

# Депрессия у больных сахарным диабетом

**ПОДГОТОВИЛА**

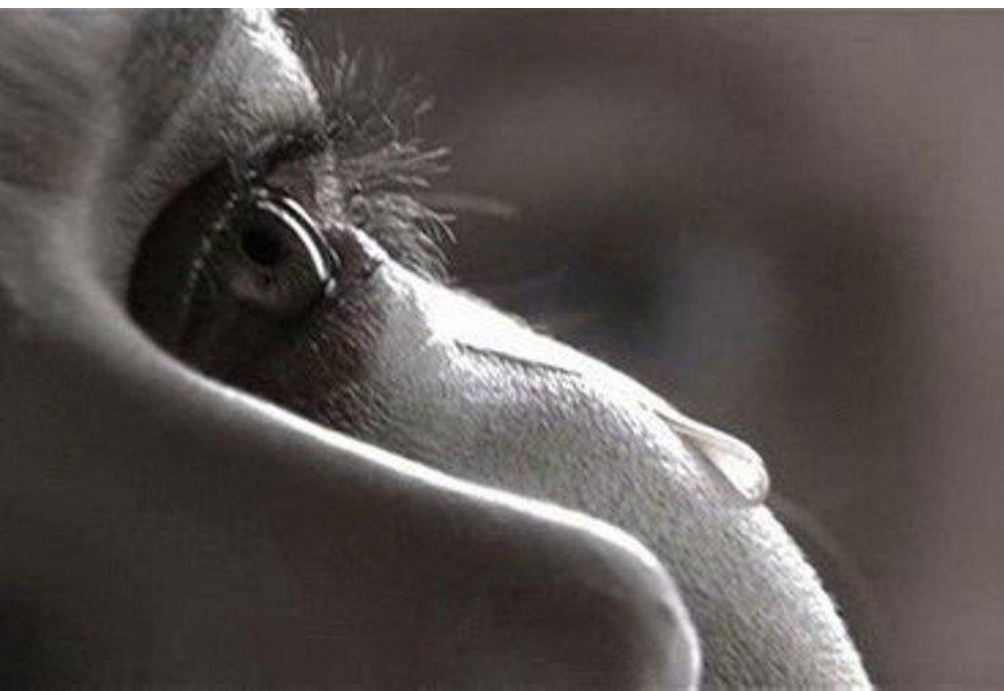
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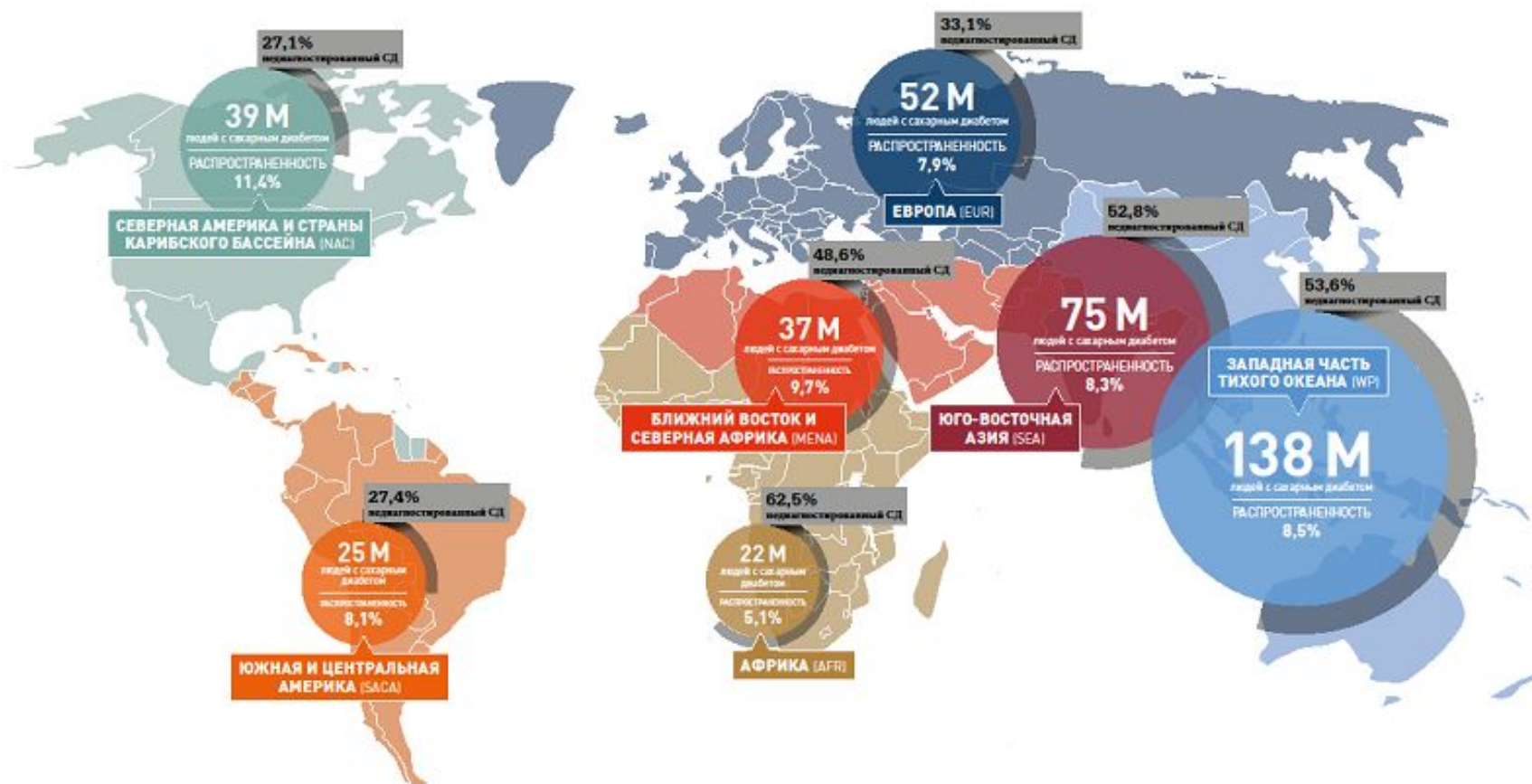
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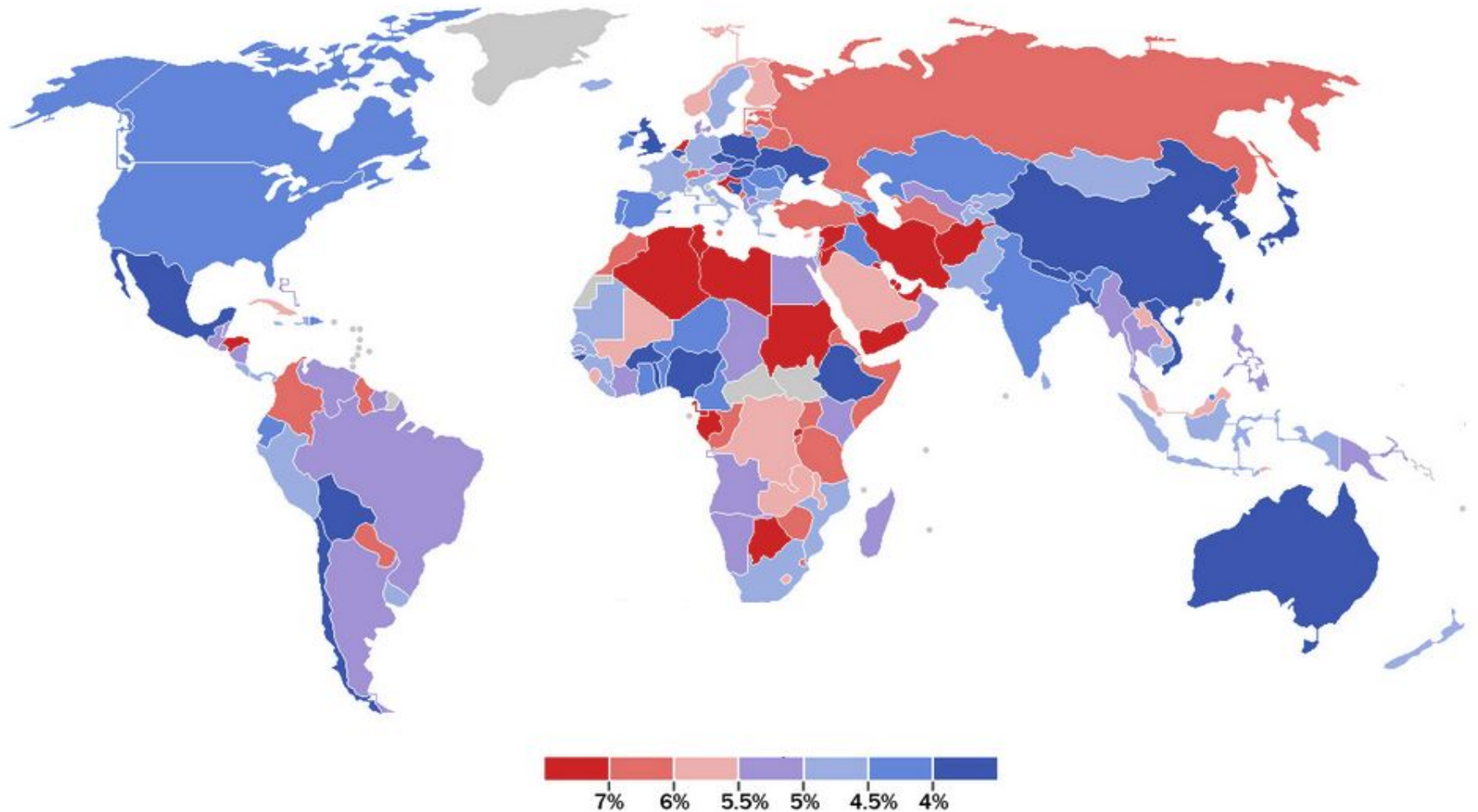


