WIKLIŃSKA, Agata, SZYDŁO, Jakub, TKACZYK, Ignacy and RYBACKA-TKACZYK, Katarzyna. Depression and somatic diseases – how are they linked? Quality in Sport. 2025;39:58457. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.39.58457
https://apcz.umk.pl/QS/article/view/58457

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 02.02.2025. Revised: 02.03.2025. Accepted: 02.03.2025 Published: 06.03.2025.

DEPRESSION AND SOMATIC DISEASES – HOW ARE THEY LINKED?

Agata Wiklińska

Medical Centre ENEL-MED S.A., Zgrupowania AK „Kampinos" 15, 01-943 Warsaw, Poland

https://orcid.org/0009-0008-8758-5860

agata.wiklinska@gmail.com

Jakub Szydło

Independent Public Team of Outpatient Healthcare Facilities Warsaw Żoliborz-Bielany, Klaudyny 26B, 01-684 Warsaw, Poland

https://orcid.org/0009-0009-1092-2571

jakubszydlorekrutacja@interia.pl

Ignacy Tkaczyk

Independent unit of public Outpatient Healt Care Institutions, Fabryczna 1, 05-500 Piaseczno, Poland

https://orcid.org/0009-0002-0647-9940

ignacytkaczyk@gmail.com

Katarzyna Rybacka-Tkaczyk
Mantyk Clinic, Nocznickiego 25/U13, 01-918 Warsaw, Poland
https://orcid.org/0009-0004-3889-6583
praktykastomatologicznakrt@gmail.com

ABSTRACT

Introduction and aim of study: Depressive disorder is one of the most common diseases involving mental health. It is known as a stress-dependent disease. It triggers a number of mechanisms, which are supposed to ensure homeostasis to the body. However, under prolonged stress, they become harmful to the organism, causing a number of somatic diseases. The aim of this paper was to discuss the cause-effect relationship between depression and somatic comorbidities.

Materials and methods: Databases such as PubMed and Google Scholar were searched to review the scientific literature on the association between depression and somatic comorbidities. The following keywords were used for the search: depression, somatic diseases, inflammation, HPA axis and lifestyle.

Results: A review of the literature showed an increased prevalence of cardiovascular diseases, obesity, diabetes, infections and cancer among patients with depressive disorder. The most important processes underlying these correlations were: hyperactivity of the HPA axis, hyperactivity of the sympathetic nervous system and inflammation.

Conclusion: In patients suffering from depression, attention should be paid to the increased incidence of somatic diseases. Both oncological and internal medicine vigilance should be increased in the treatment.

Keywords: depression, somatic diseases, inflammation, HPA axis, lifestyle

BACKGROUND

Major Depression Disorder (MDD) is one of the most common diseases affecting mental health worldwide with a lifetime prevalence of 20%. [1] World Health Organization (WHO) estimates that in 2019, 280 million people, including 5% of all adults, experienced depression. [2] By 2030, it is likely to be the leading cause of disability worldwide. [3] Depression is a significant risk factor for premature death. Not only a greater suicide rate is responsible for this, but also the concomitance of somatic diseases. [1,4,5] Their comorbidity is therefore a very important issue in the context of multidirectional treatment management. [6]

Depression is known as a stress-related disorder, which is considered one of the main risk factors for the development of this disease. [7-9] Several biological mechanisms crucial to the development of concomitant somatic diseases are activated in individuals struggling with depressive disorder. In stressful conditions for the organism, activation of the HPA axis, the autonomic nervous system and the inflammatory response are designed to ensure homeostasis. However, they can also lead to damage to the body. [10] The purpose of this paper was to discuss the cause-effect relationship between the occurrence of depression and somatic comorbidities.

MATERIALS AND METHODS

The authors searched databases such as PubMed and Google Scholar as well as the WHO website to review the scientific literature on the correlation between depression and comorbid somatic diseases. The following keywords were used to find relevant sources of knowledge: depression, somatic diseases, inflammation, HPA axis, lifestyle. For this review, information from 44 research papers was used.

