



Managing the Microvascular and Macrovascular Complications of Diabetes

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The following program is a taped presentation by Deborah Hinnen.

Deborah Hinnen, RN, ARNP, BC-ADM, CDE, FAAN, has been a diabetes educator for nearly 30 years. She is a clinical nurse specialist and education program coordinator, working with a multidisciplinary team at Mid-America Diabetes Associates to deliver a comprehensive self-management day course, as well as evening and gestational diabetes classes.

Ms. Hinnen is involved extensively with the American Association of Diabetes Educators (AADE), having served as their national President in 1993-1994. She was awarded their prestigious Distinguished Service Award in the summer of 2001. She has also served on the national board of directors for the American Diabetes Association (ADA), and has just finished serving as associate editor for *Diabetes Spectrum*. Ms. Hinnen continues to volunteer with many other organizations. Her faculty positions are with the Pharmacy Department at the University of Kansas, and Graduate Nursing Department and Physician Assistant Department at Wichita State University. She was inducted as a Fellow into the American Academy of Nursing in 2003.

Her career has focused on diabetes patient and professional education with many publications in both areas. In addition to diabetes efforts, she is currently serving as a Trustee for Butler Community College, a college with 7 sites and more than 14,000 students.



Program Objectives

- Describe the micro- and macrovascular complications of diabetes and their impact on morbidity and mortality
- Discuss the rationale for comprehensive risk management to improve patient outcomes
- Review glycemic, blood pressure, and lipid guidelines as well as other recommendations for the prevention and treatment of diabetes complications

The objectives for this program are to:

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- Discuss the rationale for comprehensive risk management to improve patient outcomes
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Diabetes

- **Classification**
 - Type 1 diabetes
 - Type 2 diabetes
 - Specific types due to other causes
 - Gestational diabetes mellitus
- **Diagnosis**
 - Symptoms + casual plasma glucose ≥ 200 mg/dL
 - FPG ≥ 126 mg/dL
 - 2-hour plasma glucose ≥ 200 mg/dL during OGTT
- **Prediabetes**
 - IFG = FPG 100–125 mg/dL
 - IGT = 2-hour plasma glucose 140–199 mg/dL

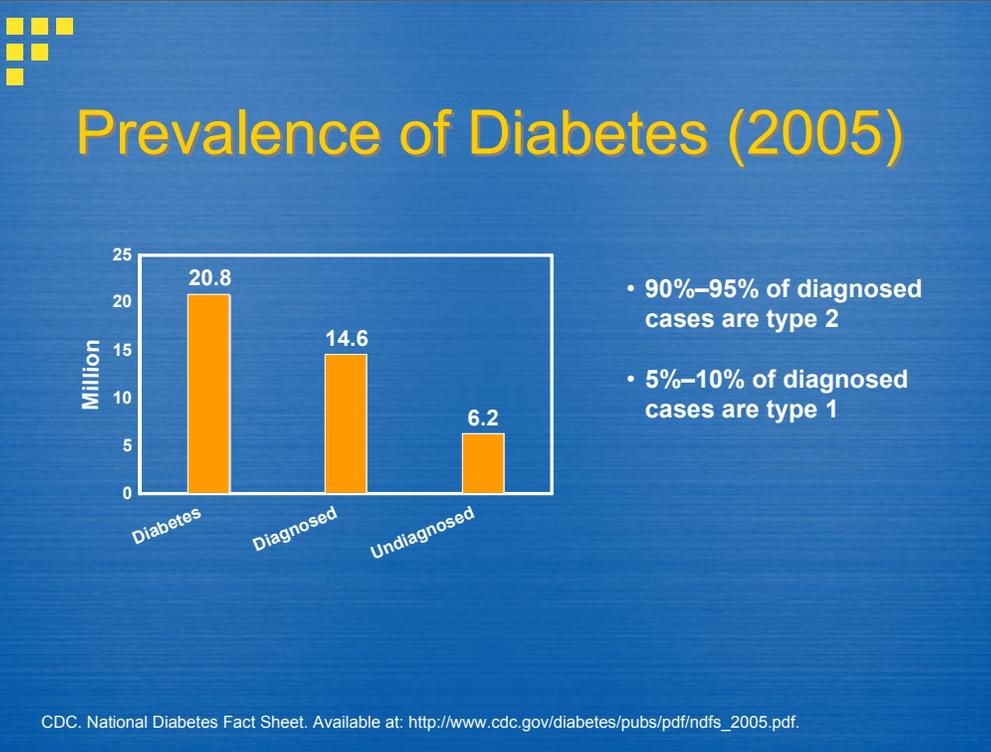
FPG = fasting plasma glucose; OGTT = oral glucose tolerance test; IFG = impaired fasting glucose; IGT = impaired glucose tolerance.
 ADA. *Diabetes Care*. 2006; 29:S4–S42.

Diabetes can be classified into 4 clinical types:

- Type 1 diabetes is an autoimmune disease, which results from β -cell destruction that usually leads to absolute insulin deficiency
- Type 2 diabetes, which results from a progressive insulin secretory defect with underlying insulin resistance
- Other specific types of diabetes due to other causes, such as medication-induced diabetes, and, finally,
- Gestational diabetes, which is elevated blood glucose diagnosed during pregnancy

The fasting plasma glucose (FPG) is the preferred test for diagnosing diabetes. A diagnosis can be made in 1 of 3 ways (each must be confirmed on a subsequent day unless unequivocal symptoms of hyperglycemia are present): initially, symptoms of diabetes, such as polyuria, polydipsia, and unexplained weight loss, in combination with plasma glucose ≥ 200 mg/dL recorded at any time of day without regard to the time since the last meal; an FPG ≥ 126 mg/dL; or, finally, 2-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test.

Elevated glucose levels not high enough to meet the diagnostic criteria for diabetes are referred to as prediabetes and this includes impaired fasting glucose diagnosed by an FPG 100 to 125 mg/dL and/or impaired glucose tolerance diagnosed by an oral glucose tolerance test of 140 to 199 mg/dL.



Diabetes is a highly prevalent disease. Approximately 20.8 million Americans were affected by the disease in 2005. Of these cases, 14.6 million were diagnosed and 6.2 million were estimated to be undiagnosed.

Type 2 diabetes accounted for the majority of diagnosed cases of diabetes (~90%-95%) and type 1 diabetes for approximately 5% to 10% of all diagnosed cases



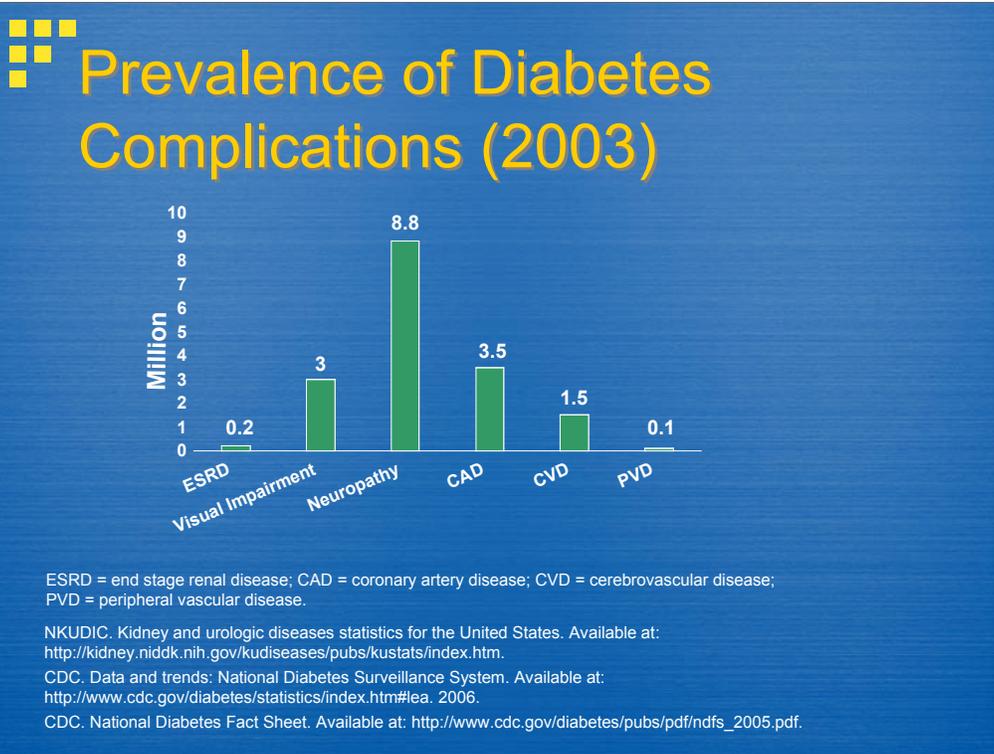
Diabetes Complications

- **Microvascular**
 - Nephropathy - kidneys
 - Retinopathy - eyes
 - Neuropathy - nerves
- **Macrovascular**
 - Coronary artery disease (CAD) - heart
 - Cerebrovascular disease (CVD) - brain
 - Peripheral vascular disease (PVD) - legs

Numerous complications affecting various organ systems can develop as a result of diabetes out of control. These complications can be divided into 2 major categories: microvascular and macrovascular.

Microvascular complications affect smaller blood vessels and can lead to damage in the kidneys (nephropathy) and eyes (retinopathy). Neuropathy is nerve damage that affects the nerves and is complicated by microvascular damage. It is sometimes considered in a separate category.

Macrovascular complications primarily affect large blood vessels and can lead to heart disease (coronary artery disease), stroke (cerebrovascular disease), and poor circulation in the lower extremities (peripheral vascular disease).