# Эпидемиология сахарного диабета



Атлас Диабета IDF

# Эпидемиология депрессии



A stunning map of depression rates around the world. Washington Post. 2013

# Томас Уиллис (1621-1675)



Сахарный диабет  
является  
следствием «грусти  
или длительной  
печали»





# Depression and All-Cause and Coronary Heart Disease Mortality Among Adults With and Without Diabetes

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**OBJECTIVE** — The aim of this study was to evaluate the effect of depression on all-cause and coronary heart disease (CHD) mortality among adults with and without diabetes.

**RESEARCH DESIGN AND METHODS** — We studied 10,025 participants in the population-based National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study who were alive and interviewed in 1992 and had complete data for the Center for Epidemiologic Studies Depression Scale. Four groups were created based on diabetes and depression status in 1992: 71 no diabetes, no depression (reference group); 21 no diabetes, depression present; 30 diabetes present, no depression; and 49 diabetes present, depression present. Cox proportional hazards regression models were used to calculate multivariate-adjusted hazard ratios (HRs) of death for each group compared with the reference group.

**RESULTS** — Over 8 years (83,624 person-years of follow-up), 1,925 deaths were documented, including 222 deaths from CHD. Mortality rate per 1,000 person-years of follow-up was highest in the group with both diabetes and depression. Compared with the reference group, HRs for all-cause mortality were no diabetes, depression present, 1.20 (95% CI 1.03–1.40); diabetes present, no depression 1.18 (1.03–1.37); and diabetes present, depression present, 2.43 (1.66–3.58). HRs for CHD mortality were no diabetes, depression present, 1.39 (1.03–1.88); diabetes present, no depression 1.26 (1.00–1.61); and diabetes present, depression present, 2.43 (1.66–3.58).

**CONCLUSIONS** — The coexistence of diabetes and depression is associated with a significantly increased risk of death from all causes, beyond that due to having either diabetes or depression alone.

*Diabetes Care* 28:1339–1345, 2005

Depression is highly prevalent in the U.S., affecting ~18.5 million adults or about 9.5% of the U.S. population aged ≥18 in a given year (1). Depression is a leading cause of disability, workplace absenteeism, diminished or lost productivity, and increased use of health care resources (2,3). There is fairly consistent evidence that depression is associated with increased mortality (4–9). A recent meta-analysis, which included 25 studies and 109,628 subjects, found that the hazard ratio (HR) for all-cause mortality in depressed subjects was 1.81 (95% CI 1.58–2.07) compared with that for nondepressed subjects (10).

Diabetes is also highly prevalent in the U.S. (11), and multiple studies have documented an increased prevalence of depression in individuals with diabetes (12). It is estimated that 10–20% of people with diabetes have coexisting depression and that people with diabetes have twofold increased odds of having depression compared with individuals without diabetes (12,13). The coexistence of depression and diabetes is known to be associated with poor glycemic control (14,15), an increased risk of complications (16–18), a decreased quality of life (19), an increased disability burden (20,21), and increased health care use and costs (19,22,23). However, no study has examined whether the coexistence of depression and diabetes is associated with increased risk of mortality. In particular, there are no data that compare the effect of depression on the risk of death in people with and without diabetes.

To address these issues, we examined mortality in a large nationally representative cohort of adults aged 25–75 years in 1971–1975 (24), who were reinterviewed in 1992 and followed until 2002 (25,26). We compared all-cause and coronary heart disease (CHD) mortality among four subsets of participants based on their diabetes status at the 1992 interview.

