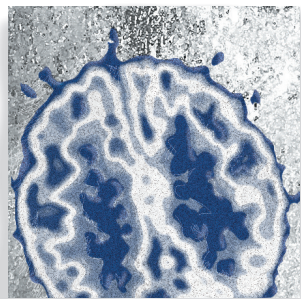


Depression and diabetes

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The comorbidity of mental and physical disorders is a major challenge for health care worldwide. Its prevalence is increasing and is likely to continue to grow due to the increase in life expectancy and a variety of other reasons. The comorbidity of depression and diabetes can be seen as a prototypical example of mental/physical comorbidity. The prevalence of both conditions is growing, and depression is twice as frequent in people with diabetes compared with those without diabetes. Health services are by and large inadequately prepared to deal with comorbid depression and diabetes, and the increasing specialization (and fragmentation) of medicine will probably make things worse. This paper reviews the epidemiology and risk factors of the comorbidity of depression and diabetes and describes areas that should be given attention in order to reduce problems arising as a result of the comorbidity of these two conditions.

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Introduction

The main challenges for medicine in the 21st century are newly emergent diseases and the management of comorbidity. The first of these two challenges should be met by enhancing research aimed at the prevention and treatment of emergent diseases. Meeting the second challenge requires, as a first step, changes in the organization of health services and in the training of health workers.

Simultaneous occurrence of noncommunicable diseases—such diabetes, cancer, chronic obstructive pulmonary disease, and cardiovascular ailments—has been at the center of attention of specialists in oncology, internal medicine, and its subspecialties—such as nephrology and endocrinology—and a top item on the agenda of general practitioners, particularly in highly developed countries. Significant progress has been made in the management of these conditions; the recognition of their public health importance and of their impact on economy led to political action by the United Nations (UN), which held a special session on this topic in 2012. Ahead of the UN session, several meetings had been organized by professional associations assembling specialists in the “four giants”: diabetes, cancer, cardiovascular diseases, and chronic obstructive pulmonary

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diseases, usually with the strong support of the World Health Organization. Further joint action is planned.

For a variety of reasons, mental disorders were not included among the conditions discussed at the UN meeting, and professional organizations of psychiatrists have not been invited to participate in discussion about joint action against noncommunicable diseases. The Sustainable Development goals (N°3) of the UN, adopted in 2017, include mental disorders. This omission is, to say the least, curious, and from the point of view of public health, erroneous. Mental and neurological disorders constitute a significant proportion, roughly one-third, of all disability due to illness, and in 2013, of the 25 disorders that produced the highest number of disability-adjusted life years, seven, were mental disorders.¹ Mental disorders are often comorbid with diabetes, cardiovascular illness, and cancer, worsening the prognosis of these diseases and increasing costs associated with their treatment. People with mental disorders live 10 years less than people without mental disorders, and noncommunicable diseases are the main reason for their death. In addition, recent research indicates that mental disorders and some of the noncommunicable diseases may have a similar pathogenesis and depend on some of the same risk factors, eg, adverse experiences in early childhood.

This paper will discuss one of the forms of comorbidity of mental and other noncommunicable diseases, that of depression and diabetes. The frequencies of diabetes and depression are growing faster than the prevalence of the other mental and other noncommunicable diseases, and appropriate action could make a major difference for people with this form of comorbidity and for the societies to which they belong. Both have moved up on the list of diseases ranked by the disability they produce: diabetes is currently in seventh place, and depression has ascended to second place among all diseases of the world population.¹

The increasing incidence and prevalence of diabetes could be related to changes in lifestyle and diet worldwide. The reasons for the growing prevalence of depression may be related to higher life expectancy at all ages, but the growth of incidence is less easy to explain although several possible causes have been identified.²

Epidemiology of comorbidity of depression and diabetes

The association of depression and diabetes had already been described long ago; in the late 17th century, Willis

wrote that people who experienced “significant life stress, sadness or long sorrow” are more likely to suffer from diabetes.³ Similar clinical observations were reported in other countries, but it was not until the second part of the 20th century that a series of epidemiological studies demonstrated that depression is more likely to occur in people with diabetes regardless of whether the individuals are aware of their diabetes. In addition to depressive disorders, people with diabetes are also registering significant levels of diabetes-specific distress,⁴ which is clearly distinguishable from depressive disorders but can act as a risk factor for depression. Epidemiological studies of depression and diabetes and their comorbidity have been carried out in the United States of America (USA), the United Kingdom, and some other high-income countries. The situation in other parts of the world is not as well documented, but reports that do exist indicate that the situation is similar in other countries as well.⁵

The current estimates of the worldwide prevalence of depression indicate that 350 million people suffer from it, and similarly, the worldwide prevalence of diabetes is estimated to be more than 400 million people.⁶ The prevalence of depressive disorders in diabetics is in the general range of 10% to 15%, which is approximately twice as high as the prevalence of depression in nondiabetics.^{3,7,8-10} Comorbidity significantly worsens the prognosis of both diseases and increases their mortality.^{11,12} In addition to having depressive disorders that satisfy criteria given in the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* and *International Statistical Classification of Diseases and Related Health Problems (ICD)*, up to one-quarter of people with diabetes also experience depressive symptoms for which severity does not reach the threshold for diagnosis of the disorder.