HPA AXIS ACTIVATION

The body, in response to stress, activates adaptive processes to ensure homeostasis. One of these is the activation of the hypothalamic-pituitary-adrenal axis (HPA axis), closely

cooperating with the limbic system. They form a functional unit called the limbic-hypothalamic-pituitary-adrenal axis. [11]

To understand the effect of HPA axis activation on the organism, it is necessary to trace the pathway that is initiated by a stress stimulus. The stimulus is registered by the nervous system, and the information reaches the sensory areas of the thalamus, then via the cerebral cortex the amygdala. The cortex can be omitted, but then the information does not reach consciousness. The neocortex structures, which create sensory representations of information about external stimuli, are also involved in the stress response. The information is transmitted from these structures to the hippocampus, where it is analyzed. After analysis, the hippocampus sends information to the amygdala, to the paraventricular nucleus (PVN) in the hypothalamus, and back to the neocortex. Thus, the limbic system initiates the activation of the HPA axis. The PVN produces corticotropin-releasing hormone (CRH), which, acting on the anterior lobe of the pituitary gland, stimulates the secretion of adrenocorticotropic hormone (ACTH) into the blood. Reaching the adrenal cortex, ACTH enables the synthesis and release of glucocorticoids. [10] Under physiological conditions, after responding to transient stress, the body aims to reestablish homeostasis via negative feedback loop. Cortisol binds to receptors for glucocorticoids in the pituitary gland, hippocampus and PVN inhibiting further CRH release. [1] The functioning of the limbic-hypothalamic-pituitary-adrenal axis is depicted in Figure 1. [1,10,11]

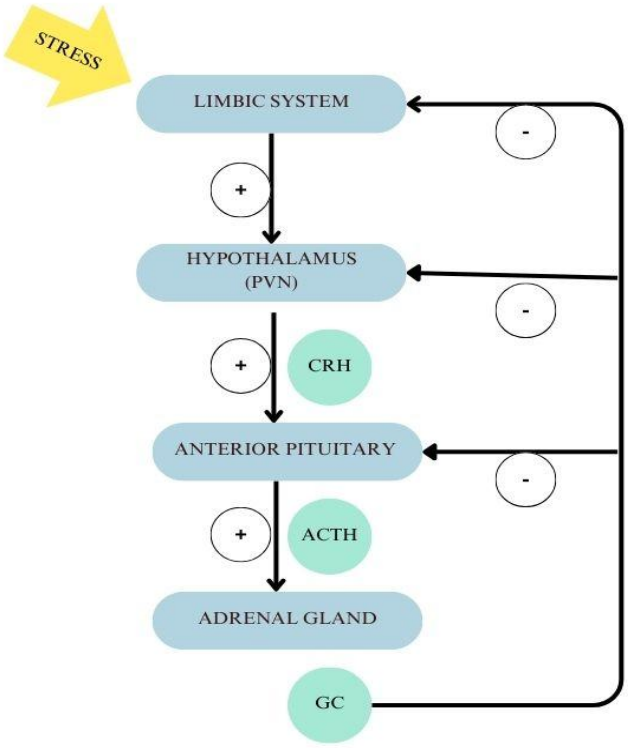

Figure 1. Limbic-Hypothalamic-Pituitary-Adrenal axis. [1,10,11]

In case of chronic stress, cortisol ceases to be secreted in a diurnal rhythm. This leads to desensitization of glucocorticoid receptors and thus resistance to glucocorticoids. [12,13] Sustained elevated cortisol levels over a long period of time can lead to impaired carbohydrate metabolism, followed by insulin resistance and visceral fat accumulation. [14] Elevated glucocorticoid levels also cause structural changes in brain regions such as the prefrontal cortex, amygdala, hippocampus and hypothalamus. This can result in the development of depressive symptoms. [15]

DYSREGULATION OF THE AUTONOMIC NERVOUS SYSTEM

The hypothalamus is the control center not only for the functioning of the HPA axis, but also for the sympathetic-adrenal system. Sympathetic-adrenal system is activated in the first minute of the stress response and is meant to manage the stress-inducing problem quickly. Activation of this system is responsible for the fight-or-flight response, which is intended to provide adequate blood supply to skeletal muscles and the brain. It is crucial for handling a

stressful situation. Also the process of glycogenolysis is intensified to increase the level of glucose in the blood, which is an affordable source of energy. In response to the stress factor, the sympathetic nervous system is activated and the secretion of catecholamines in the adrenal glands is increased. Interacting with receptors in internal organs, they cause mobilization of the body to fight the stressful situation. [11]

People affected by depression experience changes in the autonomic nervous system. Under physiological conditions, the activity of the sympathetic and parasympathetic nervous systems remains in balance, but in depressed people the sympathetic nervous system dominates. [3,16,17]