**RESEARCH DESIGN AND METHODS** — The National Health and Nutrition Examination Survey (NHANES) I was a multistage, stratified, national probability sample of the civilian noninstitutionalized population of the U.S., aged 1–74 years (24). The survey was conducted between 1971 and 1975 and included a standardized examination and questionnaire that addressed various health topics. Persons living in poverty

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## Depressive Symptoms and Mortality among Persons with and without Diabetes

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Although people with diabetes mellitus have a high risk of depression and depression may increase mortality among people with other conditions, the impact of depression on mortality risk among people with diabetes needs further examination. Using survival analysis, the authors analyzed longitudinal data from the NHANES I Epidemiologic Follow-up Study (1962–1992). This finding showed that the presence of severe depressive symptoms significantly elevated mortality risk among US adults with diabetes; the same pattern was not observed among people without diabetes. After results were controlled for sociodemographic, lifestyle, and health status variables, diabetic persons with Centers for Epidemiologic Studies Depression (CES-D) Scale scores of 16 or more had 54% greater mortality than those with scores under 16 ( $p = 0.004$ ). After exclusion of participants who died during the first year of follow-up, mortality remained higher among those with CES-D scores greater than or equal to 22 as compared with those with CES-D scores less than 16, but not among those with CES-D scores between 16 and 21. No significant relation between depression and mortality was found in the nondiabetic population. This analysis indicates that diabetes modifies the effect of depression on mortality. It also demonstrates the importance of obtaining subgroups, rather than aggregated populations, when examining the effect of depression on mortality.

depression; diabetes mellitus; mortality

**Abbreviations:** CES-D, Centers for Epidemiologic Studies Depression [Scale]; NHANES I, First National Health and Nutrition Examination Survey; NHFHS, NHANES I Epidemiologic Follow-up Study.

The prevalence of diabetes mellitus in the United States has increased rapidly in recent years, with a 49 percent increase in diagnosed cases during the period between 1990 and 2001 (1). During 2002, it was estimated that 18.2 million Americans had the disease—13.6 million diagnosed and 4.6 million undiagnosed (2). Diabetes is a leading cause of death in the United States. During 2000, the disease accounted directly for 69,301 deaths and contributed to 213,062 deaths among persons aged 25 years or older (3). Diabetes is also a major cause of losses of quality-adjusted life years, largely because of vascular complications (4).

Diabetes is associated with depression and depressive symptoms, but the strength and causal direction of these associations are unclear (4–10). In two recent studies that used data from the First National Health and Nutrition Examination Survey (NHANES I) but utilized different instruments to measure depressive symptoms, investigators came to different conclusions about the role of depression as a cause of diabetes mellitus (11, 12). In a study using the Centers for Epidemiologic Studies Depression (CES-D) Scale, found no evidence to support an etiologic relation between depression and diabetes (11). In contrast, in a study using the General Well-Being Depression subscale, found that if social factors were taken into account, depression was associated with an increased incidence of diabetes among

## Depression and Diabetes: A Potentially Lethal Combination

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**OBJECTIVE** — To assess whether Medicare fee-for-service beneficiaries with depression and diabetes had a higher mortality rate over a 2-year period compared with beneficiaries with diabetes alone.

**DESIGN** — Evidence of depression was based on a physician diagnosis or self-reported prescription of an antidepressant in the year prior to screening, or a score of ≥20 on the Patient Health Questionnaire two-item questionnaire. Mortality was assessed bi-monthly by checking Medicare claims and eligibility files or from information from telephone contact with the participant's family. Cox proportional hazards regression models were used to calculate adjusted hazard ratios of death in depressed versus nondepressed beneficiaries with diabetes.

**PARTICIPANTS** — A total of 10,704 beneficiaries with diabetes enrolled in a disease management program were surveyed with a health assessment questionnaire and followed over a two-year period.

**MAIN RESULTS** — Control depression in Medicare beneficiaries with diabetes participating in a disease management program was associated with an increased risk for all-cause mortality over a two-year period (approximately 20% to 28% depending on the definition of depression that was used). No significant increase in rates of cause-specific mortality from macrovascular diseases were found in depressed versus nondepressed beneficiaries.

**CONCLUSION** — Among a large Medicare cohort of fee-for-service beneficiaries with diabetes, controlled depression was associated with an increase in all-cause mortality over a two-year period. Future research will be required to determine whether the increase in mortality associated with depression is due to potential behavioral modifiers (i.e., smoking, poor adherence to diet) or physiologic abnormalities (i.e., hypothalamic-pituitary axis dysregulation) associated with depression.

**KEY WORDS:** depression; diabetes; mortality.

The ideas expressed in this article do not necessarily represent the views of the National Institute of Mental Health, the National Institutes of Health, the Department of Health and Human Services, or the United States government.  
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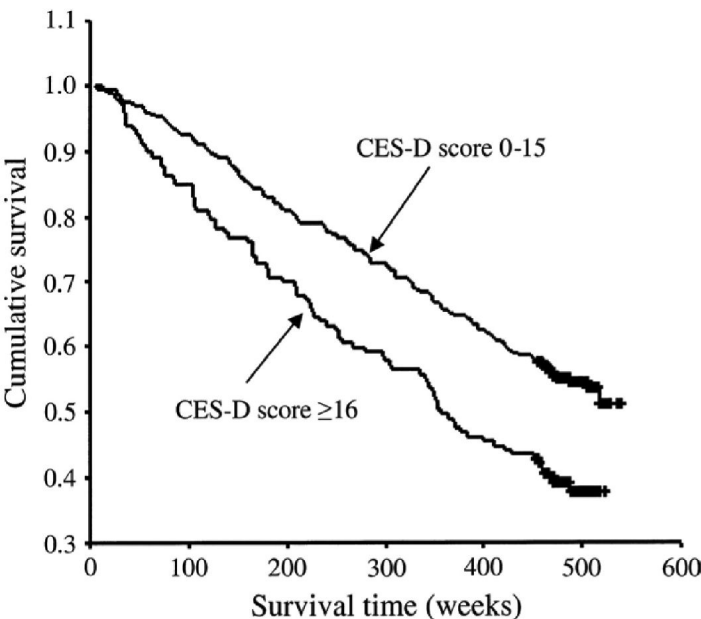
## INTRODUCTION