According to data from the Centers for Disease Control (CDC) and the National Kidney and Urologic Diseases Information Clearinghouse, a large number of people with diabetes suffer from micro- and macrovascular complications. In 2003:

- ~200,000 people with diabetes had end stage renal disease
- ~3 million were visually impaired as a result of diabetes
- ~8.8 million were hospitalized for diabetic neuropathy
- ~3.5 million people with diabetes had coronary artery disease
- ~1.5 million people with diabetes had cerebrovascular disease (stroke), and
- ~100,000 people were hospitalized for diabetes associated with peripheral vascular disease



Impact of Diabetes-Related Microvascular Complications

- **Diabetic Nephropathy**
 - Leading cause of ESRD (44% of new cases in 2003)
- **Retinopathy**
 - Leading cause of new cases of blindness in adults
- **Neuropathy**
 - Severe forms are major contributing cause of lower-extremity amputations

ESRD = end stage renal disease
CDC. National Diabetes Fact Sheet. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2005.pdf.

Epidemiologic data from the CDC also demonstrate the horrific impact of diabetes and its complications on morbidity and mortality:

- Diabetic nephropathy is the leading cause of end stage renal disease accounting for ~44% of new cases in 2003
- Diabetic retinopathy is the leading cause of new cases of blindness in adults
- Severe forms of diabetic neuropathy are a major contributing cause of lower-extremity amputations



Impact of Diabetes-Related Macrovascular Complications

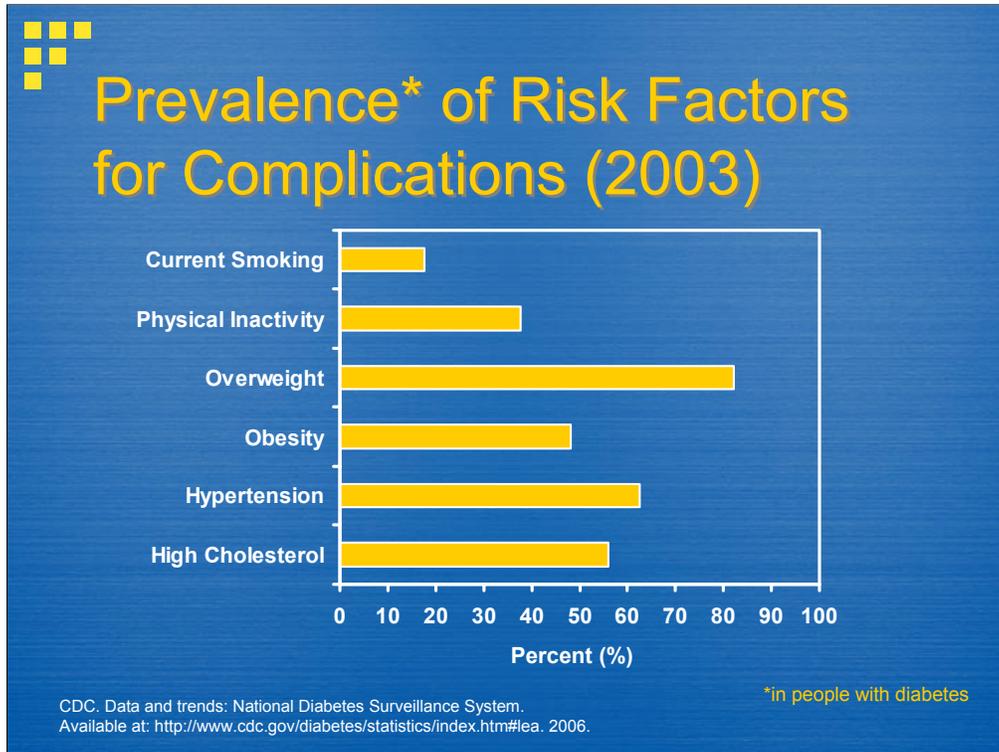
- **CAD and CVD in patients with diabetes**
 - Account for ~65% of deaths
 - Death rate from CAD 2–4 x higher
 - Risk for CVD ~2–4 x higher
 - Death rate from CVD ~2.8 x higher

- **PVD in patients with diabetes**
 - Risk factor for lower limb amputation
 - More than 60% of nontraumatic lower limb amputations occur in patients with diabetes

CDC. National Diabetes Fact Sheet. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2005.pdf.
Adler AI, et al. *Diabetes Care*. 1999;22:1029–1035.

The impact of macrovascular complications is overwhelming. Approximately 65% of deaths among people with diabetes are caused by coronary artery disease or cerebrovascular disease. The death rate from coronary artery disease and risk for cerebrovascular disease is ~2 to 4 times higher among people with diabetes than those without diabetes. The risk for developing cerebrovascular disease is also ~2.8 times higher in people with diabetes as compared to those without diabetes.

Peripheral vascular disease is a risk factor for lower limb amputation and >60% of all nontraumatic lower limb amputations occur in patients with diabetes.



In addition to the direct link between hyperglycemia and diabetes complications, numerous other risk factors contribute to poor outcomes among people with diabetes. These risk factors, which include smoking, physical inactivity, overweight, obesity, hypertension, and high cholesterol, have a high prevalence rate of ~20% to 80%.



Rationale for Comprehensive Risk Management

- **Glycemic control**
 - Each 1% drop in A1C reduces risk of microvascular complications ~40%
- **Blood pressure control**
 - Reduces risk for CAD or CVD ~33%–50%
 - Reduces risk of microvascular complications ~33%
- **Lipid control**
 - Reduces risk for CAD or CVD ~20%–50%

CDC. National Diabetes Fact Sheet. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2005.pdf.

Landmark research studies have demonstrated that, in addition to the basics of diet and exercise, avoiding smoking, controlling glucose, controlling blood pressure, and controlling lipid levels can significantly reduce the risk for diabetes complications. It is not just about controlling blood glucose anymore.

Specifically, the data from major clinical trials have shown that:

- Each 1% drop in A1C can reduce the risk of microvascular complications by ~40%
- Blood pressure control can reduce the risk of coronary artery disease and cerebrovascular disease by ~33% to 50% and the risk for microvascular complications by ~33%
- Reducing cholesterol levels can reduce the risk for coronary artery disease and cerebrovascular disease by ~20% to 50%



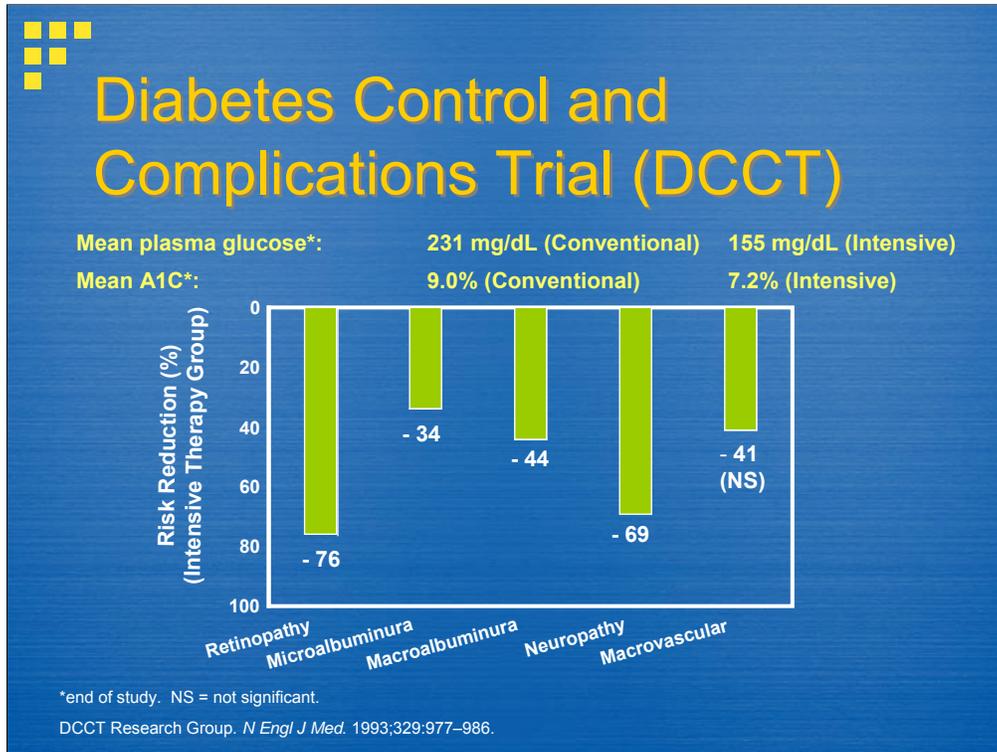
Rationale for Comprehensive Risk Management (Cont.)

- **Nephropathy detection and treatment**
 - Reduces decline in kidney function ~30%–70%
- **Retinopathy detection and treatment**
 - Reduces severe vision loss ~50%–60%
- **Foot care**
 - Reduces amputation rates ~45%–85%

CDC. National Diabetes Fact Sheet. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2005.pdf.

Other important prevention strategies that can significantly reduce the risk and severity of diabetes complications include:

- Screening and treatment of nephropathy, which can reduce the decline in kidney function by ~30% to 70%
- Screening and treatment of retinopathy can reduce severe vision loss by ~50% to 60%
- Regular foot care can reduce amputation rates by ~45% to 85%



The benefits of intensive diabetes control have been demonstrated in several large studies. The Diabetes Control and Complications Trial (DCCT) evaluated the effects of different treatment approaches on the long-term complications of type 1 diabetes.

