/dL (esp. 200-499 mg/dl)
- Non-HDL goal: LDL goal + 30 mg/dL

Specific Dyslipidemias: Low HDL Cholesterol

Management of Low HDL

- LDL is primary target of therapy
- Weight reduction and increased physical activity (if the metabolic syndrome is present)
- Non-HDL is secondary target of therapy (if triglycerides ≥ 200 mg/dL)
- Consider nicotinic acid or fibrates (for patients with CHD or CHD risk equivalents)

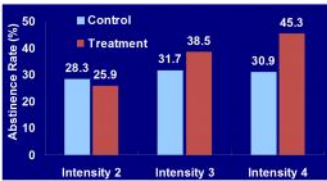
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Effectiveness of Smoking Cessation Interventions for CVD Admissions

- Smoking cessation intervention
 - MI = "teachable moment"
 - JCAHO/CMS core measure for MI care
- Meta-analysis of 18 RCTs in CVD, by intensity of intervention
- Only extended support programs significantly improved abstinence




Summary OR	1.14	1.07	1.81
95% CI	0.9-1.4	0.7-1.6	1.5-2.2

Journal of Acute Care Med 2009; 18(3): 150-159

The 5 "A's" for Effective Smoking Intervention

1. **ASK** about smoking
2. **ADVISE** to quit
3. **ASSESS** willingness to make a quit attempt
4. **ASSIST** if ready - offer therapy and consultation for quit plan and if not, then offer help when ready
5. **ARRANGE** follow up visits

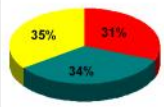
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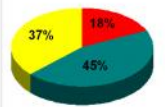
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Most Cardiovascular Patients Have Abnormal Glucose Metabolism

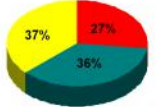
GAMI
n = 164



EHS
n = 1920



CHS
n = 2263



■ Normoglycemia
■ Prediabetes
■ Type 2 Diabetes

GAMI = Glucose Tolerance in Patients with Acute Myocardial Infarction Study
EHS = Euro Heart Survey
CHS = China Heart Survey

Atsahara M, et al. Rev Cardiovasc Med 2008;9:29-38

Diagnostic Criteria for Metabolic Syndrome: Modified NCEP ATP III

≥3 Components Required for Diagnosis

Components	Defining Level
Increased waist circumference Men Women	≥ 40 in ≥ 35 in
Elevated triglycerides	≥150 mg/dL (or Medical Rx)
Reduced HDL-C Men Women	<40 mg/dL <50 mg/dL (or Medical Rx)
Elevated blood pressure	≥130/≥85 mm Hg (or Medical Rx)
Elevated fasting glucose	≥100 mg/dL (or Medical Rx)

AHA/NHLBI Scientific Statement. Circulation 2005; 112:e885-e898.

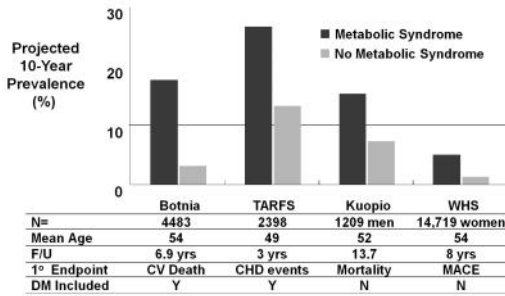
IDF Criteria: Abdominal Obesity and Waist Circumference Thresholds

	Men	Women
Europid	≥ 94 cm (37.0 in)	≥ 80 cm (31.5 in)
South Asian	≥ 90 cm (35.4 in)	≥ 80 cm (31.5 in)
Chinese	≥ 90 cm (35.4 in)	≥ 80 cm (31.5 in)
Japanese	≥ 85 cm (33.5 in)	≥ 90 cm (35.4 in)

- AHA/NHLBI criteria: ≥ 102 cm (40 in) in men, ≥ 88 cm (35 in) in women
- Some US adults of non-Asian origin with marginal increases should benefit from lifestyle changes. Lower cutpoints (≥ 90 cm in men and ≥ 80 cm in women) for Asian Americans

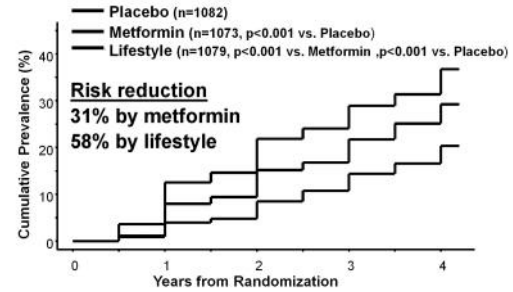
Aburto KGMM et al. Lancet 2005;366:1058-1062 | Grundy SM et al. Circulation 2005;112:2735-2752.