Depression may adversely impact outcomes of chronic diseases, such as diabetes. In several ways, depression has been shown in patients with diabetes to be associated with poor adherence to medical regimens, such as glucose monitoring, diet, exercise regimens and taking medications as prescribed. Depression has been linked to having a higher number of Framingham risk factors (i.e., smoking, obesity, systolic/diastolic blood pressure, diabetes in patients with diabetes). Depression is also associated with physiologic dysregulation of the hypothalamic-pituitary axis (HPA) and sympathetic nervous system<sup>1–3</sup> as well as an increase in inflammatory markers,<sup>4,5</sup> which may also adversely affect the course of diabetes. Given the adverse effect on self-care and physiologic dysregulation, it is not surprising that longitudinal studies have also shown that depression is linked with an increased risk of microvascular and macrovascular complications.<sup>6–10</sup> Recent data has also suggested that comorbid depression is not only linked to a higher risk for diabetic complications, but also a higher risk for mortality.<sup>11–13</sup>

Since 2003, five studies from data sets have examined the association of depression in patients with diabetes with mortality.<sup>14–18</sup> At least half of the patients with diabetes in these samples were in Medicare age groups 65 years of age. The age of the study group is important because diabetes has been shown to decrease longevity in those who develop the disease before but not after age 75.<sup>19</sup> Four out of these recent five studies have shown that depression is associated with an increased risk of mortality in patients with diabetes.<sup>14–17</sup> The total number of patients with diabetes examined in these five prior studies was approximately 6,800. In this paper, we examined the impact of comorbid depression on all-cause mortality and macrovascular mortality in an older cohort of over 10,000 fee-for-service Medicare beneficiaries with diabetes enrolled in Green Ribbon Health care management program.

## METHODS

Green Ribbon Health (GRH) serves over 1 million FFS beneficiaries in nine counties in the state of Florida. GRH's care management program began operations on November 1, 2003. The core of the



## Association of Coexisting Diabetes and Depression With Mortality After Myocardial Infarction

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**OBJECTIVE** — Diabetes and depression are both linked to an increased mortality risk after myocardial infarction (MI). Population-based studies suggest that having both diabetes and depression results in an increased mortality risk, beyond that of having diabetes or depression alone. The purpose of this study was to examine the joint associations of diabetes and depression with mortality in MI patients.

**RESEARCH DESIGN AND METHODS** — Data were derived from two multicenter cohort studies in the Netherlands, comparing 2,799 patients who were hospitalized for MI. Depression, defined as both Depression Inventory score ≥10 and diabetes were assessed using longitudinal data. Mortality data were retrieved for 2,525 patients (93%).

**RESULTS** — During an average follow-up of 4.6 years, 430 patients died. The mortality rates were 14% (23/161) in patients without diabetes and depression, 26% (94/361) in patients with diabetes only, 22% (11/64) in patients with depression only, and 47% (46/98) in patients with both diabetes and depression. After adjustment for age, sex, smoking, hypertension, left ventricular ejection fraction, prior MI, and follow-up, hazard ratios for all-cause mortality were 1.36 (95% CI 1.05–1.76) for patients with diabetes only, 1.36 (1.01–1.81) for patients with depression only, and 1.80 (1.27–2.57) for patients with both diabetes and depression.

**CONCLUSIONS** — We observed an increased mortality risk in post-MI patients with both diabetes and depression, beyond the association with mortality of diabetes and depression alone.

*Diabetes Care* 28:500–509, 2005

Myocardial infarction (MI) is an important cause of morbidity and mortality worldwide (1). Major depression after MI is present in ~20% of all MI patients (2). A meta-analysis showed that depression is associated with an almost 2.5-fold increased risk for mortality in post-MI patients, independent of whether established risk factors for mortality (3). Likewise, diabetes is common in MI patients and is independently associated with increased risk for cardiovascular morbidity (4) and mortality (5,6). Depression and diabetes are known to interact in the general population, and their combination results in poor health outcomes. The prevalence of depression

in high-risk patients with diabetes, affecting ~10–15% of type 2 diabetic patients (7). Depression can impair diabetes management and diabetes outcomes through behavioral or biological pathways (8). For example, depression appeared to be associated with less optimal diabetes self-care behaviors and subsequent poor glycemic control (9). In addition, depression was related to hypothalamic-pituitary-adrenal hyperactivity, which subsequently can affect glucose metabolism (10). It has also been proposed that diabetes and depression may share a common underlying pathogenesis (9). Among diabetic patients, several studies show that depression is an independent risk factor for an increased

recurrence of depression in a current depressive episode (11–14). Because the two studies were highly comparable in patient recruitment, inclusion and exclusion criteria, and depression assessment, data from these studies were combined for the present analysis. Both studies were approved by the local ethical committees of the participating hospitals, and all patients gave informed consent.

**RESEARCH DESIGN AND METHODS** — Data were derived from the Depression and Myocardial Infarction Study (DepMI) (18) and the Myocardial Infarction and Depression-Investigation Trial (MIND-IT) (19). In these studies, we enrolled 1,138 and 1,174 MI patients, respectively, were screened for depression. Patients were recruited from 14 hospitals (including 1 emergency hospital) located in different parts of the Netherlands. Patients were recruited from September 1997 through September 2000 in DepMI and from October 1999 through November 2002 in MIND-IT. They met established criteria for MI (20). Exclusion criteria were cognitive dysfunction, not being able to speak or read Dutch, hospitalization for other reasons than MI (except angina pectoris), and a life expectancy of <1 year of most of noncardiovascular disease. In MIND-IT, patients were also excluded if they were already receiving psychiatric treatment for a current depressive episode (11–14). Because the two studies were highly comparable in patient recruitment, inclusion and exclusion criteria, and depression assessment, data from these studies were combined for the present analysis. Both studies were approved by the local ethical committees of the participating hospitals, and all patients gave informed consent.

