

# Stress and Diabetes: A Review of the Links

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## Abstract

Evidence suggests that stressful experiences might affect diabetes, in terms of both its onset and its exacerbation. In this article, the authors review some of this evidence and consider

ways in which stress might affect diabetes, both through physiological mechanisms and via behavior. They also discuss the implications of this for clinical practice and care.

In recent years, the complexities of the relationship between stress and diabetes have become well known but have been less well researched. Some studies have suggested that stressful experiences might affect the onset and/or the metabolic control of diabetes, but findings have often been inconclusive. In this article, we review some of this research before going on to consider how stress might affect diabetes control and the physiological mechanisms through which this may occur. Finally, we discuss the implications for clinical practice and care. Before going any further, however, the meaning of the term *stress* must be clarified because it can be used in different ways. Stress may be thought of as *a*) a physiological response to an external stimulus, or *b*) a psychological response to external stimuli, or *c*) stressful events themselves, which can be negative or positive or both. In this article, we address all three aspects of stress: stressful events or experiences (sometimes referred to as stressors) and the physiological and psychological/behavioral responses to these.

### Role of Stress in the Onset of Diabetes

Stressful experiences have been implicated in the onset of diabetes in individuals already predisposed to developing the disease. As early as the beginning of the 17th century, the onset of diabetes was linked to “prolonged sorrow” by an English physician.<sup>1</sup>

Since then, a number of research studies have identified stressors such as family losses and workplace stress as factors triggering the onset of diabetes, both type 1 and type 2. For

example, Thernlund et al.<sup>2</sup> suggested that negative stressful experiences in the first 2 years of life may increase the risk of developing type 1 diabetes in children. Other factors, such as high family chaos and behavioral problems, were also implicated. Other research has also supported the hypothesis that stressful experiences can lead to increased risk for developing type 1 or type 2 diabetes.<sup>3–5</sup>

In a large population-based survey of glucose intolerance, Mooy et al.<sup>6</sup> demonstrated an association between stressful experiences and the diagnosis of type 2 diabetes. Although this was a cross-sectional study, the authors investigated stress levels in people with previously undetected diabetes in order to rule out the possibility that the disease itself influenced reports of stressful experiences. They also took other factors into account, such as alcohol consumption, physical activity level, and education.

Bjorntop<sup>7</sup> has attempted to explain the physiological links between stressful experiences and the onset of diabetes. He argues that the psychological reaction to stressors of defeatism or helplessness leads to the activation of the hypothalamo-pituitary-adrenal (HPA) axis, leading in turn to various endocrine abnormalities, such as high cortisol and low sex steroid levels, that antagonize the actions of insulin. At the same time, an increase in visceral adiposity (increased girth) is seen, which plays an important role in diabetes by contributing to insulin resistance.<sup>8</sup> Increased visceral adiposity can be measured by waist-to-hip ratio. In the Mooy et al. study of type 2 diabetes,<sup>6</sup> there was only a weak

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association between stressful experiences and waist-to-hip ratio, suggesting that other factors, so far unidentified, may play a mediating role.

Where stressful experiences have been implicated in the onset of type 1 diabetes, researchers have often attempted to explain this in terms of the effects of stress on the autoimmune system.<sup>2</sup> Bottazo et al.<sup>9</sup> hypothesized that environmental factors (e.g., viruses or toxic agents) trigger the autoimmune destruction of the  $\beta$ -cells in genetically predisposed individuals.

However, not all studies have demonstrated a link between stressful experiences and the development of diabetes. In a recent review, Cosgrove<sup>10</sup> argued that many of the studies that have demonstrated a link between stressful events and type 1 diabetes have been of small size and lacked appropriate control groups. Cosgrove cited one large Swedish study<sup>11</sup> indicating that there was no association between stressful events and the onset of type 1 diabetes. However, this study included a wide age range (15–34 years) of newly diagnosed people. Often quite vast differences in the type and intensity of life changes are found at the different ages within this range, and changes in social supports (known to be a buffer to stress) are frequent during these years, especially in the teenage years. This may have masked any association between stressful experiences and the development of diabetes.

Given the numerous measurement strategies and different study populations that have been investigated through the years, definite conclusions are difficult to reach. Smaller in-depth studies have usually demonstrated a link between stress and diabetes, whereas larger studies using self-report checklists to measure the occurrence of stressful experiences have sometimes failed to support this link. Much more conclusive is the evidence regarding the relationship between stressful experiences and metabolic control in those already diagnosed with diabetes, and it is to this research that we now turn.