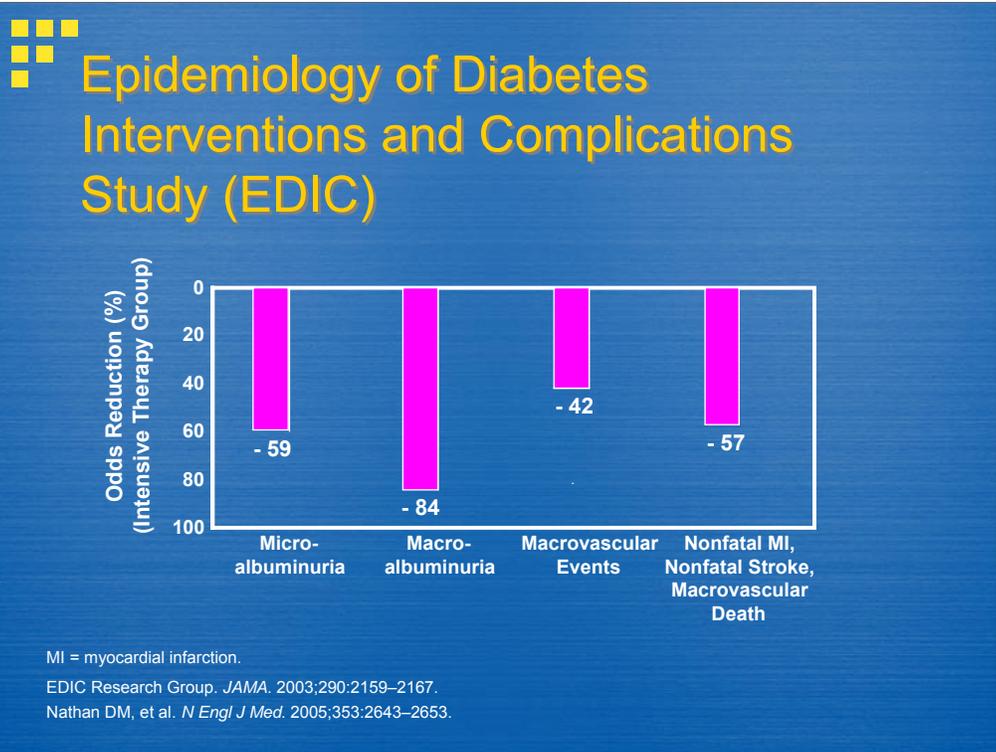
1441 Participants were randomized to intensive therapy with an insulin pump or 3 or more daily insulin injections and frequent glucose monitoring OR conventional therapy with 1 or 2 daily insulin injections.

At about 6.5 years of follow-up, intensive efforts to achieve glucose control with either multiple daily injections of insulin or insulin pumps was associated with better glycemic control and lower risk of complications than twice-a-day insulin.

The mean plasma glucose among those who received conventional therapy was 231 mg/dL and A1C averaged 9.0%. This is compared to a mean plasma glucose of 155 mg/dL and A1C of 7.2% among patients who received intensive therapy.

The percent risk reduction in 3-step background retinopathy was 76%, microalbuminuria reduced 34%, macroalbuminuria 44%, and neuropathy 69% among patients who received intensive therapy.

The relative youth of the patient population made detection of treatment-related differences in the rate of macrovascular disease unlikely. While not statistically significant, a dramatic 41% reduction in macrovascular risk was noted.

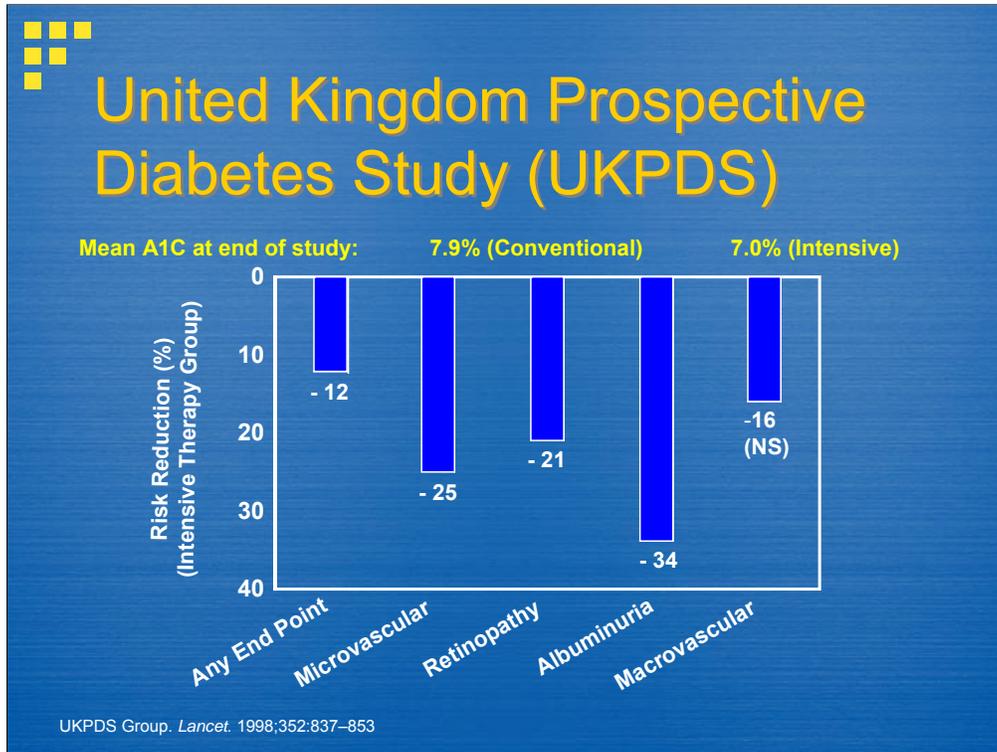


The Epidemiology of Diabetic Interventions and Complications (EDIC) study followed the same patients after the DCCT study for an additional 8 years to determine whether the effects of intensive therapy could be sustained.

After closeout of the DCCT study, the difference in A1C levels between the intensive and conventional treatment groups diminished. The intensive control group relaxed with an A1C of ~8% and the conventional group tightened their control to ~8%. Yet, the differences in the outcomes between the 2 groups, including the risk for developing micro- and macrovascular complications, persisted. The EDIC study demonstrated:

- 59% reduction in odds of new cases of microalbuminuria
- 84% reduction in odds of new cases of macroalbuminuria
- 42% reduced risk of any cardiovascular disease event, and
- 57% reduced risk of nonfatal myocardial infarction, nonfatal stroke, and death from cardiovascular disease

The beneficial reduction in both micro- and macrovascular end points among those initially treated aggressively has been attributed to a “metabolic memory” of good and poor glucose control that persists over time. Results of the EDIC study, thus, suggest that tight glycemic control early in diabetes may have big payoffs later as it relates to the complications of diabetes. Further, at any stage of diabetes, glycemic control can have long-term benefits.

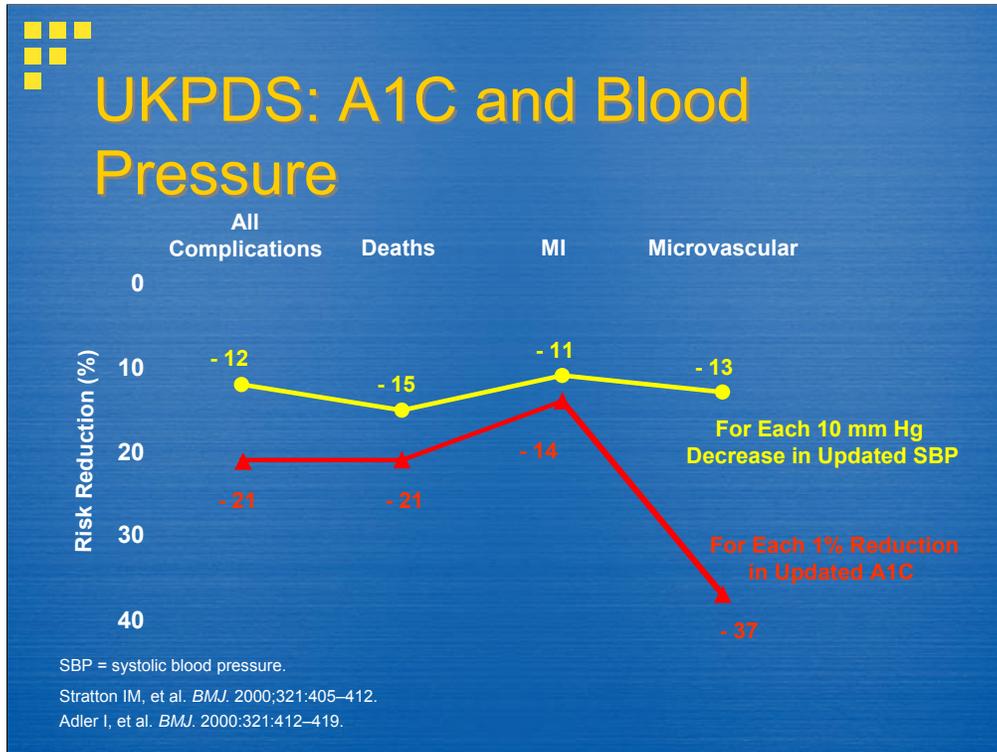


Whereas the DCCT and EDIC studies evaluated the effects of intensive therapy in people with type 1 diabetes, the United Kingdom Prospective Diabetes Study (UKPDS) evaluated the effects of intensive therapy in people with type 2 diabetes.

The largest and most comprehensive study of people with type 2 diabetes to date, the UKPDS randomized 3867 patients with newly diagnosed type 2 diabetes to intensive therapy with a sulfonylurea, metformin, or insulin OR to conventional therapy with diet.