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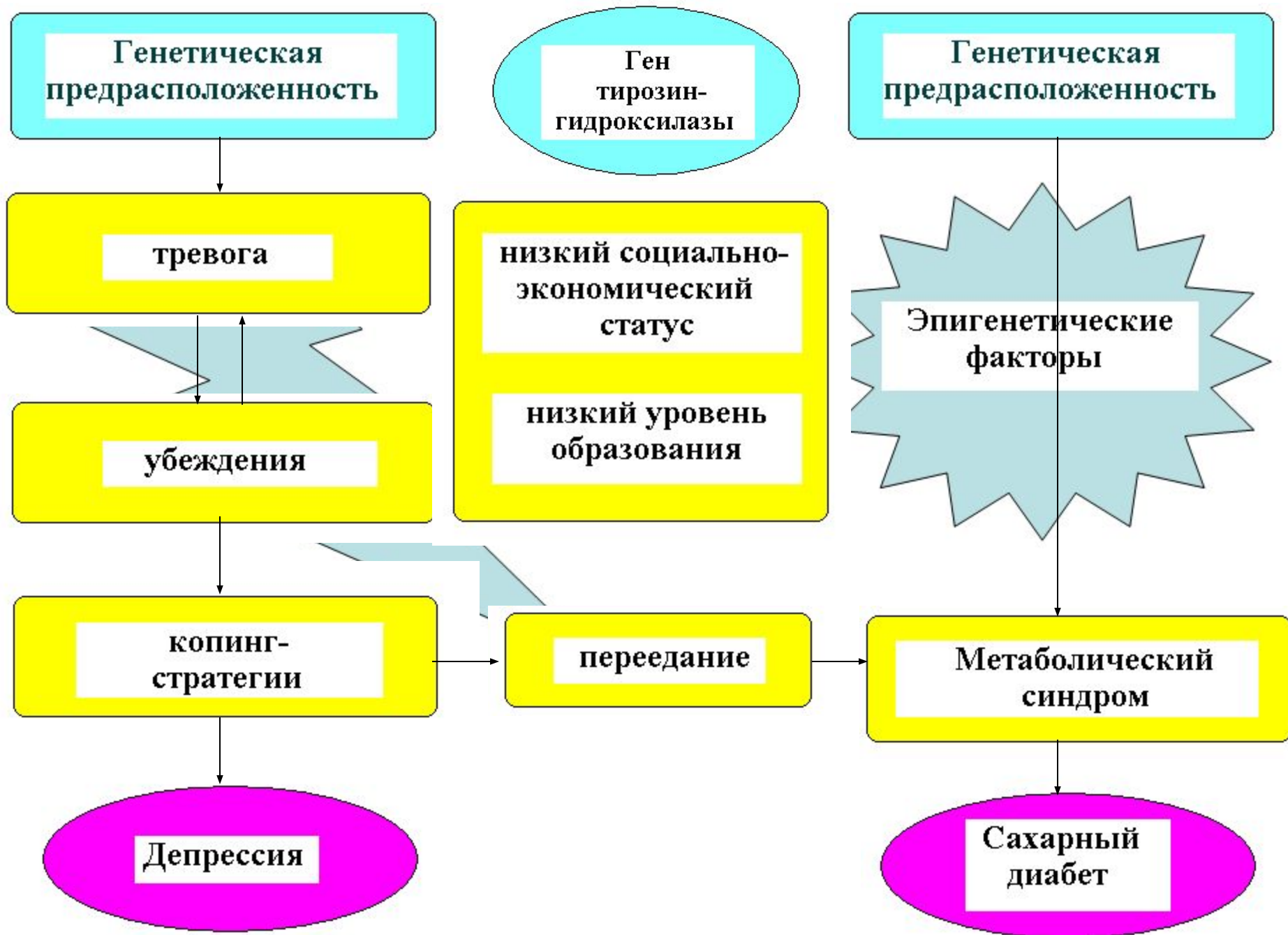
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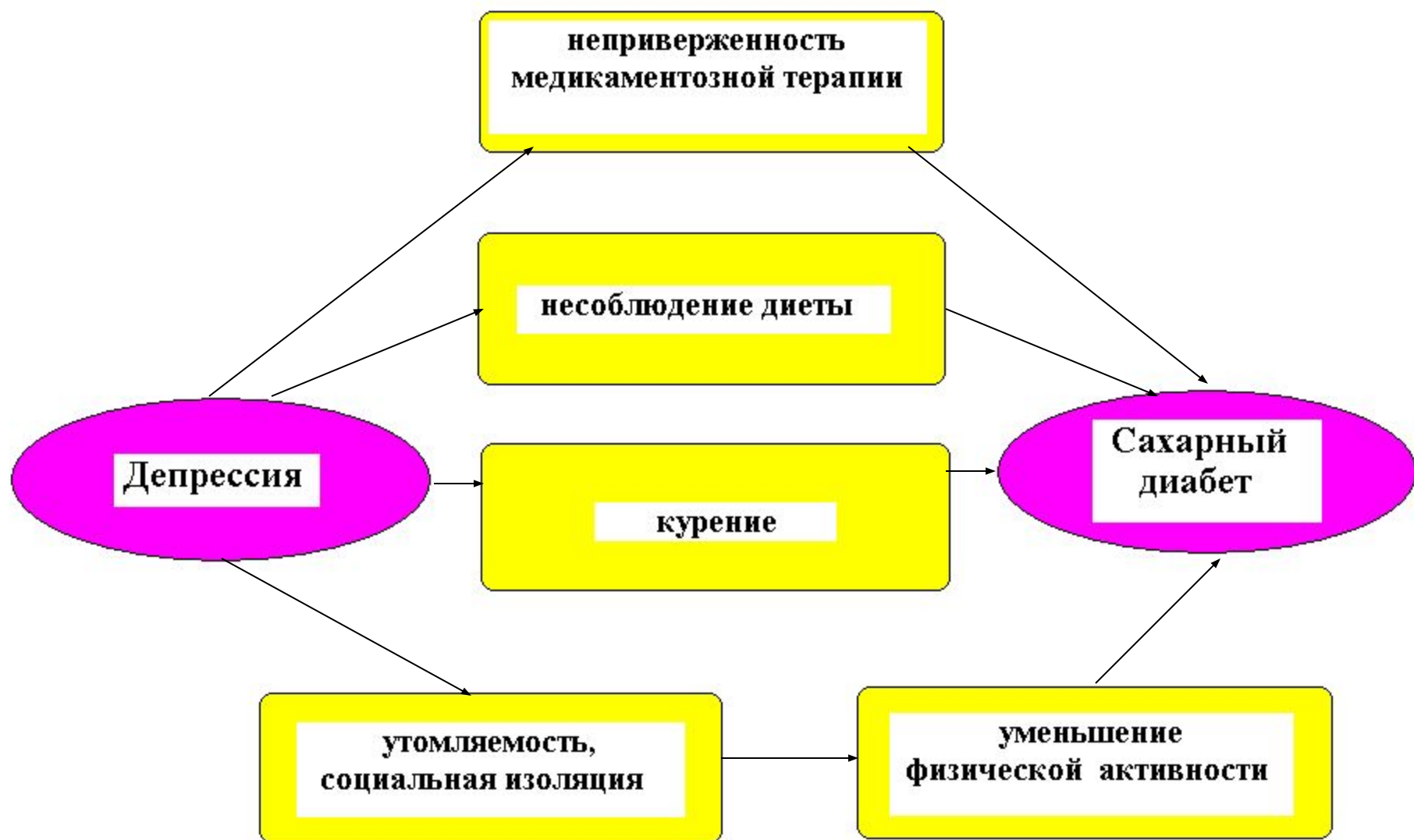
