

The Relationship and Impact of Diabetes and Cardiovascular Disease

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Summary

The prevalence of type 2 diabetes and obesity are both increasing. Because these are both major risk factors for the development of cardiovascular disease, the prevalence and mortality of cardiovascular disease is likely to increase. In order to prevent this, strategies for preventing diabetes, treating diabetes to accepted goals, and targeting associated CVD risk factors should be implemented.

Key Points

- CVD mortality has been declining over the past few decades.
- The rise in prevalence of two important risk factors – obesity and diabetes – is projected to reverse this trend.
- Preventing diabetes, glucose lowering to accepted goals, and targeting associated CVD risk factors are essential to curb the risk of CVD in the next century.
- The earlier control of glycemia occurs, the better the delay in development in CVD.

CHRONIC DISEASES ARE THE LEADING causes of mortality and disability in the United States. They account for 70 percent of all deaths in the U.S. or 1.7 million deaths each year. Chronic diseases result in morbidity in 1 out of 10 Americans. However, they are also among the most preventable of all diseases.

Cardiovascular disease (CVD) is the leading cause of mortality in the U.S., accounting for 27 percent of all deaths. Exhibit 1 shows the changes in CVD mortality since 1900.¹ Although CVD mortality has been declining since the 1970s, the rate has plateaued in men and women under the age of 35. This has likely occurred because of the rising trends in two important risk factors for CVD – diabetes and obesity.

Obesity increases risk for CVD.² Currently, 66 percent of American adults are overweight (BMI >25 kg/m²) and 32 percent are obese (BMI >30 kg/m², Exhibit 2).³ The current cohort of obese adolescents will account for a 100,000 new cases of CVD and an increase in excess deaths from CVD in the next 10 years.⁴ With the increasing trend of obesity in young people, there is a significant chance that the trend of declining rate of CVD mortality will be reversed.

There is a parallel trend with type 2 diabetes that

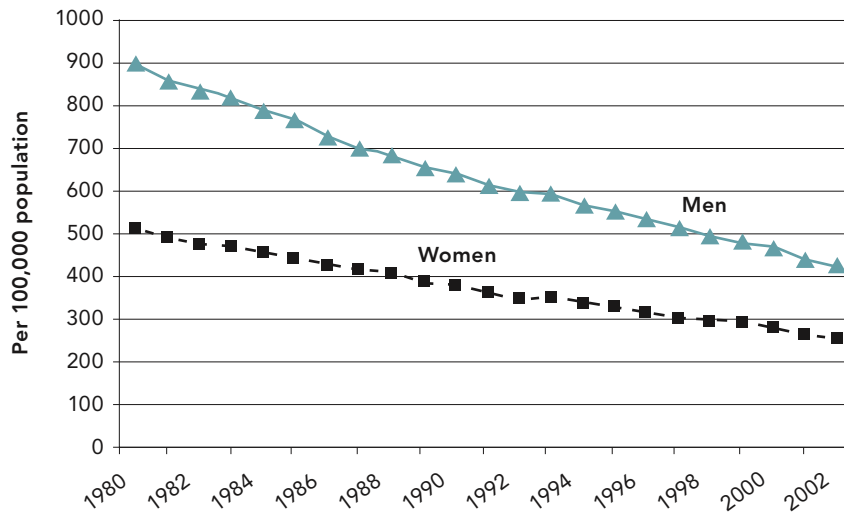
correlates with the rates of obesity. There was a steep rise in the prevalence of diabetes in the mid 90's and it is continuing to rise (Exhibit 3). Twenty four million Americans have diabetes. Even more challenging, is the rate of undiagnosed diabetes. At least five percent of patients with diabetes are thought to be undiagnosed. Additionally, diagnosis often comes too late; 50 percent of patients have at least 1 complication at the time of diagnosis. The onset of disease starts at least 10 years before the onset of classical symptoms during which time underlying damage to organ systems is occurring.

Diabetes is an independent risk factor for heart disease and occurs commonly with other associated risk factors – dyslipidemia, hypertension, increased coagulation, and obesity. Because of the amount of atherosclerosis already present at diagnosis, diabetes is considered a cardiovascular risk equivalent.

Prediabetes, as either impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), is a strong predictor of the development of diabetes. Prediabetes is also associated with an increased risk for CVD, the number one cause of mortality in patients with diabetes (Exhibit 4).⁵

Prevention of diabetes is essential. Given the strong association between diabetes (and even pre-

Exhibit 1¹: Age-Adjusted CHD Mortality Age > 35 years



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diabetes) and CVD, early detection and treatment are required. Randomized controlled trials have shown the efficacy of intensive treatment of risk factors in reducing the risk of CVD in patients with diabetes.