### Stress and Diabetes Control

In recent years, some researchers have turned their attention to the possibilities of stressful experiences influencing diabetes control.<sup>12–15</sup> This potential

influence is important, not only for the often debilitating effects poor blood glucose control can have on daily life, but also because of the known association between chronically high blood glucose levels and the development of diabetes complications.<sup>16</sup>

It is a complex area of research, much of it having been conducted in children and adolescents, with fewer studies in adults or in those with type 2 diabetes, and using a number of different measurement tools. Stressful experiences have been recorded using anything from simple checklists to longer self-report questionnaires, to in-depth interviewing techniques. Most studies in this area have not determined the type or severity of stress that may influence changes in glycemic control, nor have they been able to fully address the role of other factors in mediating the impact of stress on glycemic control. Moreover, it is difficult to determine the temporal relationship between stress and health, not least because poor health often leads to adverse experiences.

A number of laboratory studies have been conducted to demonstrate the effects of specific stressful situations (for example, arithmetic problem solving, unpleasant interviews) on blood glucose levels. Many of these studies have demonstrated that these types of stressors can destabilize blood glucose levels, at least for hours at a time.<sup>17</sup> However, a major criticism of this approach is that it does not mirror the real world in which individuals with diabetes live.

Other studies have focused on that real world and have attempted to measure naturally occurring stress.<sup>18–21</sup> These later studies are not without problems however, such as, the myriad possibilities for measurement and/or observation, which makes cross-study comparisons difficult. Stress may take the form of day-to-day hassles, and it may be that major life events (death of a close relative, losing a job) are an added layer of complexity, along with long-term chronic difficulties (e.g., providing long-term care for a relative or long-term unemployment).

In an attempt to overcome some of the previous methodological limitations, a prospective in-depth investigation into the relationship between

stressful experiences and changes in glycemic control over time was designed.<sup>21</sup> Individuals with type 1 diabetes were interviewed using an in-depth interview schedule and then followed up quarterly for a year with measures of diabetes control (hemoglobin A<sub>1c</sub> [A1C]). Unlike previous studies, the participants were asked about both negative and positive stressors in their lives. The results showed that those whose glycemic control deteriorated over time were more likely to report negative stress, whereas those whose control improved over the follow-up period reported positive stress. Negative stressors included interpersonal conflicts, death of a close tie, and disturbed behavior of someone close, whereas positive stressors were events such as engagement to be married, birth of a child, or a desired change in employment (Figure 1).

Studies such as the one reported above have their limitations. For example, not all individuals perceive stressors in the same way; what is a negative stressor in one person's life might actually be a positive one in another's, so the context in which stress occurs is also important. Some people react to stressful events in a way that makes them psychologically vulnerable, for example, they may experience feelings of hopelessness or anxiety, particularly in the context of social isolation or poverty. Others may respond to stress in positive terms or as a "challenge," or they may feel better able to cope with the stress because they have several social supports or the support of a loving family. It is easier to categorize major stressors into those that are positive and those that are negative; it is more difficult for more minor stress or "hassles." Long-term chronic difficulties are also important, but may change in perceived level of severity or negativity over time.

Findings from Smith's study<sup>22</sup> of women's experiences of diabetes-related stress indicated that a wide variety of factors were important, including relationships with other people (including health care professionals), the interaction between diabetes and daily life and work, and fear of the future. Minor stressors and hassles were seen as an integral part of living with diabetes in this study and were