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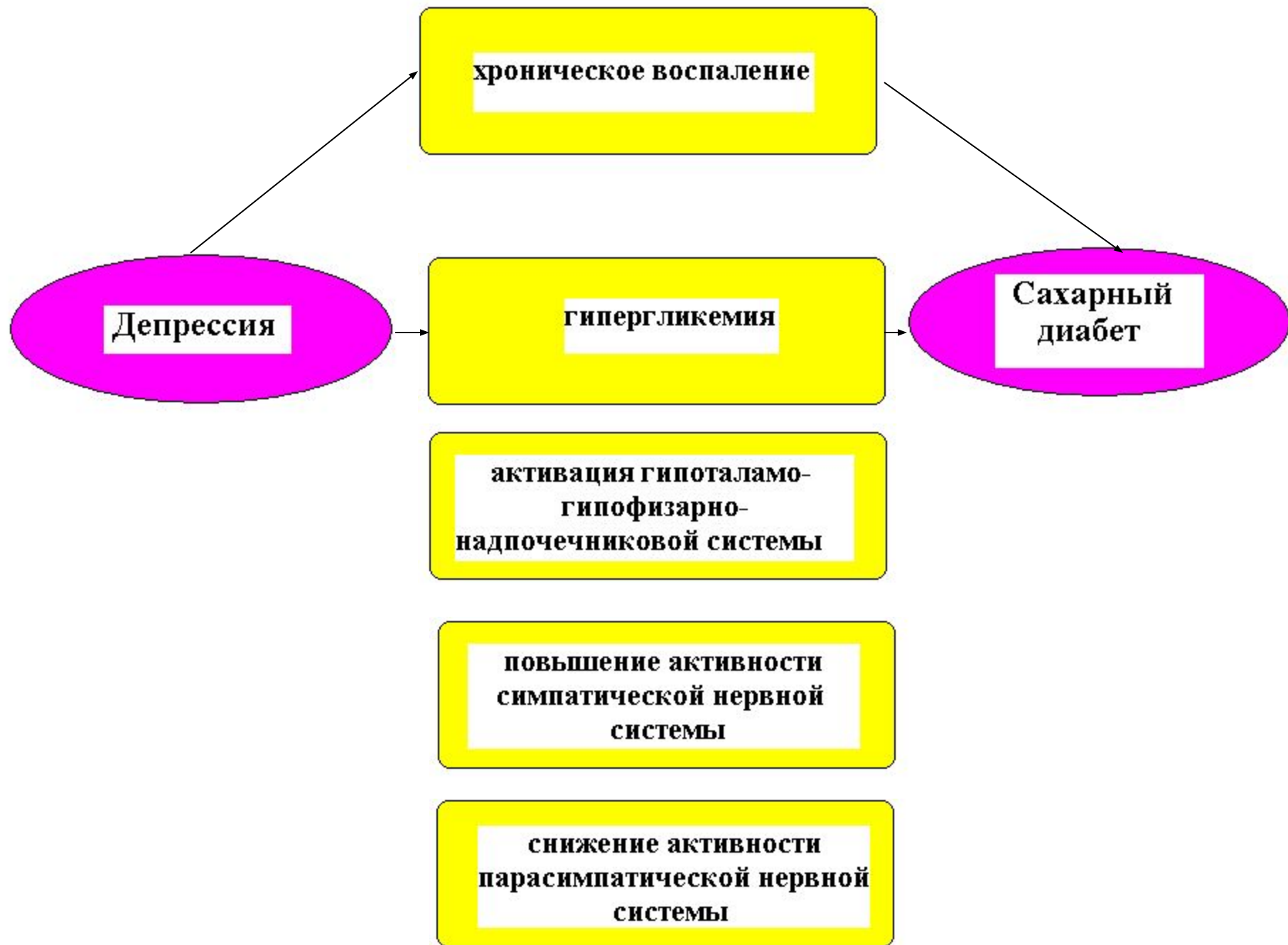
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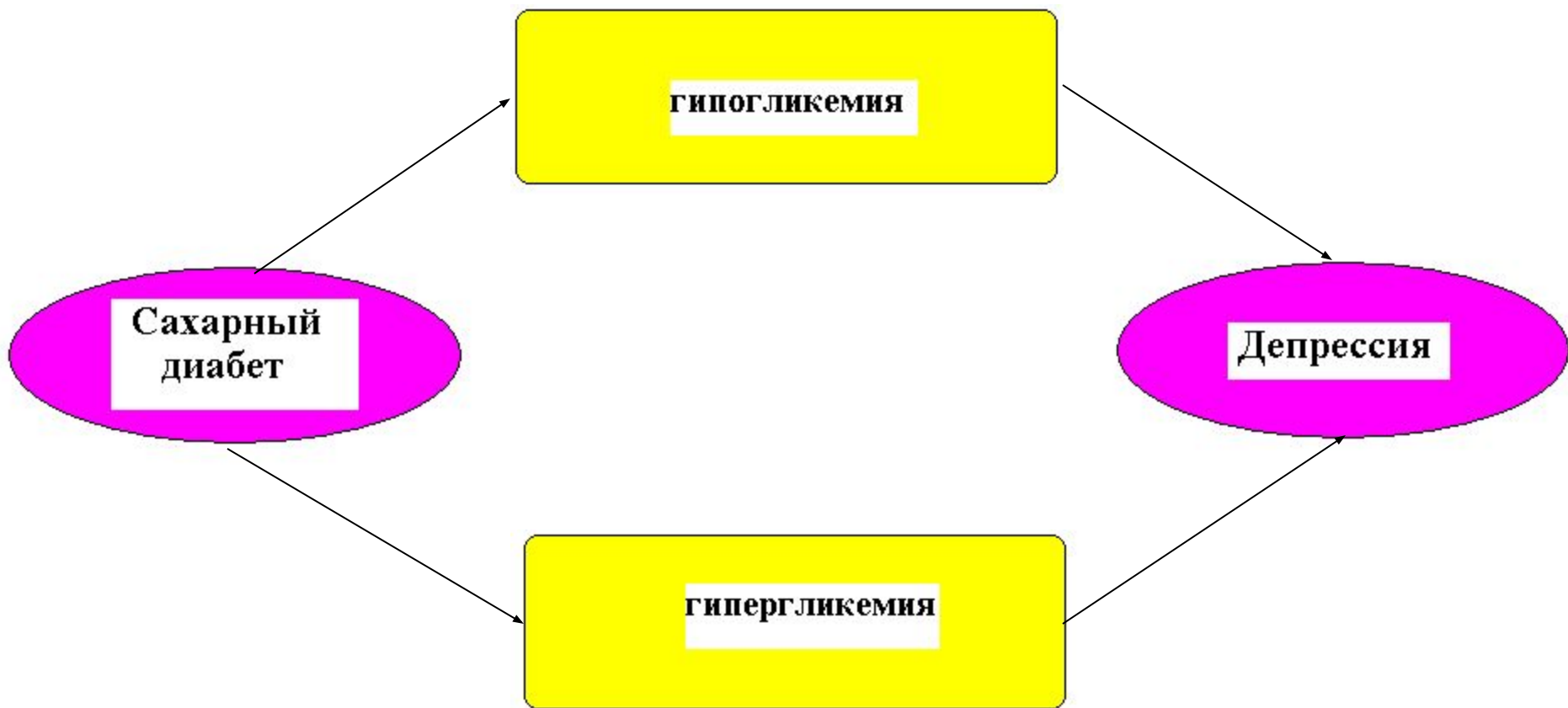