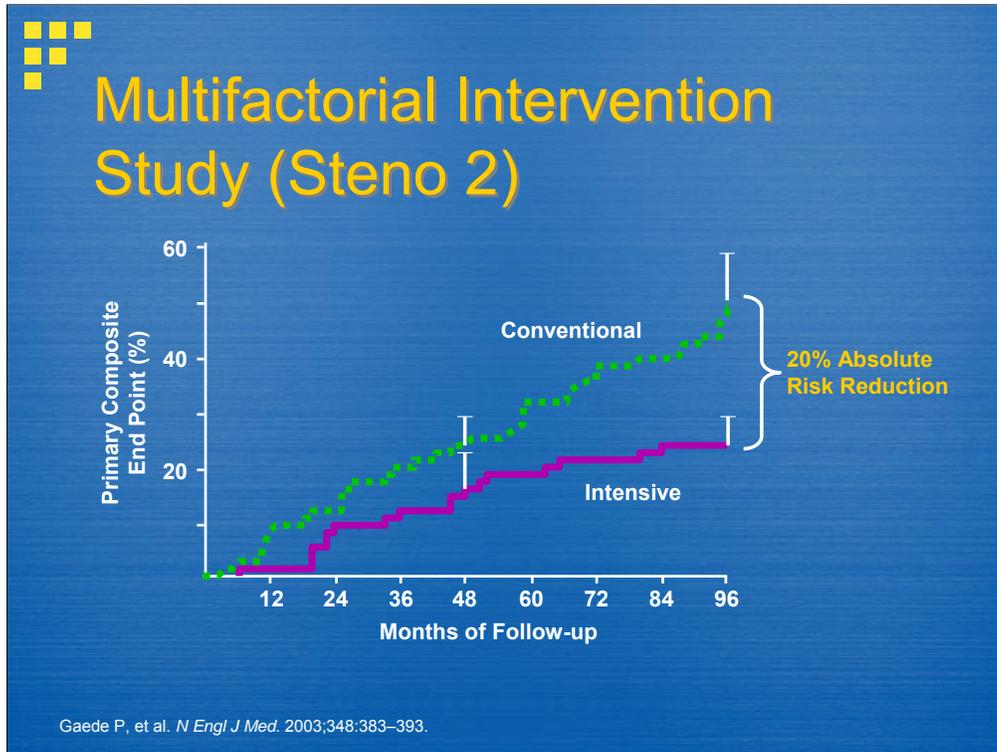
Over 10 years, participants who received intensive therapy maintained an A1C level of 7.0% as compared to an A1C level of 7.9% among those who received conventional therapy.

Intensive therapy was associated with clinically and statistically significant reductions in the risk of developing the diabetes-related complications shown in the slide above. The risk of developing any diabetes-related complication was reduced by 12%, microvascular complications were reduced by 25%, retinopathy was reduced by 21%, and albuminuria risk was decreased by 34%.



More dramatically than the benefits of glycemic control, the UKPDS study evaluated the effects of lowering systolic blood pressure. For each 10-mm Hg reduction in systolic blood pressure, a 12% reduction in the incidence of all clinical complications, 15% reduction in deaths, 11% reduction in myocardial infarction, and 13% reduction in microvascular complications was observed.

In comparison, each 1% reduction in A1C resulted in a 21% reduction in the incidence of all clinical complications, 21% reduction in deaths related to diabetes, 14% reduction in myocardial infarction, and 37% reduction in microvascular complications, with no threshold for any end point.



Another study that evaluated the benefits of intensive therapy on the development of diabetes complications was the Steno 2 study. This multifactorial intervention study compared the benefits of targeted, intensified intervention with that of conventional therapy in outcomes in patients with type 2 diabetes.

80 Patients with type 2 diabetes and microalbuminuria were assigned to receive conventional therapy according to national guidelines, while another 80 received intensive treatment with a stepwise implementation of behavior modification and pharmacologic therapy that targeted hyperglycemia, hypertension, dyslipidemia, and microalbuminuria along with secondary prevention of cardiovascular disease with aspirin.

After ~8 years of follow-up, intensive multifactorial intervention reduced the risk of microvascular and cardiovascular end points by about 50%.

This graph shows the Kaplan-Meier estimates of the composite end point of death from cardiovascular causes, nonfatal myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, nonfatal stroke, amputation, or surgery for peripheral vascular disease between the 2 treatment groups. The study estimated a 20% absolute risk reduction in the risk of cardiovascular events with intensive multifactorial intervention.



Question

The most prevalent complication of diabetes is:

- A. Coronary artery disease
- B. Visual impairment
- C. Cerebrovascular disease
- D. Neuropathy

Now, let's take a moment to test our understanding.

The most prevalent complication of diabetes is:

- A. Coronary artery disease
- B. Visual impairment
- C. Cerebrovascular disease
- D. Neuropathy

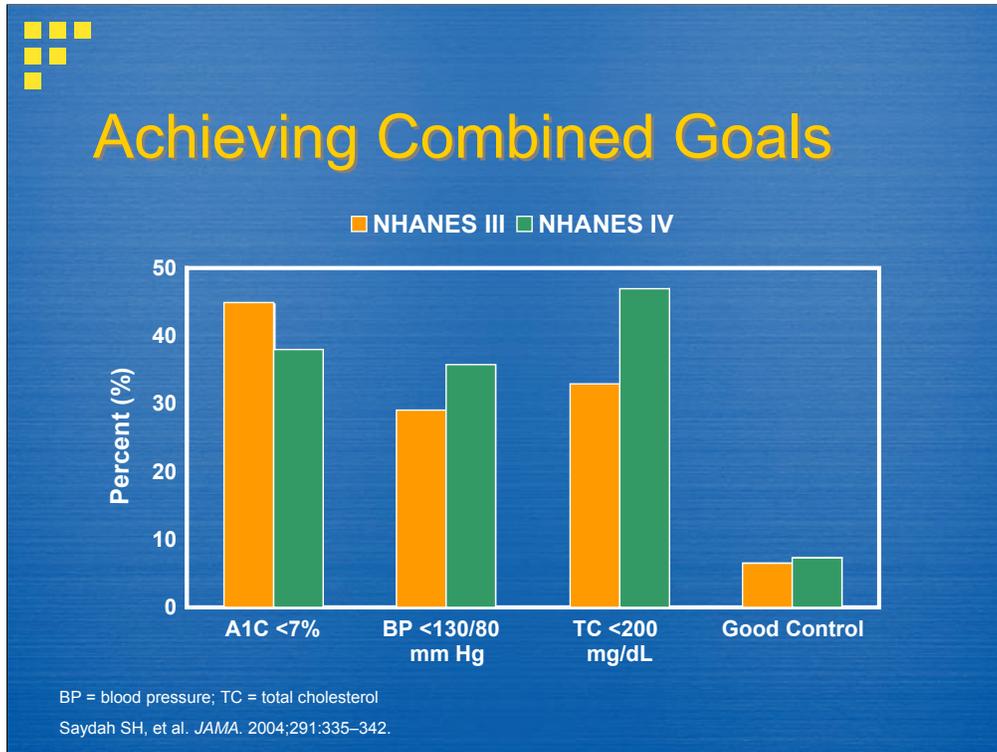


Answer

The most prevalent complication of diabetes is neuropathy, which accounted for 8.8 million hospitalizations in 2003.

The correct answer is D.

The most prevalent complication of diabetes is neuropathy, which accounted for 8.8 million hospitalizations in 2003.



Knowing all this research, are we doing a good job helping our patients with good control of the major risk factors for long-term complications? Are we at target for glycemic control, blood pressure control, and lipid management? Sadly, no.

According to analyses of data from the Fourth National Health and Nutrition Examination Survey (NHANES), conducted 1999–2000, only 7.3% of adults with diabetes attain the combined targets of A1C <7.0%, blood pressure <130/80 mm Hg, and total cholesterol <200 mg/dL.

The percentage of patients achieving individual A1C goals was 37%, blood pressure control 35.8%, and total cholesterol goals 51.8%. Compared with data from NHANES III, conducted 1988–1994, these percentages have either remained unchanged or worsened. These findings signify tremendous deficiencies in the management of diabetes and diabetes complications.

Not making clinical management changes when parameters such as A1C, blood pressure, and lipids are above target is termed *clinical inertia*. Academic and clinical training centers are developing strategies to facilitate healthcare providers' decision-making skills.



Glycemic Control

Goal	ADA	AACE
A1C (Twice a year in those meeting goals, quarterly and as needed in those not meeting goals)	<7% (Individualize to as close to normal [<6%] as possible)	≤6.5%
Preprandial plasma glucose (Individualize frequency of testing)	90–130 mg/dL	<110 mg/dL
Postprandial plasma glucose (Individualize frequency of testing)	<180 mg/dL (1 hour)	<140 mg/dL (2 hour)

ADA. *Diabetes Care*. 2006; 29:S4–S42.
AACE. *Endocrine Practice*. 2002;8:5–11.