10-Year CVD Risk Estimates Associated with Metabolic Syndrome



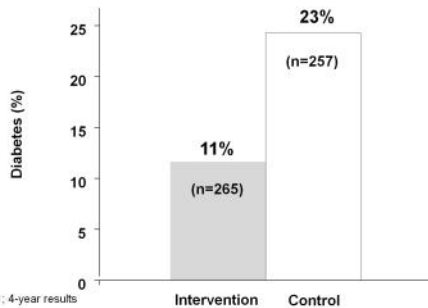
Isomaa B et al. Diabetes Care 2001; 24: 683. Crut A et al. Atherosclerosis 2002; 165: 285. Lakka HM et al. JAMA 2002; 288: 2709; Ridker PM et al. Circ 2003; 107: 391.

Management Opportunity: Prevent Diabetes



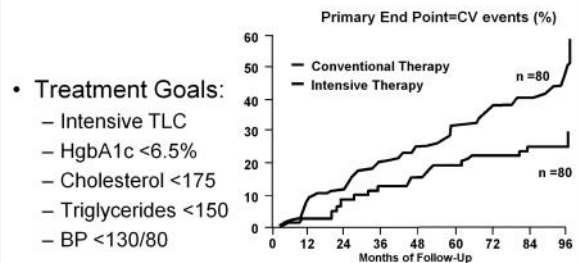
NEJM 346:983-993, 2002

Finnish Diabetes Prevention Study: Reduction in Risk for Diabetes*



Tuomiheho J et al. N Engl J Med 2001;344:1343-1350.

Benefit of Comprehensive, Intensive Management: STENO 2 Study



Gaede P et al. NEJM 2003;348:990-993

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Physical Inactivity: A Call to Arms



10,000 Steps Daily



30 minutes most days

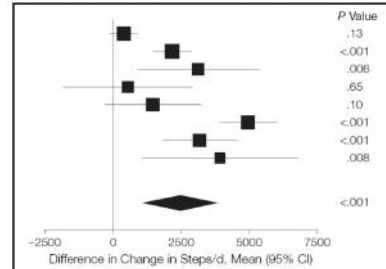
Take an Exercise History and Encourage Increased Physical Activity

- Brisk walking is an ideal physical activity for those without orthopedic issues
- Walking uses the patient's increased body weight to increase energy expenditure
- Pedometers provide daily feedback - 10,000 Steps Per Day



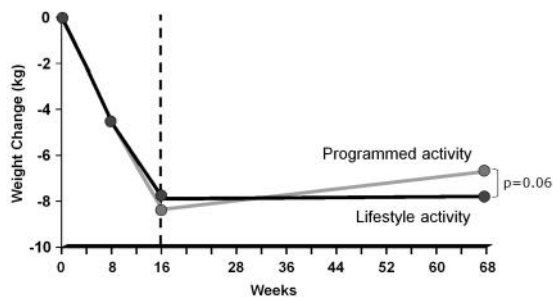
RCT Trial Assessment of Pedometer Interventions

N=277; 8 Trials
Pedometer increased steps by 2500/day



Bravata, DM et al. JAMA 2007; 298:2296-2304

Lifestyle Activity as an Alternative to "Working Out"



Andersen RE, et al. JAMA 1999;281:335-340

National Weight Control Registry

- Successful Losers: >10% Body weight for 1 year
- 3000 Registrants, 80% Women
- Average Loss = 30 kg; Time = 5.5 yrs
- How?
 - ~Low Fat Diet
 - ~Self-monitoring
 - ~Physical Activity
- 81% Reported More Physical Activity

Wing & Hill Annu Rev Nutr 2001;21:323-41

Physical Activity Recommendations


Mode of exercise	Frequency	Intensity	Duration	Class and level
Cardio-respiratory (large muscle)	3-7 d/week	Moderate intensity OR	150 min/week	1 (A)
Cardio-respiratory (large muscle)	3 d/week	Vigorous Intensity	90 min/week	1 (A)
Resistance	3 d/week	2-4 sets of 8-10 reps		1 (A)

