

# Depression: A Potentially Modifiable Risk Factor for Diabetes and Its Complications

## In Brief

The epidemic rise in diabetes in the United States has prompted scientists to expand the search for modifiable risk factors, for both the disease itself and associated morbidity. In this From Research to Practice section, the authors review mounting evidence pointing toward depression as a medical risk factor for the development of type 2 diabetes and for progression of complications from either type 1 or type 2 diabetes. They offer practical advice for the management of depression in patients with diabetes, including 1) how to identify people in need of help, 2) how to get people to accept the help they need, and 3) what to expect from treatment options in the practice setting.

## Section I: Preface

### Identifying Novel Approaches to Diabetes Prevention and Treatment: the Example of Depression

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Diabetes is becoming the most common chronic medical illness in the United States, with roughly 1.3 million new cases diagnosed annually.<sup>1</sup> Approximately 18.2 million people now have type 1 or type 2 diabetes (6.3% of the population), including 5.2 million people whose type 2 diabetes remains undiagnosed. Another 20.1 million adults in the United States (21.1% of the population > 20 years of age) have pre-diabetes, glucose regulation abnormalities that place them at risk for diabetes and coronary heart disease (CHD). In all, there are 38.3 million people in the United States with overt diabetes or pre-diabetes. The number represents a more than fivefold increase over the previous 35 years and parallels the epidemic rise of obesity in our population.

People with diabetes are significantly more likely to be disabled, incapacitated, or unemployed and have per capita and out-of-pocket medical expenditures two to five times greater than those without diabetes.<sup>2</sup> The annual total direct and indirect cost of diabetes in the United States exceeded

\$132 billion in 2002, or one in ten health dollars.<sup>1</sup>

Not only burdensome and expensive, diabetes dramatically reduces longevity, taking its toll primarily through micro- and macrovascular disease complications. Diabetes is the sixth leading cause of death in the United States and the leading cause of blindness, nontraumatic limb amputation, and end-stage renal disease.<sup>1</sup>

Diabetes is a powerful independent risk factor for atherosclerosis, particularly CHD. In turn, atherosclerosis accounts for > 80% of all deaths from diabetes and 75% of hospitalizations for diabetes complications.<sup>3</sup> The risk of CHD and death from heart disease is two to four times greater in diabetes than in the general population and is disproportionately apparent in women with diabetes. In fact, diabetes is the only disorder that causes women to have as much heart disease as men. The increased incidence of type 2 diabetes, particularly among people under the age of 20 years (a group that may account for up to 15% of new-onset cases), is likely to

slow the decline in age-adjusted CHD and signal a new epidemic of cardiovascular disease in the United States.<sup>4</sup>

The aim of diabetes treatment is to attain glycemic control sufficient to reduce the risk of acute and chronic complications. The efficacy of conventional treatment in large, randomized clinical trials is well documented, with improved glycemic control leading to sustained reductions in microvascular and neuropathic complication rates. However, there is no definitive proof that lowering hemoglobin A<sub>1c</sub> (A1C) decreases the risk of macrovascular complications, the principal cause of death from diabetes. Other factors that often antedate frank hyperglycemia, including insulin resistance, obesity, hypertension, and dyslipidemia, also may influence the course of cardiovascular disease in diabetes.

Furthermore, the level of glycemic control achieved by subjects in the landmark trials is significantly better than that of average patients with diabetes. In general clinical practice settings, two of every three patients are not able to maintain the level of glycemic control recommended by the American Diabetes Association (A1C < 7.0%), even with intensive treatment and systematic follow-up.<sup>5</sup>

It is disconcerting to observe the epidemics of diabetes and obesity occurring in the context of significant

advances in the treatment of these problems—and in the face of a U.S. population preoccupied with its weight. It is alarming to witness the encroachment of these problems into the ranks of our children. The situation has stimulated a search for novel, modifiable factors that could lower the risk for diabetes or prevent its complications.

Depression may be one such factor. The evidence supporting this hypothesis is outlined and discussed throughout this From Research to Practice section, wherein a number of empirical observations are examined. Depression severe enough to warrant intervention is present in as many as one in every four patients with type 1 or type 2 diabetes.<sup>6</sup> Not only is depression associated with hyperglycemia and with increased risk for complications (especially CHD), but it is also an independent risk factor for type 2 diabetes, doubling the likelihood of its development.

The mechanisms by which depression adds to the risk of type 2 diabetes and worsens the course of established diabetes are unclear. Depression adversely affects a number of behaviors that could mediate these outcomes, including dietary behavior, tobacco use, physical activity, and adherence to medical treatment, but these behavioral factors alone have not

explained the importance of depression in influencing outcomes. Other features of depression, e.g., glucocorticoid dysregulation, increased sympathetic activity, and alterations in inflammatory processes, may contribute directly to insulin resistance and hyperglycemia and thereby potentiate the atherogenic effects of diabetes.

For this research section, we selected a number of publications, most of which came from our own research group, that provide a scientific basis for evaluating depression as a medical risk factor. Each article is framed within a hypothesis, and the hypotheses are linked and examined as logical elements of an argument. The contributing authors summarize the articles and comment on their clinical importance. In the final section, we discuss the remaining gaps in defining depression as a true risk factor and the steps required to implement depression management in the routine care of patients with diabetes. We have provided a single reference list at the end of the discussion to avoid unnecessary repetition of citations throughout the section.

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