INFLAMMATION

Dysregulation of both the innate and adaptive immune systems is an important pathophysiological process in people with depression. Evidence of abnormalities in immune cell numbers, antibody titers and inflammatory markers continues to mount. Increased levels of proinflammatory cytokines and acute phase proteins have been demonstrated particularly highlighting the role of IL-1β, Il-6, CRP and TNF as biomarkers of inflammation in depression. [5,18] Cytokines can reduce the synaptic availability of monoamines in several various ways, which is thought to be an important pathomechanism of depression. [18,19] High levels of cytokines also lead to neuroinflammation by modulating key brain areas associated with depression, causing impairment of plasticity, neurochemistry and activation of neuroendocrine axes. [19] The important role of glucocorticoids in suppressing the inflammatory response should also be mentioned. Under physiological conditions, they activate the expression of anti-inflammatory genes and suppress inflammatory signaling pathways. As a result of prolonged stress associated with depression, this function is impaired. Due to the resistance to glucocorticoids common in depression, there may also occur a loss of sensitivity to their suppressive effects. These events promote inflammation. [19]

LIFESTYLE

Depression is characterized by a low mood or loss of pleasure or interest in activities. [20] This is related to the specific lifestyle led by individuals struggling with this disease. Compared to the healthy population, the frequency of smoking is greater in these patients.

Their meals, despite a significant caloric load, often have little nutritional and vitamin content. What is more, physical activity is often neglected by patients. Moreover, social isolation may lead to reduced attention to medical care resulting in worse treatment compliance. [3,21,22] There are premises that physical activity, diet or sleep interventions can benefit not only mood, but also cardiovascular health. [23]

CARDIOVASCULAR DISEASES

The issue that is best documented in terms of the co-occurrence of depression and somatic diseases is its association with cardiovascular diseases. They are linked by a strong bidirectional correlation. Depression increases the risk of new cardiovascular events, causes progression of existing ones and affects the prognosis. [19, 21, 22, 24] On the other hand, patients with cardiovascular diseases are more likely to reveal an increased susceptibility to MDD. [3]

C. Krittanawong et. al performed a meta-analysis of 26 studies involving 1,957,621 individuals. It showed a significantly increased risk of subsequent development of all cardiovascular diseases in people with depression. It was associated with increased risk of incident stroke, myocardial infarction, and congestive heart failure. Moreover, it was shown to raise all-cause mortality, cardiovascular disease mortality and congestive heart failure mortality. [25]

A study involving 74,285,160 people with low incomes was conducted in the United States of America. Its goal was to identify the correlation between depressive or anxiety symptoms and hypertension. It was shown that people experiencing depressive symptoms and those taking medication for this reason had a higher prevalence of hypertension. 12% of patients with hypertension reported depressive symptoms daily, 12% weekly, and 10% monthly. [26]

In 2004, the large INTERHEART study was conducted. It examined the effect of modifiable risk factors on myocardial infarction. It showed that not only elevated ApoB/ApoA1 ratio, smoking, history of hypertension, abdominal obesity, daily consumption of fruits and vegetables, regular alcohol consumption, physical activity or diabetes, but also socioeconomic factors (depression, locus of control, perceived stress, and life events) had a significant impact on the risk of acute myocardial infarction. [27] Most of the risk factors taken into

consideration in this study represent links between depression and cardiovascular disease showing how important a healthy lifestyle is in the prevention of cardiovascular events.

In addition to an unhealthy lifestyle, it is important to emphasize the previously mentioned hyperactivity of the sympathetic nervous system, which increases the risk of poor cardiovascular outcomes. [3] To measure its functioning, a sensitive and non-invasive indicator - Heart Rate Variability (HRV) - is used. Among other parameters, it consists of two oscillatory components: low frequency (LF) and high frequency (HF). HF depicts mainly parasympathetic activity, while LF depicts the activity of both parasympathetic and sympathetic systems. [28] The LF/HF ratio which provides information about sympatho-vagal balance is also determined. Depressed patients have been shown to have reduced HRV parameters and a significant increase in LF/HF ratio, which suggests reduced vagus nerve impulsation. Decreased HRV is a significant risk factor for adverse cardiovascular events and cardiovascular mortality. [28-29]

Depression with cardiovascular disease may also be linked by processes such as inflammation, activation of the HPA axis, mental stress-induced ischemia, platelet activation or other disorders of the clotting cascade, subclinical vascular changes and genetic factors. [3]