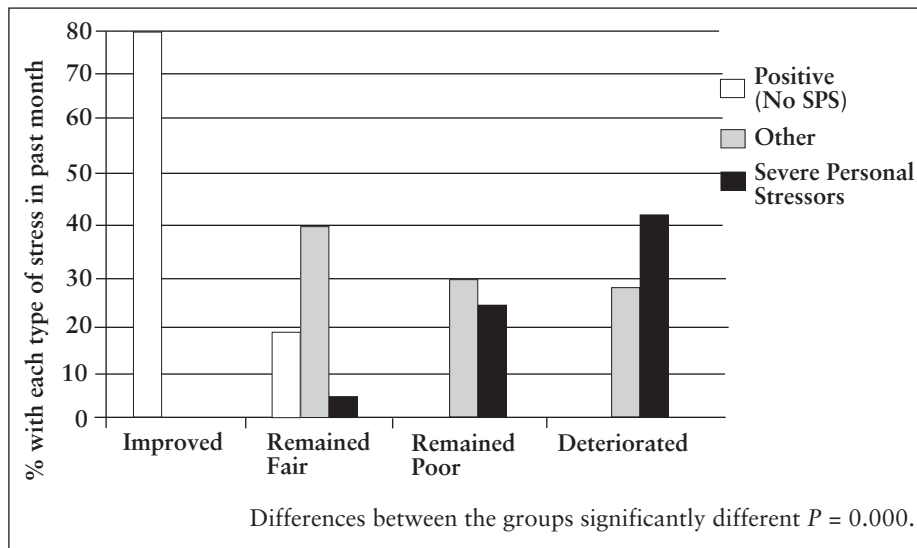


Figure 1. Relationship between stress and glycemic control. From Ref. 21.

related to both work and family life, which often took priority over the management of diabetes.

The impact of stressful experiences on diabetes is clearly varied and may depend on other psychosocial factors. One of these is social support, and research has shown this may provide a buffering effect in times of stress.<sup>13</sup> Psychological support is also important. In a recent meta-analysis of randomized controlled trials, Ismail et al.<sup>23</sup> concluded that people with type 2 diabetes who received behavioral-based diabetes education or psychological interventions were likely to show improvements in both glycemic control and psychological distress.

The relationship between stressful experiences and metabolic control is thought to differ greatly among individuals in terms of both the strength and the direction of the relationship,<sup>24</sup> and these differences have serious implications for the design of effective interventions to reduce the impact of stressors. Precisely how stressors affect glycemic control remains controversial, and there may be both physiological and behavioral pathways between stressors and health status. The mechanisms through which this may take place may be direct (through physiological effects on the neuroendocrine system)<sup>25</sup> or indirect (through alterations in health care practices in times of stress).<sup>18,26</sup> It is to these pathways that we now turn.

## Behavior

The behavioral mechanisms through which stressful experiences might

affect diabetes control are varied and often complex. There are, of course, many different types of stress, there are shorter- and longer-term stressors, and people may respond to these very differently. Difficulties in measurement such as those mentioned above also apply to measuring behavior. At the same time, differences in resources such as social supports, ability to cope, and other psychosocial variables will all affect both the response to and the behavior resulting from stressful experiences.

Reactions to external stressors, for example, feelings of anxiety or depression, may lead to difficulties with self-care manifested through less physical activity, poorer diet, or difficulties with medication taking.<sup>27,28</sup> Experiences of stress may lead to other unhealthy behaviors, such as smoking, which in turn are linked to poor blood glucose control but also to a greater risk of developing diabetes complications.<sup>29</sup> Data from Smith's study<sup>22</sup> indicated a range of behavior described as occurring in response to stress. These behaviors ranged from unhealthy lifestyle patterns associated with alcohol and tobacco consumption to increased physical activity and relaxation, such as walking, yoga, swimming, meditation, and hypnotherapy.

One particular type of stress was investigated in a Swedish study. Agardh et al.<sup>30</sup> demonstrated that work stress, as indicated by low decision latitude (or fewer opportunities for decision making), along with a low sense of coherence, significantly

increased risk for type 2 diabetes. Low sense of coherence is thought to negatively affect people's ability to cope with stressors<sup>31</sup> and also to be linked to unhealthy lifestyle patterns that could lead to poor health.

Research also supports the behavioral link. Peyrot et al.<sup>32</sup> found that stress and coping affected glycemic control by interfering with self-care practices. Coping behavior was also shown to affect glycemic control in a study of type 1 and type 2 diabetes that used sophisticated statistical techniques to demonstrate a "network" of interlinked variables in relation to the achievement of treatment goals.<sup>33</sup> For example, active coping behavior was associated with higher self-efficacy and greater satisfaction with doctor-patient relationships. The researchers suggested that their findings have clinical implications for diabetes care because coping behavior (a key factor in their analysis) was linked to self-care but could also be influenced by the health care professionals involved in that care. However, little work has been carried out to try to implement the findings of coping research into clinical practice.<sup>34</sup> Changes in clinical practice have usually involved behavioral interventions (task-oriented) rather than cognitive ones or have only included coping implicitly rather than explicitly.<sup>34</sup>