These symptoms are, to an extent, similar to the symptoms of diabetic distress, a condition that seems to be separate from depressive disorders and can be measured with relevant standardized instruments.

Risk factors for comorbidity of depression and diabetes

The risk for depression is increased in people with diabetes, and the risk of diabetes is elevated in people with depressive disorders.^{13,14} There are a number of risk factors that have been identified as relevant for the occurrence of diabetes and depression, including low birth

weight, adverse events in childhood, lifestyle, and obesity,^{3,10} and there is good evidence that complications of diabetes significantly increase the risk of depression.¹⁵

The relation between depression and the complications of diabetes (and the distressing experience of living with diabetes) is not likely to be explicable by a simple stress disease model. It is more probable that common risk factors operate through a variety of biological mechanisms. For example, it could be that adverse childhood experiences prepare the ground for depressive disorders but, at the same time, lead to cell-mediated cytokine production, which in turn may lead to insulin resistance (and type 2 diabetes) as well as influence the hypothalamic-pituitary-adrenal (HPA) axis and the occurrence of other disorders, eg, those related to endothelial dysfunction.¹⁶ The sibling recurrence risk for type 2 diabetes and the familial aggregation of diabetes has also in recent times been linked to inflammatory genes, which might have a role in the origin of depressive disorders.

Women are at higher risk than men of developing depressive disorders, with or without diabetes. A systematic review of evidence indicated that 27% of women with diabetes developed depressive disorders, which was roughly one-third higher than for men with diabetes, of whom 18% developed depression.⁷ This could be explained in part by the fact that women experience more negative life events, and experience significant hormonal changes during pregnancy and postpartum: during the perinatal period; women with diabetes had two times more depression than their nondiabetic peers.¹⁷ Cognitive dysfunction increases the risk for depression; conversely, poor glycemic control leads to functional disability, higher rates of depression, and cognitive problems. In addition, comorbid depression and diabetes also increase the risk for dementia.¹⁸

Migration is associated with higher rates of depression, higher rates of diabetes, and higher rates of comorbidity of depression and diabetes in migrants. Reasons for this include the stresses related to migration and significant changes in lifestyle and dietary patterns.¹⁹

Consequences of comorbidity of depression and diabetes

The outcome of depression and of diabetes is worse when they appear together. The presence of depression is linked to higher rates of complications in diabetes, to

more disability,²⁰ and to loss of years of life.¹² As with other mental disorders, the pattern of causes of death does not differ from the patterns seen in the population without a depressive disorder. In children and adolescents, the presence of depression affects glycemic control.¹³ An important study of 30 022 adults in the USA showed that the risk of functional disability in people with diabetes was 2.42 times higher than in people who did not have diabetes; that in people with depression alone, it was 3 times higher than in people without depression; and that the risk for those who had depression and diabetes, the risk was 7.15 times higher than in people who did not have depression or diabetes.²⁰ Cost of treatment of diabetes when depression is present is 4.5 times higher than the treatment of diabetes alone.²¹ Similar increases in cost of treatment have been found in other studies in the USA.

The presence of depression in people with diabetes also leads to poorer self-care (including lacking in physical exercise, non-adherence to diet, irregular intake of medications for any purpose) and to behavior that may increase the risk of cardiovascular illness and microvascular and macrovascular complications.²²

Treatment of comorbid depression and diabetes

Alonso et al²³ showed that in the highly developed countries of Europe, most of those (92%) with diabetes receive regular treatment, but as much as half of those with mental disorders do not receive appropriate care. In the US, 51% of people with diabetes who also had depression were recognized as having depression and offered treatment.²² Being female, having panic attacks, and having made more than seven visits to the health care provider were factors that contributed to the recognition of depression. However, not all those who were given a diagnosis of depression received treatment recommended by the relevant guidelines for their condition. These figures are probably too optimistic: in an international study carried out in developed and developing countries, the percentage of patients with type 2 diabetes who were recognized as having depression and received treatment is even lower.²⁴

The efficacy of treatment of depression in the presence of serious somatic illness has been examined in a series of studies summarized in a review published in 2010.²⁵ The review showed that psychotherapeutic in-

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interventions (some of which were combined with diabetes education) had a moderate-to-large effect on depressive symptoms and a moderate-to-large effect on glycemic control. Psychopharmacological treatment with selective serotonin reuptake inhibitor (SSRI) medications also had a moderate-to-large effect on depressive disorders with lesser effects on glycemic control. Although most of the studies were small in size, the findings seem to indicate that the treatment of depression by psychotherapy or with medications should be combined with education to achieve diabetes self-care and glucose control.