*«Депрессия может рассматриваться как независимый модифицируемый фактор риска сахарного диабета 2 типа и развития осложнений и смертности при СД 1 и 2 типов, стоящий в одном ряду с такими факторами риска как возраст, ожирение или низкая физическая активность»*

# Сопутствующие заболевания, повышенный риск развития которых связан с сахарным диабетом

- Нарушение слуха
- Синдром обструктивного апноэ во сне
- Жировая болезнь печени
- Снижение уровня тестостерона у мужчин
- Заболевания пародонта
- Определённые раки
- Переломы
- Когнитивные нарушения
- Депрессия













- *Беспокоило ли Вас чувство безнадежности или беспомощности в течение последнего месяца?*
- *Можно ли сказать, что в течение последнего месяца Вас часто беспокоило отсутствие интереса или удовольствия от какой-либо деятельности?*

# Анкета о состоянии здоровья (PHQ-9)

Как часто за последние 2 недели Вас беспокоили следующие проблемы?

(Выбранный ответ отметьте значком "✓")

	Ни разу	Несколько дней	Более половины всех дней	Почти каждый день
1. Вам было не очень интересно или не очень нравилось что-либо делать	0	1	2	3
2. Вы грустили, были подавлены или испытывали чувство безысходности	0	1	2	3
3. Вам было трудно заснуть, у Вас был прерывистый сон, или Вы слишком много спали	0	1	2	3
4. Вы были утомлены, или у Вас было мало сил	0	1	2	3
5. У Вас был плохой аппетит, или Вы переедали	0	1	2	3
6. Вы плохо о себе думали – Вы считали себя неудачником (неудачницей) или были в себе разочарованы, или считали, что подвели свою семью	0	1	2	3
7. Вам было трудно сосредоточиться, например, на чтении газеты или на просмотре телепередач	0	1	2	3
8. Вы двигались или говорили настолько медленно, что окружающие могли бы это заметить? Или наоборот, Вы были настолько суетливы или взбудоражены, что передвигались гораздо больше обычного	0	1	2	3
9. Вас посещали мысли о том, что Вам лучше было бы умереть, или о том, чтобы причинить себе какой-нибудь вред	0	1	2	3

Если бы Вам пришлось оценить свое состояние на каком-либо уровне, то насколько, насколько трудно Вам было бы работать, вести домашнее или личное и другими людьми из-за этих проблем?

Совсем не  
трудно  
□

Немного  
трудно  
□

Очень  
трудно  
□

Чрезвычайно  
трудно  
□

<b>Общий балл</b>	<b>Выраженность депрессии</b>
1-4	Минимальная депрессия
5-9	Легкая депрессия
10-14	Умеренная депрессия
15-19	Тяжелая депрессия
20-27	Крайне тяжелая депрессия



# Диагностика депрессии

- депрессивное настроение;
- значительное уменьшение интереса или удовольствия от повседневной деятельности;
- значительная потеря/увеличение веса;
- инсомния/гиперсомния;
- психомоторное возбуждение/заторможенность;
- утомление;
- чувство никчёмности/чрезмерной вины;
- трудности в концентрации/принятии решений;
- повторяющиеся мысли о смерти/суициде.