OBESITY

A meta-analysis involving 15 studies and 58,745 participants showed a bidirectional relationship between obesity and depression. Obese individuals had a 55% greater risk of developing depression over time, and those with depression had a 58% greater risk of obesity. [30] This correlation was also confirmed in the meta-analysis involving adolescents. The analysis of 13 studies showed that depressed adolescents had a 70% increased risk of obesity, and obese adolescents had a 40% increased risk of depression. [31]

The justification for this correlation is sought in inflammation, which is a common component of both diseases. Attention has been given to the role of HPA axis dysregulation, which can accompany obesity, and is an important pathomechanism underlying depression. A common link is also insulin resistance and diabetes, which can result from HPA axis hyperactivity in the course of depression, but also due to obesity. [14,30] The issue of iatrogenic obesity cannot be ignored. Antidepressant drugs affect weight gain in various ways. Among others,

fluoxetine and bupropion are considered safe medications in this aspect. In contrast, amitriptyline, paroxetine, lithium, mirtazapine or monoamine oxidase inhibitors (MAOIs) are associated with weight gain. [32,33]

DIABETES

According to WHO, the number of people suffering from diabetes increased from 200 million in 1990 to 830 million in 2022. [34] About 280 million people worldwide struggle with depression. [35] These statistics show how significant a problem they are and how important it is to treat them effectively. Studies have shown that both diseases often occur simultaneously. [36] Depression is 26,3% more common among people with diabetes compared to the healthy population. [37] In comparison, people with mood disorders such as MDD or bipolar affective disorder have a twice greater risk of developing type 2 diabetes mellitus (DM2). [38] The co-occurrence of depression with DM2 results in a 54% increased mortality rate. [39]

The main mechanisms that lead to the development of DM2 in depressed individuals are the previously discussed unhealthy lifestyle, autonomic system dysfunction, systemic inflammation and HPA axis dysregulation. Chronic stress can also lead to hepatic insulin resistance promoting the development of DM2. Looking at this correlation from the other side, adipose tissue dysfunction and hyperglycemia in DM2 patients may induce inflammation, which plays an important role in the pathogenesis of depression. Moreover, chronic inflammation is often associated with insulin resistance. Insulin has neuroprotective effects and plays an important role in the function of synapses. Lack of sensitivity to its effects can result in the development of cognitive impairment in various neuropsychiatric disorders. [40]

INFECTIONS

L. Shi et al. conducted a two-sample Mendelian randomization study using data from the Genome-Wide Association Study (GWAS). The study found a causal relationship between depression and susceptibility to infectious diseases, especially upper respiratory tract infections and urinary tract infections. [41] A greater risk of infections in people with poor

mental health was also shown in a study of 47,202 USA college students. A correlation was found between depression and increased rates of bronchitis, sinusitis, strep throat and ear infection. [42]

CANCER

Depression is common in cancer patients. [43] In a study involving 2,611,907 participants, depression and anxiety were associated with a significantly increased risk of cancer, cancer-specific mortality and mortality from any cause in cancer patients. Considering specific cancers it was shown that there was an increased risk of lung, oral, prostate and skin cancer. Cancer-specific mortality increased for lung, bladder, breast, colorectal, hematopoietic, kidney and prostate cancers, while the risk of mortality from any cause increased for patients with lung cancer. It should be noted that the study was characterized by high heterogeneity among the analyzed studies, which affected the interpretability of the results. [44] Another study found that patients with depression had an 18% higher risk of being diagnosed with cancer overall compared to patients without depression. The largest increases in risk were for lung cancer, gastrointestinal cancer, breast cancer and urinary tract cancer. [45]

This correlation is associated with increased smoking and alcohol consumption among depressed patients. Both substances demonstrate mutagenic effects and affect dysregulation of the immune system, which can lead to carcinogenesis. [45] As a result of chronic stress, which is closely associated with depression, the HPA axis and autonomic system are activated. They promote tumorigenesis and oncogenesis through inflammation, suppression of the immune response and release of stress hormones. These hormones can trigger carcinogenesis by inducing DNA damage, increasing p53 degradation and regulating the tumor microenvironment. [46]

For cancer patients, it is important to remember the importance of adherence to medical recommendations. People struggling with depression usually show worse compliance, which adversely affects prognosis. [45,47]

CONCLUSIONS

Depressive disorder often co-occurs with somatic diseases, which can increase mortality in this group of patients. In depressive disorder, various mechanisms are activated that lead to the development of concomitant diseases. Excessive and chronic activation of the HPA axis is associated with an increased risk of cardiovascular diseases, as well as cancer. Accompanying changes in carbohydrate metabolism can lead to obesity and type 2 diabetes. Shifting the balance of the autonomic system in favor of the sympathetic nervous system also adversely affects patients' cardiovascular health. Chronic activation of the immune system combined with inflammation in addition to the aforementioned diseases may also result in more frequent infections among depressed patients.