There is a strong correlation between glucose control and coronary heart disease events. Controlling hemoglobin A1C (A1C) reduces the rate of CVD events. Several studies have shown a decrease in CVD events in general and myocardial infarction (MI), stroke, nonfatal MI, and death specifically

with intensive treatment.⁶⁻⁸ In the UKPDS study in type 2 patients, intensive treatment improves microvascular disease and CVD outcomes over the long term.⁶ In addition to glucose control, intensive treatment of all CVD risk factors does reduce risk for CVD in both type 1 and type 2 patients. Exhibit 5 is an example of one study intensively controlling all CVD risk factors.⁸

Targeting the current ADA guidelines for A1C control (A1C \leq to 7 percent) is appropriate in all patients with diabetes. Based on the findings from

Exhibit 2³: Obesity Trend in the U.S.

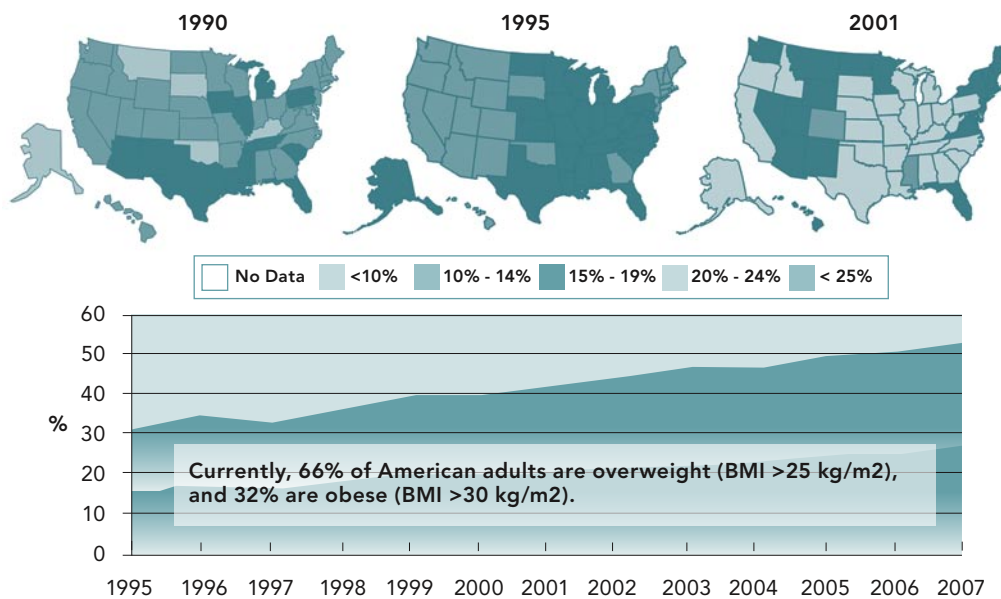
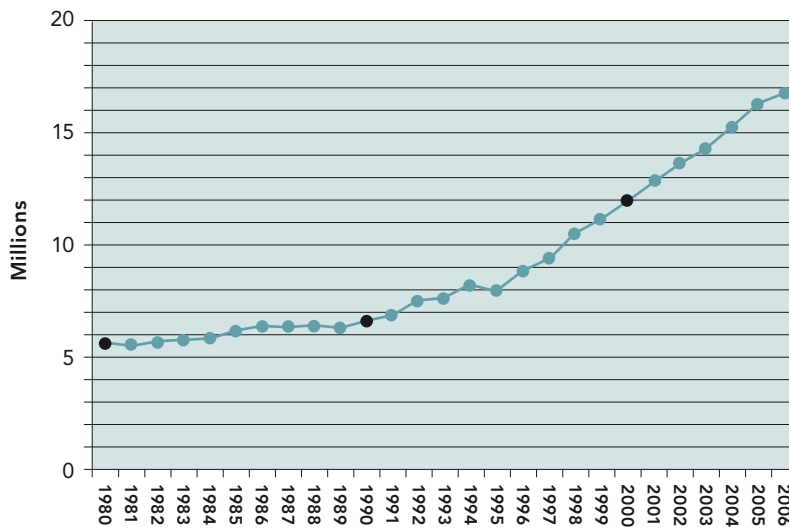


Exhibit 3: Prevalence of Diabetes



the ACCORD study of increased mortality with low A1C values, setting lower goals (< 6.5 percent) in patients with pre-existing heart disease and diabetes may not be appropriate.⁹

Type 2 diabetes can be prevented. A number of studies have assessed whether diabetes can be prevented with lifestyle modifications or pharmacologic therapy. In subjects with IGT, the use of metformin along with lifestyle changes, reduced the risk of diabetes in the Diabetes Prevention Study (Exhibit 6).¹⁰ The DREAM trial was another trial examining the issue of diabetes prevention. Rosiglitazone use reduced the incidence of diabetes development in patients with IGT.¹¹

The unanswered question is will CVD be prevented by preventing the development of DM. At least one diabetes prevention trial, STOP-IDDM, showed that delaying the development of diabetes also delayed the development of heart disease.¹² In the DREAM and Diabetes Prevention studies, reduced incidence of cardiovascular disease has not been seen but with longer term follow-up this may become evident.^{10,13}

Other CVD risk factors may be reduced with prevention of diabetes. Blood pressure values were reduced in the lifestyle treatment arm of the Diabetes Prevention study and in the rosiglitazone group in the DREAM trial. As a result of the various diabetes