Harwick TH. Circulation 2009;119:3284-92

Summary of Care: ABC's for Providers

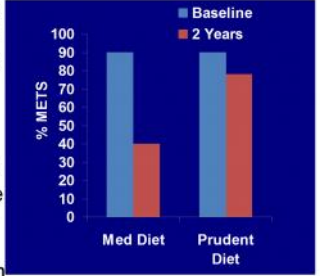
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ADA Nutritional Guidelines

- Patients with pre-diabetes should receive individualized Medical Nutrition Therapy (MNT)
- Weight loss recommended for all overweight or obese individuals who have or are at risk for diabetes
- Physical activity and behavior modification effective for weight loss and maintenance
- Fiber 14 g/1000 kcal intake
- Saturated fat 7% with minimal trans fat 

Effect of Mediterranean-Style Diet in the Metabolic Syndrome

- 180 pts with metabolic syndrome randomized to Mediterranean-style vs. prudent diet for 2 years
- Those in intervention group lost more weight (-4kg) than those in the control group (+0.6kg) (p<0.01), and significant reductions in CRP and IL-6



Diet	Baseline	2 Years
Med Diet	~90	~40
Prudent Diet	~90	~75

Esposito K et al. JAMA 2004; 292(12): 1460-6

Patient Education

- Educational Objectives
 - Ensure patients realize the link between metabolic syndrome and risk of heart disease
 - Reinforce the patient's role and control in disease management
 - Focus on significant impact even modest exercise and weight loss will have
 - Verify patients understand how to implement healthy changes to diet and physical activity level

Summary of Care: ABC's for Providers

A	A1c Target Aspirin Daily
B	Blood Pressure Control
C	Cholesterol Management Cigarette Smoking Cessation
D	Diabetes and Pre-Diabetes Management
E	Exercise
F	Food Choices

CASE STUDY

Case Study 52 Year-Old Man with ACS

- JN is a 52-year-old man who has gained 20 pounds over the past 10 years
- Many of the men in his family are overweight and have hypertension
- CAD at age 62 in his father and early 60's in his paternal grandfather. Both were diabetic

52 Year-Old Man with ACS

- "Borderline" HTN over the past 3-4 years
- No history of hyperlipidemia or diabetes
- Lifelong non-smoker
- He was advised to lose weight and start an exercise plan, but did not follow through
- He has a sedentary job and does minimal walking as a part of his daily routine

52 Year-Old Man with ACS

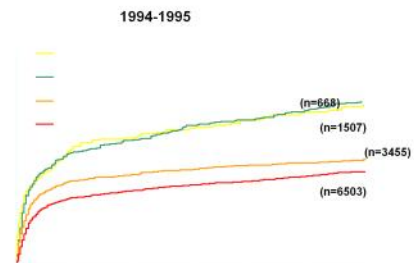
- At 5:30 a.m. he awoke with chest heaviness that worsened over the next 30 when he called 911
- Exam on arrival to the Emergency Room:
 - Diaphoretic. BP 190/90, HR 78, Ht. 5'10", Wt 220 (BMI 32kg/m²)
 - CV and lung exams were normal
 - His abdomen was obese
 - no edema and his pulses were 2+
- Given aspirin and SL NTG with relief of his symptoms

52 Year-Old Man with ACS

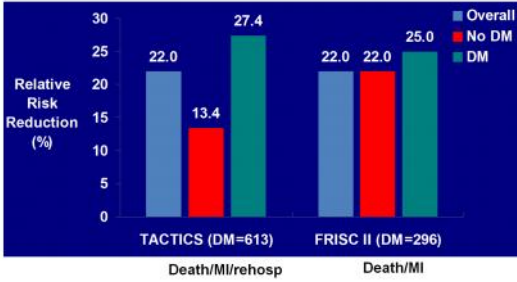
- The 12 Lead EKG showed ST depressions in leads II, III, aVf and V6
- Labs on Admission:

Blood glucose	248 mg/dL
TG	252 mg/dL
LDL-C	153 mg/dL
HDL-C	35 mg/dL
Initial Troponin I	2.3 ng/ml
HbgA1C was	7.2 %

High Risk of Diabetes Independent of ST-Segment Status



Effect of Primary Invasive Strategy of ACS by Diabetes Status at 6 Months



Canon CP, et al. NEJM 2001; 344: 1879-87
Waltertsch L, et al. Lancet 2000; 356: 9-16