Such significant links between depressive disorders and somatic diseases appear to have substantial implications for therapeutic management. Internal medicine as well as oncology vigilance should be increased in the treatment of depressed patients.

DISCLOSURE

Author's contribution:

Conceptualization: Agata Wiklińska, Jakub Szydło

Methodology: Jakub Szydło, Ignacy Tkaczyk

Software: Katarzyna Rybacka-Tkaczyk

Check: Agata Wiklińska, Katarzyna Rybacka-Tkaczyk

Formal analysis: Ignacy Tkaczyk

Investigation: Agata Wiklińska, Jakub Szydło, Ignacy Tkaczyk, Katarzyna Rybacka-Tkaczyk

Resources: Jakub Szydło, Ignacy Tkaczyk

Data curation: Katarzyna Rybacka-Tkaczyk

Writing - rough preparation: Agata Wiklińska, Jakub Szydło, Ignacy Tkaczyk, Katarzyna Rybacka-Tkaczyk

Writing - review and editing: Agata Wiklińska

Visualization: Jakub Szydło, Ignacy Tkaczyk, Katarzyna Rybacka-Tkaczyk

Supervision: Agata Wiklińska

Project administration: Agata Wiklińska

All authors have read and agreed with the published version of the manuscript.

Funding Statement: The study did not receive special funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflict of Interest Statement: There is no conflict of interest for the authors.

Acknowledgments: Not applicable.

Declaration of generative AI and AI-assisted technologies in the writing process: Not applicable.

REFERENCES

[1] Menke A. The HPA Axis as Target for Depression. *Curr Neuropharmacol*. 2024;22(5):904. doi:10.2174/1570159X21666230811141557

[2] Depression. World Health Organization (WHO). Access 8.01.2025. https://www.who.int/health-topics/depression#tab=tab_2

[3] Whooley MA, Wong JM. Depression and cardiovascular disorders. *Annu Rev Clin Psychol*. 2013;9:327-354. doi:10.1146/annurev-clinpsy-050212-185526

[4] Penninx BWJH, Lange SMM. Metabolic syndrome in psychiatric patients: overview, mechanisms, and implications. *Dialogues Clin Neurosci*. 2018;20(1):63. doi:10.31887/DCNS.2018.20.1/BPENNINX

[5] Beurel E, Toups M, Nemeroff CB. The Bidirectional Relationship of Depression and Inflammation: Double Trouble. *Neuron*. 2020;107(2):234. doi:10.1016/J.NEURON.2020.06.002

[6] Leone M, Kuja-Halkola R, Leval A, et al. Association of Youth Depression With Subsequent Somatic Diseases and Premature Death. *JAMA Psychiatry*. 2020;78(3):1. doi:10.1001/JAMAPSYCHIATRY.2020.3786

[7] Cruz-Pereira JS, Rea K, Nolan YM, O'Leary OF, Dinan TG, Cryan JF. Depression's Unholy Trinity: Dysregulated Stress, Immunity, and the Microbiome. *Annu Rev Psychol*. 2020;71:49-78. doi:10.1146/ANNUREV-PSYCH-122216-011613

[8] Slavich GM, Irwin MR. From Stress to Inflammation and Major Depressive Disorder: A Social Signal Transduction Theory of Depression. *Psychol Bull*. 2014;140(3):774. doi:10.1037/A0035302

[9] Griep Y, Hanson LM, Leineweber C, Geurts SAE. Feeling stressed and depressed? A three-wave follow-up study of the beneficial effects of voluntary work. *International Journal of Clinical and Health Psychology*. 2023;23(3):100363. doi:10.1016/J.IJCHP.2022.100363

[10] Leistner C, Menke A. Hypothalamic–pituitary–adrenal axis and stress. *Handb Clin Neurol*. 2020;175:55-64. doi:10.1016/B978-0-444-64123-6.00004-7