Diabetes-related distress may also affect self-care behavior,<sup>35,36</sup> as demonstrated when the Problem Areas in Diabetes (PAID) scale was developed.<sup>35</sup> The scale covers negative emotions related to living with diabetes, for example, "feeling alone with diabetes" and "worrying about the future and the possibility of serious complications." Although often associated with depression,<sup>36,37</sup> diabetes-related distress has been found to be predictive of diabetes self-care behavior as well as blood glucose control.<sup>36,38</sup>

Depression and diabetes-related distress can occur together and can have serious implications for the management of diabetes, because those affected may feel unable or unmotivated to carry out self-care behaviors such as blood glucose testing or healthy eating. A different group of researchers in the United States has identified both diabetes-related stress and other stressors as important in

predicting self-care behavior.<sup>27</sup> If study participants reported, “My life is out of control because of my diabetes” or “I have other problems more serious than diabetes,” they were less likely to report attention to diet or exercise as part of their diabetes self-care.

In summary, studies strongly suggest that stressful experiences have an impact on diabetes self-care behavior; however, there are many different factors that may mediate this relationship. Before turning to the implications for clinical practice, we consider the physiological mechanisms behind stress and its impact on diabetes.

### Physiological Mechanisms Behind Stressful Experiences

Any stressful event might be judged by people in different ways, based on factors such as previous experience, psychological factors, and social influences. An event that is seen by one individual as particularly threatening might be seen as totally harmless by another individual. However, when a situation is regarded as threatening, that is, seen as having the potential to cause harm to the individual, a specific pattern of physiological responses is elicited, known as the stress response or “fight/flight” response. This pattern of responses has developed as a result of human evolution and is aimed at priming the individual for action, so that the situation can be dealt with by either fighting or fleeing the threat. The actions initiated by the central nervous system in response to a threat affect the entire body and are associated with three different bodily systems: the autonomic nervous system, the neuroendocrine system, and the immune system.<sup>39,40</sup>

The autonomic nervous system is concerned with the regulation of smooth muscle, cardiac muscle, and glands and regulates the functions over which there is no conscious control, such as cardiovascular function, digestion, and metabolism. It consists of two distinct branches: the parasympathetic and the sympathetic nervous system, the latter being the most dominant in times of stress. The sympathetic system is involved with the preparation of the body for action. It increases oxygen and nutrient supplies to the muscles by increasing the blood flow to the skeletal muscles and free-

ing glucose and lipids from its stores. It also prepares the immune system to deal with possible injury.

With regard to the effects of stress on the neuroendocrine system, the HPA axis is of considerable importance.<sup>39</sup> Upon encountering a threat or a stressor, the hypothalamus secretes corticotropin-releasing factor, which causes the release of adrenocorticotropin. This in turn travels to the adrenal cortex, where it leads to the secretion of glucocorticoid hormones, in particular cortisol.

Cortisol exerts considerable influence over bodily functions, both when the body is at rest and during stress. In normal circumstances, it is secreted according to a circadian (daily) rhythm, with cortisol levels highest in the morning and lowest in the evening. However, exposures to stress stimulate the HPA axis to release additional amounts of cortisol to maintain homeostasis and reduce the effects of stress. Cortisol influences a wide range of processes, including the breakdown of carbohydrates, lipids, and proteins to provide the body with energy. It also has an effect on bone and cell growth and may modulate salt and water balance. Cortisol has an immunosuppressive effect and therefore plays a role in the regulation of immune and inflammatory processes.

That the central nervous system communicates with and exerts an influence on the immune system is now well established; brain lesions can alter a variety of immune measures, and both the autonomic and the neuroendocrine system have been shown to influence the state of the immune system.<sup>41</sup> Because both the neuroendocrine and the autonomic system are influenced by psychosocial factors, it follows that the immune system is also affected by such factors, although the precise nature of these complex interactions remains to be determined.

Although there is still much unknown about the effects of acute stress on the immune system and studies have been limited in the number of immune parameters studied, one review<sup>42</sup> revealed that stress influences both circulating cell numbers and the function of immune cells. The cells generating the immune defense are generally known as white blood cells and consist of several subgroups

including the lymphocytes ( $\beta$ -cells, T-cells, and natural killer cells), which have received much attention in stress research.<sup>41</sup>

Although research into the effects of stress continues, it seems clear that there is a range of responses to stressful experiences, both physiological and behavioral/emotional. The final section of this article focuses on the implications of stress research for practice in the care of individuals with diabetes.