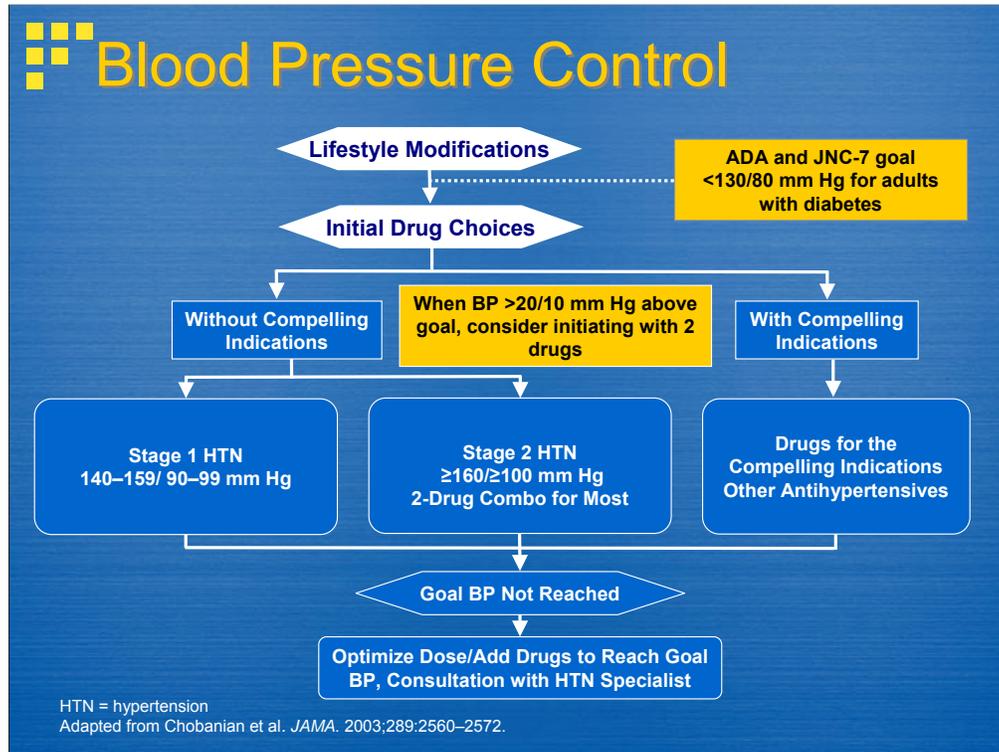
Evidenced-based clinical care is the gold standard. Let's review the targets.

For glycemic control in adults with diabetes, the American Diabetes Association (ADA) guidelines recommend maintaining a preprandial plasma glucose of 90 to 130 mg/dL and the highest glycemic excursion (at about 1-hour postprandially) plasma glucose of <180 mg/dL. A1C levels should be checked at least twice a year and be maintained at <7% or as close to normal (<6%) as possible.

However, the American Association of Clinical Endocrinologists (AACE) guidelines recommend a preprandial plasma glucose <110 mg/dL, a 2-hour postprandial plasma glucose <140 mg/dL, and A1C ≤6.5%.

While these numbers may seem at odds, the postprandial targets are based on slightly different testing times. At 1 hour after the meal, the blood glucose would be higher than at 2 hours. Considering that, the numbers are fairly consistent.

With the ADA taking a stronger stand on A1C as near normal as possible for most populations, the leading US organizations are indeed quite similar in their quest for exceptional glucose control.



Now, let's talk about blood pressure targets.

The ADA and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) both recommend a blood pressure of <130/80 mm Hg for people with diabetes.

The JNC-7 guidelines further recommend that treatment and prevention of high blood pressure begin with lifestyle modifications, such as weight reduction in obese persons; adoption of the Dietary Approaches to Stop Hypertension, known as the DASH diet; and adequate physical activity.

Patients with diabetes who have blood pressures above the target range are noted to be at high risk and require special attention. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are recommended as initial therapy. Additional agents used in combination may be required.

Consultation with a specialist is recommended for patients who do not attain their blood pressure goals after optimal dosages and a trial of additional drugs.



Lipid Control

ADA Goals

LDL <100 mg/dL	HDL, Male >40 mg/dL
TG <150 mg/dL	HDL, Female >50 mg/dL

Test at least annually for lipid disorders in adults, more often if needed to achieve goals.

NCEP ATP III

Suggest an LDL <70 is a reasonable clinical strategy in patients considered very high risk (ie, multiple major risk factors [especially diabetes], severe and poorly controlled risk factors [continued smoking], multiple risk factors of the metabolic syndrome, and patients with acute coronary syndrome)

LDL = low density lipoprotein; HDL = high density lipoprotein; TG = triglyceride.
ADA. *Diabetes Care*. 2006;29:S4–S42.
Grundy SM, et al. *Circulation*. 2004;110:227–239.

This slide reviews lipid targets.

The ADA recommends checking lipid levels annually in patients with diabetes or more frequently if needed to achieve goals.

Both the ADA and the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults recommend maintaining the low-density lipoprotein (LDL) level <100 mg/dL. Both the ADA and Adult Treatment Panel (ATP) III guidelines suggest an optional LDL goal of <70 mg/dL in people with diabetes who are considered high-risk individuals. People with diabetes are considered a cardiac risk equivalent and placed in the same category as if they have already had a heart attack. Add to that anyone with a family history of cardiac disease, and they are at “high risk.”

In addition to the primary LDL goals, the ADA recommends that men attain a high-density lipoprotein (HDL) >40 mg/dL and women an HDL >50 mg/dL, and all persons with diabetes a triglyceride level <150 mg/dL.



Question

What percentage of patients with diabetes achieve the combined goals of A1C <7%, blood pressure <130/80 mm Hg, and total cholesterol <200 mg/dL?

- A. 45%–55%
- B. 35%–45%
- C. 25%–35%
- D. 15%–25%
- E. <10%

Saydah SH, et al. *JAMA*. 2004;291:335–342.

Now, it is time for another short quiz.

What percentage of patients with diabetes achieve the combined goals of A1C <7%, blood pressure <130/80 mm Hg, and total cholesterol <200 mg/dL?

- A. 45%–55%
- B. 35%–45%
- C. 25%–35%
- D. 15%–25%
- E. <10%



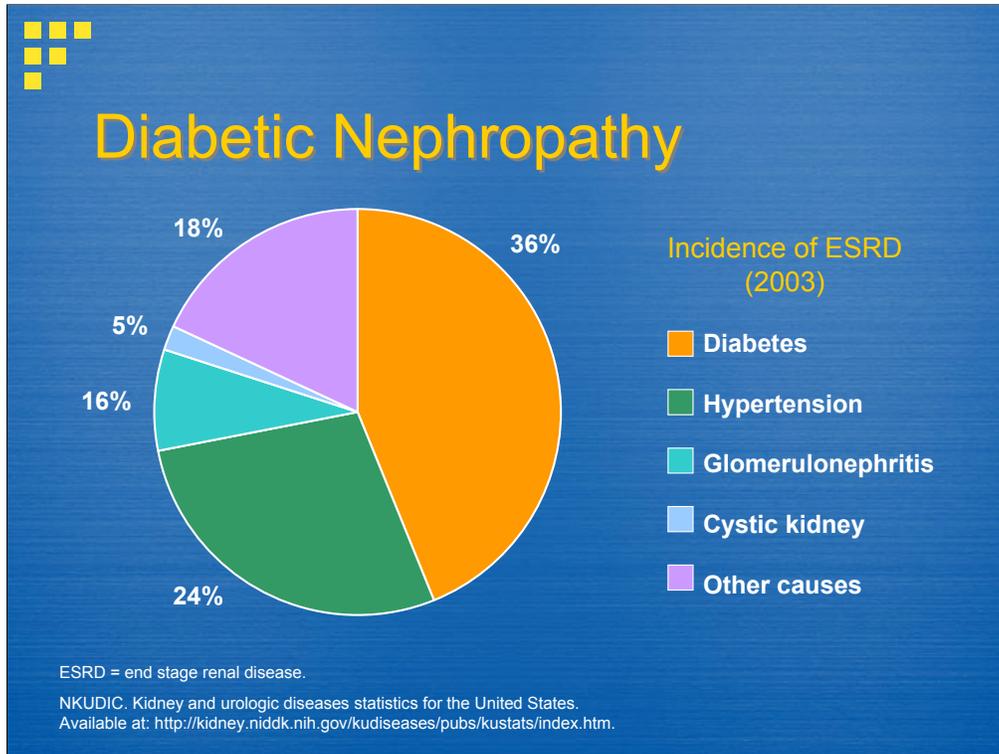
Answer

Less than 10% of patients with diabetes achieve the combined goals of A1C <7%, blood pressure <130/80 mm Hg, and total cholesterol <200 mg/dL.

Saydah SH, et al. *JAMA*. 2004;291:335–342.

The correct answer is E.

Despite the proven benefits of aggressive comprehensive risk-factor management on diabetes outcomes, <10% of patients with diabetes achieve the combined goals of A1C <7%, blood pressure <130/80 mm Hg, and total cholesterol <200 mg/dL.



Now, let's shift our discussion to nephropathy.

Among the primary causes of end stage renal disease, diabetes accounts for the largest proportion of new cases at 36%.



Stages of Nephropathy

Stages	Characteristics	Clinical Manifestations
1	Functional Changes (hypertrophy, hyperfiltration)	Asymptomatic
2	Structural Changes (renal lesions)	Asymptomatic
3	Incipient Nephropathy (microalbuminuria)	Normal or slightly elevated blood pressure, generally asymptomatic
4	Overt Nephropathy (proteinuria)	Nephrotic syndrome, hypertension
5	Renal Failure or ESRD	Fluid retention, congestive heart failure, uncontrolled hypertension, uremia

AADE. AADE Core Curriculum: Diabetes and Complications 5th ed. Chicago, Illinois; AADE; 2003:158–159.

Diabetic nephropathy progresses through 5 different stages.

Stage 1 is characterized by hyperfiltration and renal hypertrophy. During this stage, tiny blood vessel deterioration due to atherosclerosis destroys some of the many nephrons within the kidney. Remaining nephrons increase in size and work capacity as they attempt to compensate. Renal function is reduced, but no accumulation of metabolic waste occurs.

During *Stage 2*, thickened and inflamed capillaries reduce blood flow to the glomerulus. This results in glomerular basement membrane thickening, mesangial expansion (expansion of phagocytic cells of the mesangium), and diffuse intercapillary glomerulosclerosis (a degenerative process resulting in scarring of the renal glomeruli).

During *Stage 3*, also referred to as incipient diabetic nephropathy, microscopic amounts of albumin (microalbuminuria) inadvertently slip through sclerosed glomerular membranes, signifying a progressive deterioration in kidney filtration. Metabolic waste begins to accumulate in the blood because unaffected nephrons can no longer compensate, and responsiveness to diuretic therapy decreases.