Exhibit 4⁵: Glucose Tolerance Status and CVD

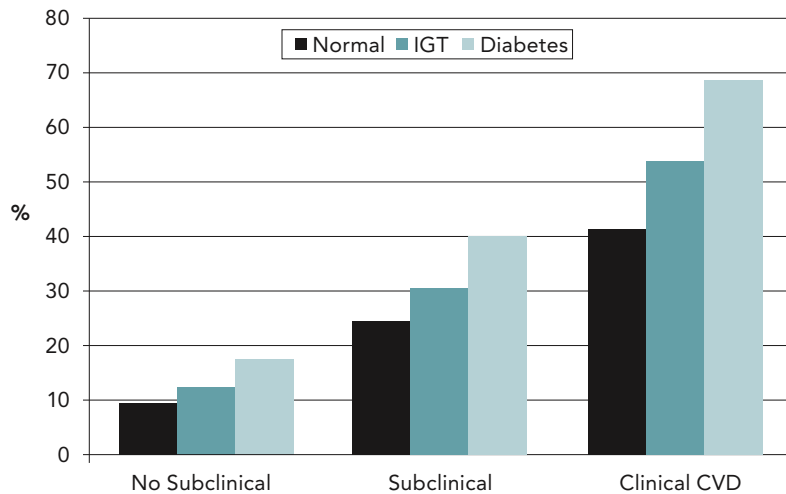


Exhibit 5⁸: Incidence of Any CVD Event

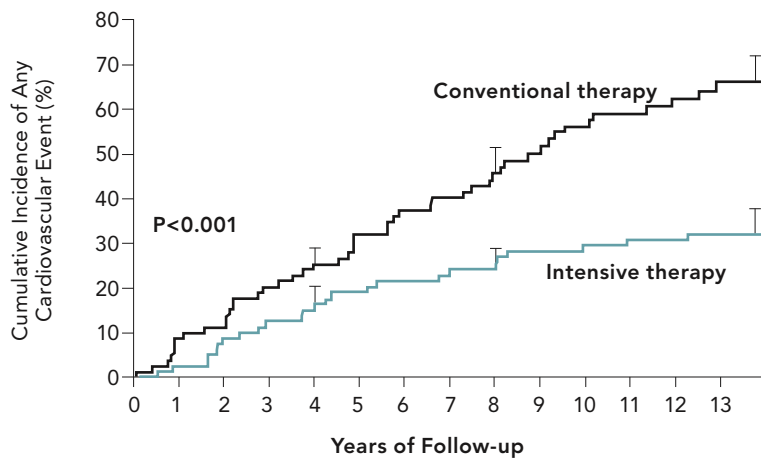
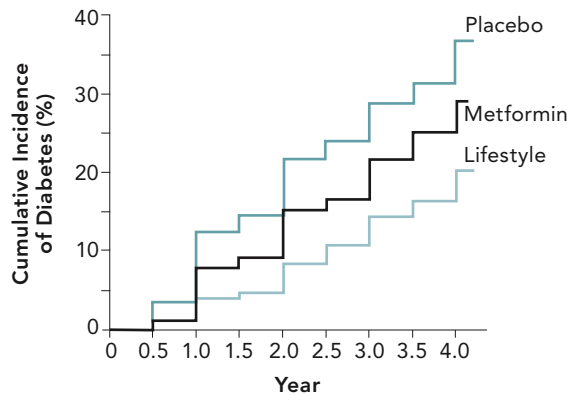


Exhibit 6¹⁰: Diabetes Prevention



prevention trials, the ADA recently published a consensus statement that suggests that anyone with pre-diabetes should be offered lifestyle modifications.¹³ Patients should lose 5 to 10 percent of body weight, if overweight, and should engage in 30 minutes of moderate physical activity daily. If patients have both IFG and IGT and any one of the following young: BMI greater than 35, family history in a first degree relative with type 2 diabetes, elevated triglyceride levels, low high density lipoprotein levels, hypertension, or an A1C greater than 6 percent, metformin should be considered in addition to lifestyle changes. Metformin is the best studied and has the least adverse effects. Unfortunately, about 12 to 15 percent of the U.S. adult population would meet the criteria for metformin prevention therapy. To date, no study of diabetes prevention with medications has determined cost effectiveness.

Diabetes therapy in general does not cost as much as heart disease, cancer, or hypertension but there

are many costs associated with the long-term complications of the disease. Health care expenditures for patients with diabetes are approximately twice that of someone without the disease. The per capita health care expenditures for diabetes are over \$11,000 per year. The indirect costs of diabetes are also significant. In 2007, the indirect costs of diabetes were estimated as 58 billion dollars. Costs for patients who have both diabetes and CVD are almost quadruple. The costs peaks at an earlier age when CVD is present and increase over time.

Conclusion

CVD mortality has been declining over the past few decades. However, important risk factors – obesity and diabetes – have been on the rise. Therefore, incident CVD is projected to increase in the next 30-50 years. Preventing diabetes and targeting the associated CVD risk factors are essential to curb the risk of CVD in the next century. The earlier control

of glycemia occurs, the better the delay in development in CVD. *JMCM*

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