### Implications For Practice: Stress Management

In addition to the physiological impact that stress has on glycemia, research has shown that stress interferes with the ability to self-manage diabetes. Doing everyday self-care tasks, such as monitoring glucose frequently, following a meal plan, and correctly preparing or remembering to take insulin or oral medications at the right time, is difficult during times of stress. Moreover, diabetes self-management tasks themselves may become a source of stress. Learning to prevent and control the negative responses to stress is helpful, particularly if the causes are relatively permanent. For example, if cooking dinner, bathing children, and doing laundry constitute a typical stressful evening, that stress is a relatively permanent part of life for several years and must be dealt with accordingly.

Assessment of stress levels in practice is a relatively underdeveloped area. One approach is to identify those life events during the previous year that typically act as stressors. Using a scale such as the Recent Life Change Questionnaire<sup>43</sup> or the Revised Social Readjustment Rating Scale,<sup>44</sup> individuals identify events that have occurred in their life from a list that includes births, deaths, marriage, retirement, social issues, financial worries, work-related stress, and so forth. The weighted ratings provide the basis for an overall score that can be compared to norms. However, these scales are rather long and take some time to complete, which may not always be appropriate in a practice setting.

Polonsky<sup>45</sup> describes a diabetes-specific exercise to help people with diabetes develop an understanding of the relationship between stress and blood glucose levels. In this exercise, individ-

uals rate their perceived stress each evening on a 0–10 Likert scale and record their glucose levels before breakfast and dinner and at bedtime. The individual then looks for blood glucose level patterns for days when perceived stress is high, medium, and low. The premise behind this exercise is that those individuals whose blood glucose levels are sensitive to stress may be more sensitive to stress management strategies. Although validation data are not available, individuals may find this approach helpful in understanding and managing stress-related aberrant glucose readings. Finally, surveys tools, such as the individual items on the PAID scale that measure diabetes-related distress, may also reflect accumulated stress resulting from living with diabetes. PAID scores are associated with A1C levels.<sup>35,36,38</sup>

Clinicians must take care to differentiate stress response from depression and anxiety. Depression is more common in diabetes than in the general population.<sup>46,47</sup> Although both under-diagnosed and under-treated,<sup>48,49</sup> depression is responsive to both medication and psychotherapy. Tools such as the Beck Depression Inventory<sup>50</sup> or the Hospital Anxiety and Depression Scale<sup>51</sup> are useful in screening for depression. Asking simple questions such as, “During the past month, have you been bothered by feeling down, depressed, or hopeless?” and “During the past month, have you been bothered by little interest or pleasure in doing things?” can be as successful as surveys when screening for depression.<sup>52</sup>

Three approaches to stress management go hand in hand, albeit with some overlap: 1) when possible, removing or minimizing the source of stress, 2) changing the response to the stressful situation, and 3) modifying the longer-term effects of stress. Some interventions directly target people with diabetes in order to prevent diabetes-related stress and improve quality of life or glycemia.

**1. Remove or minimize the source of stress.**

Time management and organizational techniques may reduce small stressors that often compound until a crescendo is reached. Self-help books<sup>53,54</sup> may be useful for patients to find success-

ful ways to put structure in their lives and manage their time and life stressors. Minimizing the source of stress is helpful. For example, if repetitive noise at work is causing stress, one solution could be substituting white noise for the repetitive noise by softly playing relaxing classical music. Setting up a meeting with the employer or coworkers to get help with one’s workload may also alleviate stress. Often, the most difficult challenge is actually identifying the source of stress and separating that source from the responses to stress. Effective problem-solving strategies are important for minimizing the source of stress.

Diabetes-specific approaches that may help individuals cope better with diabetes include setting specific, realistic self-management goals. Many individuals set global vague goals that may serve to exacerbate stress. “Lose weight,” “Take better care of my diabetes,” and “Improve my glycemic control” are examples of vague unhelpful goals. Realistic, measurable, and achievable goals specifically stating the measurement criteria that indicate success are more helpful as motivators. Examples of realistic, measurable goals are, “I will walk 20 minutes each day on Monday, Wednesday, Friday, and Saturday at 5:00 p.m.,” “I will drink diet cola instead of cola with sugar,” and “I will lose 6 lb over the next 9 weeks by following my meal plan and increasing my walking to 30 minutes, 5 days per week.” Evaluation does not neces-

sarily have to focus on whether a goal is met, but rather on how successful one’s effort has been in trying to achieve it. Thus, instead of “No, I did not reach my target A1C,” evaluation would be “My A1C has improved by 0.5 percentage points, thus, I am about half way to my first goal of a 1–percentage point improvement.”