Stage 4, also referred to as overt or clinical diabetic nephropathy, is characterized by detection of significantly large amounts of protein in the urine (albuminuria or proteinuria). Significant amounts of metabolic waste begin to accumulate, particularly urea and creatinine. Patients generally do not become symptomatic until stage 4 when oliguria, edema, and hypertension can develop.

Without, and sometimes in spite of, aggressive treatment, deteriorating vasculature or end stage renal disease results in *Stage 5*.



Screening

Test	When	Values
Blood pressure	Each office visit	Goal <130/80 mm Hg
Microalbuminuria (spot albumin-to-creatinine ratio)	Type 2: annually beginning at diagnosis Type 1: annually beginning at ≥5 years of diagnosis During pregnancy	Normal <30 µg/mg creatinine Microalbuminuria 30–299 Macroalbuminuria ≥300
Serum creatinine	Annually for estimation of glomerular filtration rate (GFR) in all adults with diabetes regardless of degree of urine albumin excretion	Normal 0.5 to 1.4 mg/dL Stage 1* GFR ≥90 Stage 2* GFR 60–89 Stage 3* GFR 30–59 Stage 4* GFR 15–29 Stage 5* GFR <15 or dialysis

GFR = glomerular filtration rate
 ADA. *Diabetes Care*. 2006; 29:S4–S42.
 AADE. AADE Core Curriculum: Diabetes and Complications 5th ed. Chicago, Illinois; AADE; 2003:158–159.

*mL/min per 1.73 m² body surface area

Screening for diabetic nephropathy should include evaluation of blood pressure at every office visit with a blood pressure goal of <130/80 mm Hg. Nephropathy screening also includes evaluating for microalbuminuria (usually with a spot urine albumin-to-serum creatinine ratio) annually beginning at diagnosis for people with type 2 diabetes and annually beginning at ≥5 years of diagnosis for people with type 1 diabetes, and during pregnancy for women. Additionally, an annual serum creatinine for estimation of the glomerular filtration rate (GFR) in all adults with diabetes regardless of the degree of urine excretion should be done. The estimated GFR is used to estimate the stage of diabetic nephropathy.



Prevention and Treatment of Nephropathy

- **Glycemic control**
 - A1C \leq 6.5%
 - Preprandial plasma glucose $<$ 110 mg/dL
 - 2-Hour postprandial plasma glucose $<$ 140 mg/dL
- **Blood pressure control \leq 130/80 mm Hg**
 - Angiotensin-converting enzyme inhibitors (ACEIs)
 - Angiotensin receptor blockers (ARBs)
- **Protein restriction**
 - \leq 0.8 g/kg body weight per day (~10% of daily calories) if any degree of chronic kidney disease

AACE. *Endocrine Practice*. 2002;8:5–11.

ADA. *Diabetes Care*. 2006; 29:S4–S42.

Glycemic and blood pressure control, as recommended by national guidelines, form the basis for the prevention and treatment of diabetic nephropathy.

Antihypertensives recommended for patients with diabetic nephropathy include angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers.

Protein restriction should be initiated in the presence of nephropathy (\leq 0.8 g/kg body weight per day [~10% of daily calories]). This level of protein intake essentially reflects the national recommendation of daily protein intake, which may in practice be a restricted amount.



Treatment of ESRD

- **Hemodialysis**
 - Fistula
 - Graft
- **Peritoneal dialysis**
 - Continuous ambulatory peritoneal dialysis (CAPD)
 - Continuous cycler-assisted peritoneal dialysis (CCPD)
 - Combined CAPD and CCPD
- **Kidney transplant**
 - Cadaveric kidney
 - Related or nonrelated living donor kidney

National Kidney Foundation. Dialysis. Available at: <http://www.kidney.org/atoz/atozItem.cfm?id=39>.

For patients who progress to end stage renal disease, treatment may include hemodialysis, peritoneal dialysis, or kidney transplant.

In hemodialysis, a fistula or graft is created for access to the bloodstream. Wastes, excess water, and salt are removed from the bloodstream using a dialysis machine. Hemodialysis is generally performed 3 times a week and can be done at a medical facility or at home.

In peritoneal dialysis, waste products and extra fluid pass from the blood into the dialysis solution via the peritoneum, which lines the wall of the abdominal cavity. A dialysis machine is not required for the most common form of peritoneal dialysis known as continuous ambulatory peritoneal dialysis (CAPD). Patients are able to be mobile with the dialysis solution in their abdomen. Other forms of peritoneal dialysis require a machine called a cycler to fill and drain the abdomen. Peritoneal dialysis can also be done using a combination of both CAPD and continuous cycler-assisted peritoneal dialysis.

Kidney transplantation can be performed with a kidney from a nonliving or living donor. Factors that must be taken into consideration to determine a kidney/recipient match include blood type, human leukocyte antigens, and cross-matching antigens. There has been dramatic progress over the past decade in the ease of matching donors and the success of kidney transplants.



Question

At what stage of diabetic nephropathy do symptoms generally become clinically apparent?

- A. Stage 1
- B. Stage 2
- C. Stage 3
- D. Stage 4
- E. Stage 5

Here is another question to check our progress.

At what stage of diabetic nephropathy do symptoms generally become clinically apparent?

- A. Stage 1
- B. Stage 2
- C. Stage 3
- D. Stage 4
- E. Stage 5



Answer

In diabetic nephropathy symptoms generally become clinically apparent at Stage 4.

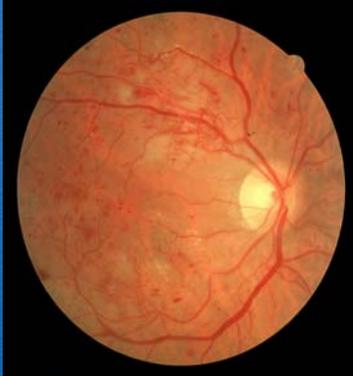
The correct answer is D.

Symptoms of diabetic nephropathy generally do not appear until late in the disease course at stage 4 when nephrotic syndrome and hypertension develop. Thus, routine screening and prevention measures are very important in the management of diabetic nephropathy.

■ ■ ■
■ ■ ■
■

Diabetic Retinopathy

- **Nonproliferative diabetic retinopathy (NPDR)**
 - Mild NPDR
 - Moderate NPDR
 - Severe NPDR
- **Proliferative diabetic retinopathy (PDR)**
- During first 2 decades of disease, nearly all with type 1 diabetes and >60% with type 2 diabetes have retinopathy



Fong, et al. *Diabetes Care*. 2004;27:S84–S87.

Blindness is the most feared complication of diabetes by patients.

Diabetic retinopathy can be classified as nonproliferative (NPDR) or proliferative (PDR).

In spite of our knowledge about good glycemic control, during the first 2 decades of disease, nearly all people with type 1 diabetes and >60% of people with type 2 diabetes have retinopathy.



Clinical Features

Progression*	Clinical Features
Mild NPDR	Increased vascular permeability, microaneurysms, intraretinal hemorrhages
Moderate NPDR	Venous caliber changes, intraretinal microvascular abnormalities (IRMAs), intraretinal hemorrhages
Severe NPDR	Retinal ischemia, IRMAs, extensive hemorrhage, and microaneurysms
PDR	Ischemia-induced neovascularization, vitreous hemorrhage, retinal traction, tears, and detachment

***Macular edema can develop at all stages of retinopathy**

ADA. Diabetic Retinopathy Slides. Available at: <http://www.diabetes.org/for-health-professionals-and-scientists/slide-sets-professional.jsp>.

The rate of progression of diabetic retinopathy varies, but generally follows the natural history shown on this slide. It begins with mild nonproliferative diabetic retinopathy (NPDR) characterized by increased vascular permeability, microaneurysms, and intraretinal hemorrhages. The next stage is moderate NPDR diabetic retinopathy, characterized by venous caliber changes, intraretinal microvascular abnormalities, and intraretinal hemorrhages. This is followed by severe NPDR, characterized by retinal ischemia, intraretinal microvascular abnormalities, extensive hemorrhage, and microaneurysms. Finally, we see proliferative diabetic retinopathy, characterized by ischemia-induced neovascularization, vitreous hemorrhage, retinal traction, tears, and detachment.

Macular edema can develop at all stages of retinopathy.



Retinopathy Screening

- **Type 1** - within 3-5 years after onset for adults and adolescents
- **Type 2** - at time of diagnosis
- **Pregnancy** - prior to conception and during 1st trimester, with close follow-up throughout pregnancy and for 1 year postpartum (does not apply to GDM)
- **Follow-up** - annually; may consider reducing to every 2–3 years in some cases
- **Examination** - dilated indirect ophthalmoscopy with biomicroscopy and 7-standard field stereoscopic 30° fundus photography

ADA. *Diabetes Care*. 2006;29:S4–S42.

Fong DS, et al. *Diabetes Care*. 2004;27:S84–S87.

GDM = gestational diabetes mellitus

Screening for diabetic retinopathy should be performed within 3 to 5 years after the onset of type 1 diabetes for adults and adolescents. For younger children, screening for diabetic retinopathy should be performed after 5 years' duration of the disease or by age 10.

For people with newly diagnosed type 2 diabetes, screening should be done soon after blood glucose has stabilized. Screening for retinopathy should occur during pregnancy in women with preexisting diabetes mellitus, but not necessarily in women with gestational diabetes mellitus.

Patients should be followed-up annually with dilated indirect ophthalmoscopy with biomicroscopy and 7-standard field stereoscopic 30-degree fundus photography.