[11] Gołyszny M. An „old" and „new" neuropeptides as modulators of the stress axis (hypothalamus–pituitary–adrenal). Psychiatry. 2018;15(3):135-147. Polish

[12] Knezevic E, Nenic K, Milanovic V, Knezevic NN. The Role of Cortisol in Chronic Stress, Neurodegenerative Diseases, and Psychological Disorders. *Cells*. 2023;12(23):2726. doi:10.3390/CELLS12232726

[13] Zefferino R, Di Gioia S, Conese M. Molecular links between endocrine, nervous and immune system during chronic stress. *Brain Behav*. 2020;11(2):e01960. doi:10.1002/BRB3.1960

[14] Dębski J, Przybyłowski J, Skibiak K, Czerwińska M, Walędziak M, Różańska-Walędziak A. Depression and Obesity—Do We Know Everything about It? A Narrative Review. *Nutrients*. 2024;16(19):3383. doi:10.3390/NU16193383

[15] Zhou L, Wang T, Yu Y, et al. The etiology of poststroke-depression: a hypothesis involving HPA axis. *Biomedicine & Pharmacotherapy*. 2022;151:113146. doi:10.1016/J.BIOPHA.2022.113146

[16] Koschke M, Boettger MK, Schulz S, et al. Autonomy of autonomic dysfunction in major depression. *Psychosom Med*. 2009;71(8):852-860. doi:10.1097/PSY.0b013e3181b8bb7a

[17] Penninx BWJH, Milaneschi Y, Lamers F, Vogelzangs N. Understanding the somatic consequences of depression: biological mechanisms and the role of depression symptom profile. *BMC Med*. 2013;11(1):129. doi:10.1186/1741-7015-11-129

[18] Miller AH, Raison CL. The role of inflammation in depression: from evolutionary imperative to modern treatment target. *Nat Rev Immunol*. 2016;16(1):22. doi:10.1038/NRI.2015.5

[19] Bauer ME, Teixeira AL. Inflammation in psychiatric disorders: what comes first? *Ann N Y Acad Sci*. 2019;1437(1):57-67. doi:10.1111/NYAS.13712

[20] Depression. World Health Organization (WHO). Access 11.01.2025. https://www.who.int/health-topics/depression#tab=tab_1

[21] Hare DL, Toukhsati SR, Johansson P, Jaarsma T. Depression and cardiovascular disease: A clinical review. *Eur Heart J*. 2014;35(21):1365-1372. doi:10.1093/eurheartj/eht462

[22] Penninx BWJH. Depression and cardiovascular disease: Epidemiological evidence on their linking mechanisms. *Neurosci Biobehav Rev*. 2017;74:277-286. doi:10.1016/j.neubiorev.2016.07.003

[23] Patterson SL, Marcus M, Goetz M, Vaccarino V, Gooding HC. Depression and Anxiety Are Associated With Cardiovascular Health in Young Adults. *J Am Heart Assoc*. 2022;11(24):27610. doi:10.1161/JAHA.122.027610/FORMAT/EPUB

[24] Meng R, Yu C, Liu N, et al. Association between Depression and All-cause and Cardiovascular Mortality in Chinese Adults. *JAMA Netw Open*. 2020;3(2):e1921043. doi:10.1001/JAMANETWORKOPEN.2019.21043

[25] Krittanawong C, Maitra NS, Qadeer YK, et al. Association of Depression and Cardiovascular Disease. *American Journal of Medicine*. 2023;136(9):881-895. doi:10.1016/j.amjmed.2023.04.036

[26] Shah RM, Doshi S, Shah S, Patel S, Li A, Diamond JA. Impacts of Anxiety and Depression on Clinical Hypertension in Low-Income US Adults. *High Blood Pressure & Cardiovascular Prevention*. 2023;30(4):1. doi:10.1007/S40292-023-00584-3

[27] Yusuf PS, Hawken S, Ôunpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *Lancet*. 2004;364(9438):937-952. doi:10.1016/S0140-6736(04)17018-9

[28] Tobaldini E, Carandina A, Toschi-Dias E, et al. Depression and cardiovascular autonomic control: a matter of vagus and sex paradox. *Neurosci Biobehav Rev*. 2020;116:154-161. doi:10.1016/j.neubiorev.2020.06.029

[29] Kumar C, Sakshi P, Sinha N, Sunita, Kumar T. HRV changes in young adults with depression. *J Family Med Prim Care*. 2024;13(7):2585-2588. doi:10.4103/jfmpc.jfmpc_926_23

[30] Luppino FS, De Wit LM, Bouvy PF, et al. *Overweight, Obesity, and Depression A Systematic Review and Meta-Analysis of Longitudinal Studies*. Vol 67.