Even better results can be achieved by collaborative care, combining screening for depression, and a team approach to care in population-based health services. Its components include patient education, the presence of allied health professionals in the primary care system (to track the effects of treatment, side effects, and adherence to treatment and to provide support for needed changes in behavior), and caseload supervision by a psychiatrist using stepped-care principles, ie, adjusting the intensity of care to the development of the clinical picture.²² The notion that the improved treatment of depression must go hand in hand with the treatment of diabetes and with changing adverse health behavior (eg, sedentary lifestyle, obesity, smoking) is gradually gaining general acceptance, and it is hoped that it will lead to changes in health system organization. These might include regular screening of diabetics for depression, changes in the education of personnel working in services dealing with diabetes, and—in primary health care settings—the inclusion of mental health workers in the primary health care teams, improved referral chains, education of the general population, as well as education of diabetics and other measures.

Areas for future work

Aware of huge problems related to the comorbidity of mental and physical disorders, a Geneva-based nongovernmental organization, the Association for the Improvement of Mental Health Programs (AIMHP), founded the Dialogue on Diabetes and Depression

(DDD), an initiative addressing comorbidity of depression and diabetes as a paragon of comorbidity of mental and other diseases.²⁶ In the framework of this initiative, which brought together a large number of international professional and nongovernmental organizations, the AIMHP in collaboration with the The National Institute of Diabetes and digestive and kidney diseases (NIDDK) organized the international conference Digestive and Kidney Diseases, which reviewed current knowledge and produced a series of specific recommendations concerning research that should be undertaken to facilitate the prevention of comorbidity and the provision of care to people with comorbid diabetes and depression.¹³ The recommendations address the development of methods of assessment of depressive disorders in diabetics, the mechanisms and pathogenesis of comorbidity of diabetes and depression, treatment of diabetes and depression and the relevant organization of services, the primary prevention of diabetes and depression, and the training for research and clinical care.

The organization of services that provide (or should provide) treatment and the manner in which treatment for comorbid diabetes and depression (and indeed other forms of comorbidity of mental and physical disorders) will be delivered require, as a first step, a reexamination of the current paradigms of health care and an agreement on a conceptual framework; such a framework would include the various elements and factors playing a role in the development of diabetes and depression, in their treatment, and in the prevention of functional impairment that they might produce.²⁷ A comprehensive conceptual framework, as well as current knowledge about the best ways of dealing with comorbid depression and diabetes, could serve as a basis for changes in the organization of services. That framework could also, and perhaps more importantly, serve as a roadmap for the readjustment of training of health workers and for public health interventions that would reduce the current problems related to comorbidity of mental and physical disorders and prevent their further growth. □

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Depresión y diabetes

La comorbilidad de los trastornos mentales y físicos constituye un gran desafío para la atención de salud en todo el mundo. Su prevalencia está aumentando y es probable que continúe creciendo debido al incremento en la expectativa de vida y a una variedad de otras razones. La comorbilidad de depresión y diabetes puede ser vista como un ejemplo prototípico de la comorbilidad física/mental. La prevalencia de ambas condiciones está creciendo, y la depresión es dos veces más frecuente en personas con diabetes en comparación con las no-diabéticas. En general, los servicios de salud no están preparados para enfrentar adecuadamente la depresión y la diabetes comórbidas, y el aumento de la especialización (y fragmentación) de la medicina probablemente empeorará las cosas. Este artículo revisa la epidemiología y los factores de riesgo de la comorbilidad de depresión y diabetes, y describe áreas en las que hay que poner atención para reducir los problemas que surgen como resultado de la comorbilidad de estas dos condiciones.

Dépression et diabète

La comorbilidad des troubles physiques et mentaux représente un défi majeur pour les soins de santé dans le monde. Leur prévalence augmente et continuera probablement à croître en raison de l'augmentation de l'espérance de vie et d'autres facteurs. La comorbilité de la dépression et du diabète peut être observée comme un exemple typique de la comorbilité somatique/mentale. La prévalence des deux maladies augmente et la dépression est deux fois plus fréquente chez les diabétiques que chez les non-diabétiques. Les services de santé sont dans l'ensemble mal préparés à leur prise en charge et la spécialisation (ainsi que la fragmentation) croissante de la médecine va probablement aggraver les choses. Dans cet article, nous analysons l'épidémiologie et les facteurs de risque de la comorbilité dépression et diabète et nous décrivons les domaines sur lesquels se concentrer afin de diminuer les problèmes consécutifs à cette comorbilité.