Prevention

- **Glycemic control**
 - A1C \leq 6.5%
 - Preprandial plasma glucose <110 mg/dL
 - 2-Hour postprandial plasma glucose <140 mg/dL
- **Blood pressure control <130/80 mm Hg**
- **Annual dilated eye exams**

AACE. *Endocrine Practice*. 2002;8:5–11.
ADA. *Diabetes Care*. 2006; 29:S4–S42.

General recommendations for the prevention and treatment of diabetic retinopathy include optimal glycemic control as recommended by the American College of Endocrinology with an A1C \leq 6.5%, fasting glucose <110 mg/dL, and 2-hour postprandial plasma glucose <140 mg/dL. Blood pressure control according to national guidelines should be <130/80 mm Hg. And, finally, people with diabetes should have an annual dilated eye exam.



Management

Progression	Management*
Mild NPDR	Annual follow-up
Moderate NPDR	6–12 month follow-up, color fundus photography
Severe NPDR	3–4 month follow-up, color fundus photography; possible panretinal photocoagulation
PDR	2–4 month follow-up; color fundus photography; panretinal photocoagulation (3–4 month follow-up)

*Macular edema: color fundus photography, fluorescein, angiography, photocoagulation, 3–4 month follow-up

ADA. Diabetic Retinopathy Slides. Available at: <http://www.diabetes.org/for-health-professionals-and-scientists/slide-sets-professional.jsp>.

The frequency of follow-up and management of retinopathy also differ depending on the severity of the disease.

Mild nonproliferative diabetic retinopathy (NPDR) should be followed with an annual examination.

Moderate NPDR should have follow-up in 6 to 12 months plus color fundus photography.

Severe NPDR should have more frequent follow-up, every 3 to 4 months with color fundus photography and possibly panretinal photocoagulation.

Once a person has proliferative retinopathy, follow-up should occur more frequently, probably every 2 to 4 months. Color fundus photography should continue as well as panretinal photocoagulation, with follow-up every 3 to 4 months.

Laser photocoagulation can help prevent vision loss and is recommended for the treatment of severe NPDR, proliferative diabetic retinopathy (PDR), and for macular edema, which can potentially develop at any stage of retinopathy.

Macular edema is more common in people with type 2 diabetes and requires color fundus photography, fluroscein angiography, and photocoagulation with 3 to 4-month follow-up.

Therapies include laser photocoagulation as well as 2 emerging therapies; anti-VEG-F and PKC beta inhibitors.



Diabetic Neuropathy

Heterogeneous, affecting different parts of the nervous system, and presenting with diverse clinical manifestations

Classification

Generalized symmetric

- Acute sensory
- Chronic sensorimotor
- Autonomic

Focal and multifocal

- Cranial
- Truncal
- Focal limb
- Proximal motor (amyotrophy)
- Coexisting chronic inflammatory demyelinating polyneuropathy (CIDP)

Boulton AJM, et al. *Diabetes Care*. 2005;28:956–962.

Diabetic neuropathy is seen sooner than some other complications and patients often have noticeable symptoms. While other complications may be insidious and asymptomatic, neuropathy may drive people to seek medical attention.

Diabetic neuropathies are heterogeneous, affecting different parts of the nervous system and presenting with diverse clinical manifestations.

Although many classification systems have been proposed, the ADA's position statement on diabetic neuropathy classifies it into 2 major categories—first, generalized symmetric and, second, focal and multifocal.

Symmetric neuropathy includes acute sensory, chronic sensorimotor, and autonomic neuropathy.

Focal and multifocal neuropathy includes cranial neuropathy that may present as Bell's Palsy, which looks like a stroke, truncal neuropathy, focal limb neuropathy, proximal motor neuropathy, and co-existing chronic inflammatory demyelinating polyneuropathy.



Screening

	Chronic Sensorimotor Distal Peripheral Neuropathy (DPN)	Autonomic Neuropathy
Screening in Type 1*	At diagnosis then annually	5 years after diagnosis then annually
Screening in Type 2	At diagnosis then annually	At diagnosis then annually
	Visual inspection, sensory function, ankle reflexes; foot exam at every visit or every 3–6 months for established DPN	History and exam for signs of autonomic dysfunction, test for heart rate variability

Boulton AJM, et al. *Diabetes Care*. 2005;28:956–962.
 ADA. *Diabetes Care*. 2006; 29:S4–S42.

*Boulton et al suggest screening in patients with type 1 diabetes occur 5 years after diagnosis and annually thereafter.

For both chronic sensorimotor distal peripheral neuropathy (DPN) and autonomic neuropathy, screening is recommended at 5 years after the diagnosis of type 1 diabetes and annually thereafter, and at diagnosis and annually thereafter for people with type 2 diabetes.

Screening for chronic sensorimotor DPN should include visual inspection, sensory function, and ankle reflexes as well as a foot exam at every visit. If patients have established peripheral neuropathy, screening should be done more often, potentially every 3 to 6 months.

Screening for autonomic dysfunction should include a history and exam for signs of autonomic dysfunction. Additionally testing for heart rate variability is done and usually includes R to R interval measurement.



Diagnosis and Prevention

- **Diagnosis**
 - Assess symptoms
 - Sensory testing
 - Autonomic function testing
 - Electrophysiology
- **Prevention**
 - Glycemic control
 - Manage other risk factors (no definitive prevention studies)
 - Blood pressure control
 - Lipid control
 - Avoid smoking and excess alcohol

Boulton AJM, et al. *Diabetes Care*. 2005;28:956–962.

The diagnosis of diabetic neuropathy is made based on assessment of symptoms, sensory testing, autonomic function testing, and electrophysiology. Symptoms may include muscle weakness, muscle cramps, prickling, numbness or pain, vomiting, diarrhea, poor bladder control, and sexual dysfunction.

Glycemic control represents the primary prevention and treatment measure for diabetic neuropathy. Blood pressure control, lipid control, and avoiding both smoking and excess alcohol are also suggested, although no definitive prevention studies have been performed on the benefit of managing these other risk factors.

Within the past few years newer medications have become available to treat painful neuropathy.



Acute Sensory Neuropathy

- Rare
- Tends to follow:
 - Periods of poor metabolic control
 - Sudden change in glycemic control
- Acute onset of severe sensory symptoms with marked nocturnal exacerbation
- Few neurologic signs on leg exam

Boulton AJM, et al. *Diabetes Care*. 2005;28:956–962.

Acute sensory neuropathy is rare and tends to follow periods of poor metabolic control or sudden changes in glycemic control.

The clinical features of acute sensory neuropathy are characterized by acute onset of severe sensory symptoms with marked nocturnal exacerbation and few neurologic signs on leg exam.



Chronic Sensorimotor DPN

- Most common form of diabetic neuropathy
- Diagnosis of exclusion
- Affects distal lower extremities
- Signs/symptoms
 - 50% asymptomatic
 - Paresthesia/hyperparesthesia
 - Burning pain
 - Loss of sensation
- Treatment
 - Glycemic control, foot care
 - Pharmacologic (tricyclic agents, selective serotonin and norepinephrine reuptake inhibitors, anticonvulsants, pain medications)
 - Nonpharmacologic, topical, and physical therapies

Boulton AJM, et al. *Diabetes Care*. 2005;28:956–962.

Chronic sensorimotor DPN is the most common form of diabetic neuropathy and is a diagnosis of exclusion. This may be called glove and stocking neuropathy, because it occurs in the feet and hands first.

Although as many as 50% of people are asymptomatic, signs and symptoms may include paresthesia or hyperparesthesia (some people can't stand the sheets on their feet at night), they may have burning pain (patients report that it feels like walking on needles), and loss of sensation in the later stages.

In addition to glycemic control and regular foot care, pharmacologic therapy with tricyclic agents, selective serotonin and norepinephrine reuptake inhibitors, anticonvulsants, and pain medications, as well as nonpharmacologic, topical, and physical therapies may be helpful.



Focal and Multifocal Neuropathies

- **Mononeuropathies**
 - Cranial neuropathy: primarily involves nerves II, IV, VI, and VII
 - Ulnar, median, peroneal, and medial plantar nerve entrapment, common (1/3 of patients)
- **Proximal motor (amyotrophy)**
 - Severe neuropathic pain and uni- or bilateral muscle weakness and atrophy in proximal thigh muscles; exclude spinal stenosis
- **Coexisting chronic inflammatory demyelinating polyneuropathy (CIDP)**
 - Severe predominantly motor neuropathy and progressive polyneuropathy

Boulton AJM, et al. *Diabetes Care*. 2005;28:956–962.

With regard to focal and multifocal neuropathies, several clinical features should be considered.

Mononeuropathies encompass cranial neuropathy and ulnar, median, peroneal, and medial plantar nerve entrapment. This may present as Bell's Palsy, looking like a stroke, or in the wrist and hand, making it resemble carpal tunnel syndrome.

Additionally, patients who develop severe neuropathic pain with unilateral or bilateral muscle weakness and atrophy in proximal thigh muscles should be evaluated for proximal motor neuropathy. Spinal stenosis and chronic inflammatory demyelinating polyneuropathy must also be considered.

Coexisting chronic inflammatory demyelinating polyneuropathy is often overlooked and is characterized by severe predominantly motor neuropathy and progressive polyneuropathy.

These neuropathies are not seen as commonly, and are therefore more difficult to diagnose.

Cardiovascular and Gastrointestinal Autonomic Neuropathy

	Cardiovascular	Gastrointestinal
Clinical Features	Most studied and clinically important form of distal autonomic neuropathy (DAN) Exercise intolerance Postural hypotension	Gastroparesis - anorexia, nausea, vomiting, early satiety Diabetic enteropathy - diarrhea, constipation
Treatment	Exercise intolerance – graded supervised exercise, ACEI, BB Hypotension - change posture, slow posture changes, elevate bed, increase plasma volume	Gastroparesis - small frequent meals, prokinetic agents Enteropathy - antibiotics, antiemetics, stool softeners or dietary supplements

Boulton AJM, et al. *Diabetes Care*. 2005;28:956–962.