Case

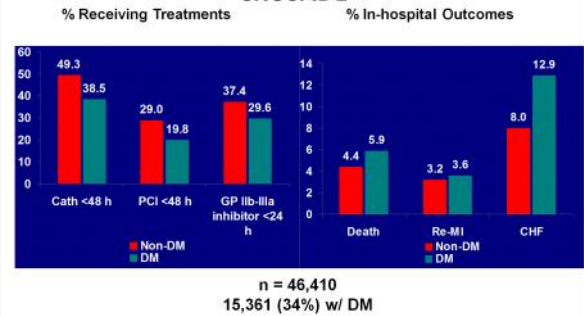
- Patient underwent catheterization with successfully PCI of his LCx artery
- He was placed on
 - Aspirin 325 mg
 - Plavix 75 mg
 - Lisinopril 20 mg
 - Carvedilol 12.5 mg bid
 - Atorvastatin 20 mg

Diabetes and NSTEMI: Help from the Guidelines

- Treatment and diagnostics for NSTEMI patients with diabetes should be similar to those without (I; A)
- Diabetes-specific recommendations
 - Gp IIb/IIIa inhibitor for all (I; A)
 - ACE Inhibitors for all (I; A)
 - Eplerenone with EF≤40; Cr<2.5; K+<5.0 (I; A)
 - CABG preferred over PCI for multi-vessel dz (IIa; B)
 - Glucose: target <150mg/dL X 1st 72 hours; 80-110 thereafter (IIa; B)

Circ 2007; 116: e148-e304

Process of Care and Outcomes by Diabetes Status: Observations from CRUSADE



Brogan et al. Diabetes Care 2006; 29: 9-14

Glucose in ACS: Help From the Guidelines?

- AACE
 - Target BG 80 - 110 mg/dL
- ADA
 - As close to 110 mg/dL as possible and generally <180 mg/dL
- ACC/AHA Guidelines
 - 2000 USA/NSTEMI
 - "Attention should be directed toward tight glucose control." (Level of evidence: B)
 - 2004 STEMI
 - Insulin infusion to normalize BG for patients with STEMI and complicated courses (I; B)
 - Insulin infusion during 1st 24-48 hrs....to normalize BG even in patients with an uncomplicated course (IIa; B)

Circ 2007; 116: e148-e304
Deedwania P, et al. Circulation 2006; 117: 1610-1619

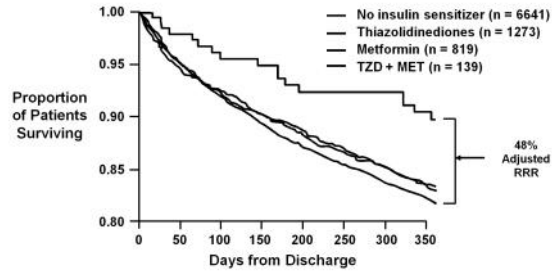
Glucose in ACS: Help From the Guidelines (cont.)

- 2007 NSTEMI
 - Aggressive insulin use for the first 72 hours with a target of <150mg/dl, 80-110 mg/dl thereafter (IIa; B)
- 2008 AHA position paper
 - Glucose target of <180mg/dl is reasonable (B)
 - Glucose target of 90-140 mg/dl is reasonable if hypoglycemia is avoided (C)

Circ 2007; 116: e148-e304
Deedwania P, et al. Circulation 2006; 117: 1610-1619

Association Between Glucose Therapy and Outcomes after MI

N=8872 w/ AMI and DM, mean age 76.4 years



Inzucchi SE et al. Diabetes Care. 2005;28:1680-9

Conclusions

- Diabetes is increasingly prevalent in ACS/AMI populations
 - Associated with especially adverse clinical outcomes
- Diabetes and hyperglycemia associated with adverse outcomes
 - Role of glucose modulation remains to be defined
 - Concerning safety signals from intensive control trials

Pre 2007; 116: e148-e304
 Galiszeria P. et al. Circulation 2008; 117: 1610-1619

Conclusions (cont.)

- Most recent recommendations endorse more conservative glucose targets
 - <180 mg/dl is a reasonable target
 - Target 90-140 mg/dl only if hypoglycemia can be systematically avoided diabetes is increasingly prevalent in ACS/AMI populations
 - Associated with especially adverse clinical outcomes
- Cornerstone remains prevention of ACS/MI
 - Continued efforts to apply chronic preventive therapies according to evidence base and guidelines

Pre 2007; 116: e148-e304
 Galiszeria P. et al. Circulation 2008; 117: 1610-1619



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