**2. Change the response to stress.**

Most stress management techniques emphasize changing the response to stress. When the response to chronic or acute stress results in rage and reactive behavior, a thought-stopping and reflective technique can be helpful in preventing negative consequences of the impulsive behaviors associated with anxiety and rage (Table 1). Other approaches involve learning how to induce a more relaxed feeling.

Benson’s relaxation response,<sup>55</sup> first reported as a means to lower blood pressure, can be useful in inducing relaxation quickly in times of stress, for example, while driving in traffic, or before taking an exam. Practicing the relaxation response is extremely important because the technique is difficult to learn. However, once learned, the relaxation response quickly brings about the physiological responses associated with relaxation.

**3. Modifying the longer-term effects of stress.**

Other approaches to stress that may be useful for individuals with diabetes include using distraction and involve-

**Table 1. A Thought-Stopping Strategy for Acute Rage**

<b>STOP</b>	To interrupt a negative spiral of anger, say “stop” out loud or to yourself.
<b>BREATHE</b>	Take several deep breaths, exhaling slowly.
<b>REFLECT</b>	Think about the situation and what could happen if . . . If you choose to act in anger, what could happen? What are all the negative things that may happen? What would you accomplish? Be thorough and reflect on the consequences of your actions, how your actions will affect others, how they will affect you in the long term.
<b>CHOOSE</b>	Based on your reflection above, decide how you will act.
<b>THEN ACT</b>	Your actions are then based on rational thought rather than on anger. The actions may not change, but what is different is that you are in control and have thought about the consequences of your actions.

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ment in pleasurable activities that help to minimize the influence of stress-producing activities. (For other examples, see Table 2.) For example, active participation in a hobby (even a sedentary one) or exercise program can help combat stress. Typically passive activities, such as watching television, may not help alleviate stress, although attending a concert, theater performance, or movie with friends can have beneficial effects as a distraction. If one is not able to put aside worries from work, then distraction may be effective.

If a person with diabetes is experiencing severe stress, referral to a mental health professional may be the most effective approach.

Reports from research investigating the effect of stress management on glycemic control have been inconsistent.<sup>56-60</sup> Several of these studies were underpowered, and others had design problems. However, recent reports have shown that stress management may affect diabetes and its treatment. In a small study with a pre-/post-design and no control group,<sup>61</sup> 20 study participants demonstrated improved glycemic control and state and trait anxiety scores after 12 weeks of treatment with an anti-anxiety medication (fludiazepam). Surwit et al.<sup>14</sup> used a randomized, controlled design to inves-

tigate the use of stress management techniques for groups of type 2 diabetes patients. They found that those using stress management had a small improvement in A1C (0.5 percentage points) at the 1-year follow-up compared to those who were not. Although Boardway et al.<sup>62</sup> found that adolescents receiving stress management improved stress levels but not glycemic control or adherence, evidence now exists that stress management training may potentiate intensive treatment. For adolescents enrolled in an intensive diabetes management clinic, Grey et al.<sup>63,64</sup> demonstrated that preventive strategies such as teaching coping skills to adolescents with type 1 diabetes in order to better prepare them for stressful life events can lead to improvements in both glycemic control and quality of life and that the improvement was maintained over time.

In summary, research has indicated that stressful experiences have an impact on diabetes. Stress may play a role in the onset of diabetes, it can have a deleterious effect on glycemic control and can affect lifestyle. Emerging evidence strongly suggests, however, that interventions that help individuals prevent or cope with stress can have an important positive effect on quality of life and glycemic control. The clinical implications of this research illustrate the need for greater understanding of the effects of stress, as well as a serious acceptance of the need for psychosocial support for people in this predicament.

**Table 2. Useful Interventions for Managing Stress**

Changing stress-producing situations

- Time management
- Improved organization skills
- Learning problem-solving skills

Changing the physiological response to stress

- Stop, Breathe, Reflect, and Choose (Table 1)
- Relaxation with or without tapes
- Deep muscle relaxation
- Head-to-toe relaxation
- Pleasant scenes
- Breath-focused relaxation
- Yoga, Tai Chi, meditation
- Hot baths, scented candles

De-emphasizing stress with distractions

- Hobbies
- Attending pleasant activities, such as theater, movies, concerts

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