ADA. Diabetic Neuropathy Slides. Available at: <http://www.diabetes.org/for-health-professionals-and-scientists/slide-sets-professional.jsp>.

Cardiovascular autonomic dysfunction or cardiac autonomic neuropathy is the most studied and clinically important form of distal autonomic neuropathy because of its potentially life-threatening consequences. Clinical features include exercise intolerance and postural hypotension. Graded supervised exercise and/or treatment with an angiotensin-converting enzyme inhibitor or a β -blocker is suggested for the management of exercise intolerance, whereas postural changes and increasing plasma volume may help in the management of hypotension.

Gastrointestinal autonomic neuropathy can cause a number of gastrointestinal symptoms. For gastroparesis, small frequent meals and prokinetic agents such as metoclopramide are recommended. Prandial or mealtime insulin management becomes a challenge, as food leaves the stomach at quite variable times. Insulin may be given after the meal with blood glucose monitoring done hourly to determine the appropriate time to inject the insulin.

For enteropathy, antibiotics, antiemetics, stool softeners, or dietary supplements may help.



Genitourinary Autonomic Neuropathy

Signs/Symptoms	Treatment
Bladder dysfunction	Bethanechol, intermittent catheterization
Erectile dysfunction	Sildenafil, verdenafil, tadalafil, prostaglandin
Dyspareunia	Lubricants

Boulton AJM, et al. *Diabetes Care*. 2005;28:956–962.

Genitourinary autonomic neuropathy can lead to bladder dysfunction, erectile dysfunction, and dyspareunia.

In addition to general preventive measures, bethanechol and intermittent catheterization may be used in the treatment of bladder dysfunction, pharmacologic therapies can be used to treat erectile dysfunction, and lubricants may help to reduce painful dyspareunia.



Question

Diabetic neuropathy affects what percentage of people with diabetes?

- A. 30%–40%
- B. 40%–50%
- C. 50%–60%
- D. 60%–70%

And now we have one last question.

Diabetic neuropathy affects what percentage of people with diabetes?

- A. 30%–40%
- B. 40%–50%
- C. 50%–60%
- D. 60%–70%



Answer

Diabetic neuropathy affects 60%-70% of people with diabetes.

The correct answer is D.

60% to 70% of people with diabetes have mild to severe forms of diabetic neuropathy.



Macrovascular Complications

- CAD**
 - Acute coronary syndrome
 - Angina
 - Unstable angina
 - Myocardial infarction (coronary thrombosis or occlusion)
- CVD**
 - Transient ischemic attacks (TIAs)
 - Ischemic stroke
 - Cerebral thrombosis
 - Cerebral occlusion
 - Hemorrhagic stroke
 - Aneurysm
 - Arteriovenous malformation
- PVD**
 - Ischemia and infarction

As previously mentioned, the macrovascular complications of diabetes include coronary artery disease, cardiovascular disease, and peripheral vascular disease.

Blockage of the coronary arteries that occurs with coronary artery disease can lead to the development of acute coronary syndromes, a constellation of clinical symptoms caused by myocardial ischemia such as: angina (chest pain that occurs with exertion), unstable angina (chest pain that occurs at rest), and myocardial infarction resulting from coronary thrombosis or occlusion.

When vessels supplying the brain become blocked, transient ischemic attacks or strokes can occur. Two types of strokes can develop. They are ischemic strokes resulting from cerebral thrombosis or occlusion, and hemorrhagic strokes resulting from rupture of an aneurysm or arteriovenous malformation.

Blockage of vessels that supply the lower extremities can cause ischemia and infarction that result in leg pain and gangrene.



Cardiovascular Risk Factors

- Hypertension*
- Cigarette smoking
- Obesity* (BMI ≥ 30 kg/m²)
- Physical inactivity
- Dyslipidemia*
- Diabetes mellitus*
- Microalbuminuria
- GFR <60 mL/min
- Age (older than 55 for men, 65 for women)
- Family history of premature cardiovascular disease (men under 55, women under 65)

*Components of the metabolic syndrome

BMI = body mass index; GFR = glomerular filtration rate
Chobanian AV, et al. *JAMA*. 2003;289:2560–2572.

Numerous risk factors, in addition to diabetes, contribute to the development of macrovascular complications. Many of these risk factors are also highly prevalent among those with diabetes as previously discussed.

Hypertension, obesity, dyslipidemia, and diabetes are all components of the metabolic syndrome. Additional risk factors include age, decreasing glomerular filtration rate, and family history of cardiovascular disease in men under 55 and women under 65.

Metabolic Syndrome

NCEP Definition	WHO Definition
<p>At least 3 of the following:</p> <ul style="list-style-type: none"> ▪ Fasting plasma glucose ≥ 110 mg/dL ▪ Abdominal obesity: waist girth men: >40 inches women: >35 inches ▪ Serum TG ≥ 150 mg/dL ▪ Serum HDL: men <40 mg/dL women <50 mg/dL ▪ Blood pressure $\geq 130/85$ mm Hg or antihypertensive medication 	<ul style="list-style-type: none"> ▪ Hyperinsulinemia (upper quartile of nondiabetic) or fasting glucose ≥ 110 mg/dL AND at least 2 of the following: <ul style="list-style-type: none"> ▪ Abdominal obesity: (1) waist-to-hip ratio, men >0.90 and women >0.85 or BMI ≥ 30 kg/m²; or (2) waist girth ≥ 94 cm ▪ Dyslipidemia: TG ≥ 150 mg/dL, HDL, men <35 mg/dL and women <39 mg/dL ▪ Blood pressure $\geq 140/90$ mm Hg or antihypertensive medication

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486–2497.
Lakka H-M, et al. *JAMA*. 2002;288:2709–2716.
Alberti KGMM, et al. *Diab Med*. 2006;23:469–480.

As we talk about cardiovascular disease, let me remind you that the metabolic syndrome represents a cluster of risk factors for cardiovascular disease.

Although the definition and pathophysiology of the metabolic syndrome are not always consistent, 2 respected organizations have defined the metabolic syndrome according to the criteria listed in this slide.

The National Cholesterol Education Program (NCEP) definition of the metabolic syndrome includes at least 3 of the following:

- Fasting plasma glucose ≥ 110 mg/dL
- Abdominal obesity (waist girth for men >40 inches, waist girth for women >35 inches)
- Serum triglycerides ≥ 150 mg/dL
- Serum HDL for men <40 mg/dL and for women <50 mg/dL
- Blood pressure $\geq 130/85$ mm Hg or antihypertensive medication.

The World Health Organization (WHO) definition of the metabolic syndrome includes:

- Hyperinsulinemia (upper quartile of nondiabetic) or fasting glucose ≥ 110 mg/dL AND at least 2 of the following:
 - Abdominal obesity: (1) waist-to-hip ratio, >0.90 in men and >0.85 in women or BMI ≥ 30 kg/m²; or (2) waist girth ≥ 94 cm
 - Dyslipidemia: triglycerides ≥ 150 mg/dL, HDL for men <35 mg/dL, and HDL for women <39 mg/dL
- Blood pressure $\geq 140/90$ mm Hg or antihypertensive medication.



Screening and Management for Macrovascular Disease

- Risk assessment (annually)
- Glycemic control ADA (or ACE)
 - A1C <7% (twice a year and as needed)
 - Preprandial plasma glucose 90–130 mg/dL
 - Peak postprandial plasma glucose <180 mg/dL
- Blood pressure control (at each visit)
 - \leq 130/80 mm Hg
- Lipid control (annually and as needed)
 - LDL <100 mg/dL, HDL males >40 mg/dL, HDL females >50 mg/dL, TG <150 mg/dL
- Lifestyle modification

ADA. *Diabetes Care*. 2006; 29:S4–S42.

General screening, prevention, and treatment measures for macrovascular disease include assessment of risk, glycemic control using American Diabetes Association or American College of Endocrinology guidelines, blood pressure, and lipid control according to national guidelines, and lifestyle modification (ie, diet, exercise, and avoiding tobacco).



Additional Recommendations for Coronary Artery Disease

- Consider ACEI for patients with or without hypertension who have increased risk for coronary artery disease
- Consider beta-blocker for patients with prior myocardial infarction or undergoing major surgery
- In patients with congestive heart failure, metformin is contraindicated and thiazolidinediones should be used with caution

ADA. *Diabetes Care*. 2006; 29:S4–S42. ACEI = angiotensin converting enzyme inhibitor

Additional ADA recommendations for the treatment of coronary artery disease in people with diabetes include treatment with an angiotensin-converting enzyme inhibitor for patients who have other cardiovascular risk factors in addition to coronary artery disease, such as a history of cardiovascular disease, dyslipidemia, microalbuminuria, or smoking.

Additional medication considerations include β -blockers for patients who have had a previous myocardial infarction or are undergoing major surgery to reduce mortality.

In people who have congestive heart failure, avoid metformin and use thiazolidinediones with caution.



Conclusion

- Diabetes is a highly prevalent disease that is associated with numerous micro- and macrovascular complications
- Comprehensive risk factor management can significantly reduce diabetes complications and improve patient outcomes
- Glycemic, blood pressure, and lipid control are essential to the prevention and management of diabetes complications

In conclusion:

- Diabetes is a highly prevalent disease that is associated with numerous micro-and macrovascular complications.
- Comprehensive risk factor management can significantly reduce diabetes complications and improve patient outcomes.
- Glycemic, blood pressure, and lipid control are essential to the prevention and management of micro-and macrovascular complications.