Соблюдение  
диеты



Соблюдение  
рекомендаций  
по физической  
активности

# АНТИДЕПРЕССАНТЫ

нарушающие  
нейрональный захват  
моноаминов

ингибиторы  
моноаминооксидазы

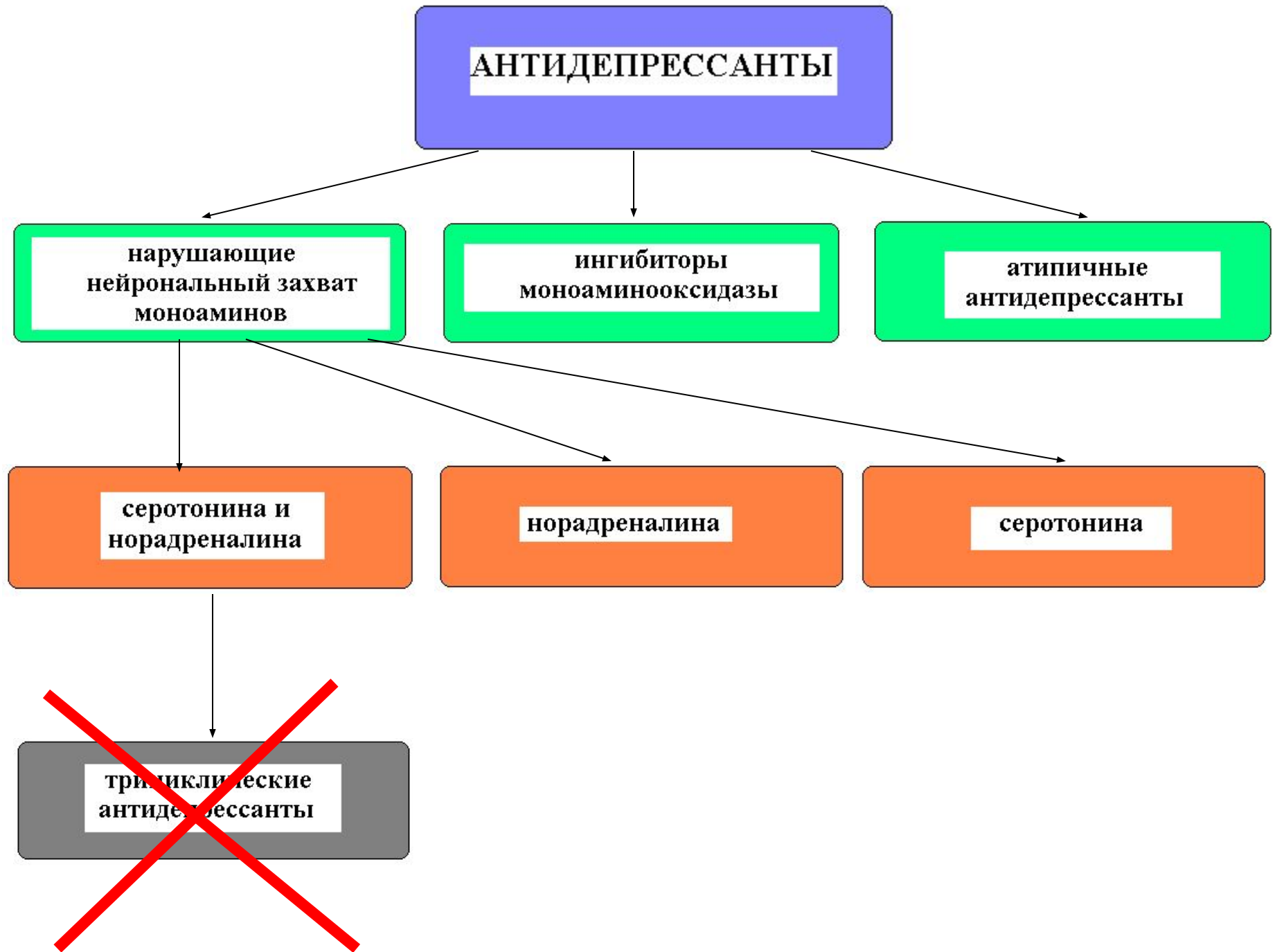
атипичные  
антидепрессанты

серотонина и  
норадреналина

норадреналина

серотонина

трициклические  
антидепрессанты



# Fluoxetine for Depression in Diabetes

## A randomized double-blind placebo-controlled trial

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LINDA S. GRIFFITH, MSW  
RAY E. CLOUSE, MD

**OBJECTIVE**— Depression is prevalent in patients with diabetes. It is associated with poor glycemic control and is linked to an increased risk for diabetic complications. In this study, we assessed the efficacy of fluoxetine for depression in patients with diabetes.

**RESEARCH DESIGN AND METHODS**— Sixty patients with diabetes (type 1,  $n = 26$ ; type 2,  $n = 34$ ) and major depressive disorder entered an 8-week randomized placebo-controlled double-blind trial. Patients were given daily doses of fluoxetine (up to 40 mg/day). The Beck Depression Inventory (BDI) and Hamilton Rating Scale for Depression (HAM-D) were used to measure the severity of depression and to determine the percentage of patients who achieved substantial improvement or complete remission. GHb levels were obtained to monitor glycemic control.

**RESULTS**— Reduction in depression symptoms was significantly greater in patients treated with fluoxetine compared with those receiving placebo (BDI,  $-14.0$  vs.  $-8.8$ ,  $P = 0.03$ ; HAM-D,  $-10.7$  vs.  $-5.2$ ,  $P = 0.01$ ). The percentage of patients achieving a significant improvement in depression per the BDI was also higher in the fluoxetine group (68.7 vs. 37.0%,  $P = 0.03$ ). Additionally, trends toward a greater rate of depression remission (48.1 vs. 25.9%,  $P = 0.09$  per the HAM-D) and greater reduction in GHb ( $-0.40$  vs.  $-0.07\%$ ,  $P = 0.13$ ) were observed in the fluoxetine group.

**CONCLUSIONS**— Fluoxetine effectively reduces the severity of depression in diabetic patients. Our study demonstrated that after only 8 weeks, this treatment also produced a trend toward better glycemic control.

*Diabetes Care* 23:618–623, 2000

Major depressive disorder is present in 15–20% of patients with type 1 or type 2 diabetes (1) and has implications that exceed its recognized adverse effects on daily functioning and quality of life (2–4). Depression has been associated with poor compliance with the diabetes regimen (5,6), poor glycemic control (7–15), and an increased risk for micro- and macrovascular complications (16–19). It is not known, however, whether

these associations can be altered by the successful treatment of depression.

In general, little is known about the efficacy of antidepressant pharmacotherapy in diabetic patients. Nortriptyline hydrochloride, a secondary amine tricyclic antidepressant, is the only agent previously tested in a placebo-controlled trial with diabetic patients (20). Reduction in depression symptoms was significantly greater in patients treated with nortriptyline compared

with those receiving placebo, but the drug had significant adverse effects on glycemic control. Path analysis, controlling for opposing effects, showed that improvement in depression had a clinically significant benefit on glycemic control; depression remission was associated with a 0.8–1.2% reduction in glycated hemoglobin over the 8-week study period (20,21).

Hyperglycemia has not been reported in patients treated with newer classes of antidepressant agents such as the selective serotonin reuptake inhibitors (SSRIs) (22,23). The efficacy of fluoxetine hydrochloride, the first SSRI available in the U.S., for treating depression in healthy patients has been established in a number of controlled clinical trials (24–26), but its usefulness in diabetic patients has been unknown. Tollefson et al. (27) found that fluoxetine was less effective in patients over age 60, which might, the study suggested, partially result from more comorbid medical illness in this age group. The efficacy of depression treatment may be limited by lifestyle restrictions, pain, impairment, and disability—realities that often accompany advancing diabetes (20,21). This study was designed to determine the antidepressant efficacy of fluoxetine in diabetic patients with major depressive disorder. A secondary aim was to study the effects of treatment and depression improvement on glycemic control.

## RESEARCH DESIGN AND METHODS

### Patients

A study to determine the usefulness of fluoxetine for depression in diabetic patients was reviewed and approved by the Human Studies Committee of Washington University School of Medicine. The study was publicized within the Washington University Medical Center community and through various advertisements in the St. Louis, Missouri, metropolitan area. Patients with type 1 or type 2 diabetes who were 21–65 years of age were eligible to participate, provided they were able to give informed consent and answer questions and fill out research forms on their own. Patients were required to meet diagnostic

Снижение уровня гликированного гемоглобина при лечении Флуоксетином больных сахарным диабетом в течение 8 недель статистически недостоверно

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Abbreviations: ANCOVA, analysis of covariance; BDI, Beck Depression Inventory; DIS, National Institute of Mental Health Diagnostic Interview Schedule; HAM-D, Hamilton Rating Scale for Depression; SSRI, selective serotonin reuptake inhibitor.

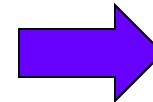
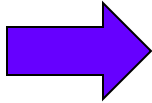
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.







# Когнитивная поведенческая терапия



Bystritsky A., Danial J., Kronemyer D. Interactions between diabetes and anxiety and depression: implications for treatment. EndocrinolMetabClin North Am. 2014. 43: 269-283.

# Электроконвульсивная терапия