[31] Mannan M, Mamun A, Doi S, Clavarino A. Prospective Associations between Depression and Obesity for Adolescent Males and Females- A Systematic Review and Meta-

Analysis of Longitudinal Studies. *PLoS One*. 2016;11(6):e0157240. doi:10.1371/JOURNAL.PONE.0157240

[32] Kumar RB, Aronne LJ. Iatrogenic Obesity. *Endocrinol Metab Clin North Am*. 2020;49(2):265-273. doi:10.1016/j.ecl.2020.02.010

[33] Gill H, Gill B, El-Halabi S, et al. Antidepressant Medications and Weight Change: A Narrative Review. *Obesity*. 2020;28(11):2064-2072. doi:10.1002/oby.22969

[34] Diabetes. World Health Organization (WHO). Access 8.01.2025. https://www.who.int/news-room/fact-sheets/detail/diabetes

[35] Depressive disorder (depression). World Health Organization (WHO). Access 9.01.2025. https://www.who.int/news-room/fact-sheets/detail/depression

[36] Khawagi WY, Al-kuraishy HM, Hussein NR, et al. Depression and type 2 diabetes: A causal relationship and mechanistic pathway. *Diabetes Obes Metab*. 2024;26(8):3031-3044. doi:10.1111/DOM.15630

[37] Basiri R, Seidu B, Rudich M. Exploring the Interrelationships between Diabetes, Nutrition, Anxiety, and Depression: Implications for Treatment and Prevention Strategies. *Nutrients*. 2023;15(19):4226. doi:10.3390/NU15194226

[38] Possidente C, Fanelli G, Serretti A, Fabbri C. Clinical insights into the cross-link between mood disorders and type 2 diabetes: A review of longitudinal studies and Mendelian randomisation analyses. *Neurosci Biobehav Rev*. 2023;152:105298. doi:10.1016/J.NEUBIOREV.2023.105298

[39] Fanelli G, Serretti A. Depression, antidepressants, and insulin resistance: which link? *European Neuropsychopharmacology*. 2022;60:4-6. doi:10.1016/J.EURONEURO.2022.04.011

[40] Fernandes BS, Salagre E, Enduru N, Grande I, Vieta E, Zhao Z. Insulin resistance in depression: A large meta-analysis of metabolic parameters and variation. *Neurosci Biobehav Rev*. 2022;139:104758. doi:10.1016/J.NEUBIOREV.2022.104758

[41] Shi L, Ren J, Jin K, Li J. Depression and risk of infectious diseases: A mendelian randomization study. *Transl Psychiatry*. 2024;14(1):245. doi:10.1038/S41398-024-02950-8

[42] Adams TB, Wharton CM, Quilter L, Hirsch T. The association between mental health and acute infectious illness among a national sample of 18- to 24-year-old college students. *Journal of American College Health*. 2008;56(6):657-664. doi:10.3200/JACH.56.6.657-664

[43] Bortolato B, Hyphantis TN, Valpione S, et al. Depression in cancer: The many biobehavioral pathways driving tumor progression. *Cancer Treat Rev*. 2017;52:58-70. doi:10.1016/J.CTRV.2016.11.004

[44] Wang YH, Li JQ, Shi JF, et al. Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies. *Mol Psychiatry*. 2020;25(7):1487-1499. doi:10.1038/s41380-019-0595-x

[45] Mössinger H, Kostev K. Depression Is Associated with an Increased Risk of Subsequent Cancer Diagnosis: A Retrospective Cohort Study with 235,404 Patients. *Brain Sci*. 2023;13(2):302. doi:10.3390/BRAINSCI13020302/S1

[46] Dai S, Mo Y, Wang Y, et al. Chronic Stress Promotes Cancer Development. *Front Oncol*. 2020;10:1492. doi:10.3389/FONC.2020.01492

[47] Young K, Singh G. Biological Mechanisms of Cancer-Induced Depression. *Front Psychiatry*. 2018;9(JUL):299. doi:10.3389/FPSYT.2018.00299