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## INFLUENCE OF DEPRESSION ON STROKE RISK FACTORS – LITERATURE REVIEW

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### ABSTRACT

**Aims:** This review aims to analyse available literature on the influence of depression on risk factors of a stroke. For the purposes of this study, we treated stroke as a unified category, without differentiating between specific subtypes. The goal of this study is to provide insight into potential risks of overlooking depression in patients with heightened risk of stroke, for example patients with atrial fibrillation.

**Methods:** Data was collected by searching publicly available database Pubmed, using articles in English, no older than 2004.

**Results:** While depression is often overlooked as a risk factor of stroke, available data implies that it increases the risk of other, more notable risk factors.

**Conclusion:** Depression should be taken into consideration by health professionals, when assessing the risk of stroke. It contributes to the elevation of risk for prevalent risk factors. It should be screened for, diagnosed and treated in patients with high risk of stroke, for example, in patients with atrial fibrillation.

### INTRODUCTION

Stroke is one of the leading causes of deaths worldwide [1]. Furthermore, it is also one of the biggest contributors to disability [2]. It imposes a significant burden on healthcare systems, lowers the quality of life of patients and reduces the independence of the patients. There is a great amount of stroke risk factors identified, many of which are modifiable. These risk factors include obesity, physical inactivity, alcoholism, diabetes, hypertension, smoking, dyslipidaemia, sleep apnea and coronary artery disease [3]. While these factors been thoroughly researched and described, some diseases that contribute to the risk of their occurrence in the first place have been overlooked. One potential illness increasing that risk is depression.

An ever-growing amount of research indicates that depression increases the risk of stroke, contributing as a factor on its own, elevating the risk of first-ever stroke by 40% in the general population [4]. It is particularly challenging to design an analysis that examines whether depression increases the risk of stroke as an independent factor or whether it just elevates the risk of other risk factors, however most of research suggests that this influence is multifactorial [5].

In this review we focused on the analysis of the influence of depression on risk factors of a stroke, specifically we investigated whether depression increases the possibility of these factors occurring. We aim to provide healthcare professionals with more tools to appropriately take care of patients with heightened risk of stroke, like patients with atrial fibrillation[6].

Even though link between depression and increased risk of stroke is well-established, it is not as often listed as other, somatic, risk factors. That often results in it being overlooked in usual screenings for potential reductions in risk. That is why it is important to highlight, how it influences the somatic risk factors. Whether it is listed as officially listed as risk factor or not, it's association with other risk factors makes it practically obligatory in screening for stroke risk factors. Understanding these associations is imperative in order to provide every patients with proper care and holistic approach.

Considering the prevalence of depression, estimated to affect 5% of adults in the world [7] and around 3% in Poland([8]. It is imperative for doctors and other health specialists to understand the impact this illness has on other ailments. Expanding our understanding of depressions influence on stroke risk factors offers valuable insight into prevention strategies. It allows for more effective screening, diagnosing and management of patients with heightened stroke risk. We hope that this review will help health practitioners provide holistic approach in stroke prevention, emphasizing the importance of early detection of conditions that may increase the possibility of unfavourable outcome.

## METHODS

In order to write the review, we have searched multiple Internet-based medical article databases PubMed, and selected relevant literature available in English. We have used the keywords "stroke", "depression", "risk factors". The studies were carefully reviewed and analysed in order to ensure the presented data was of the highest possible quality. We excluded the articles that were before year 2004. We have given priority to large scale reviews and meta-analyses and excluded case reports and non-relevant articles.

## RESULTS

A variety of risk factors for stroke have been identified, though the exact list may vary across organizations. For our study, we have chosen to focus on the following factors, that significantly contribute to stroke risk: obesity, physical inactivity, excessive alcohol consumption, diabetes, hypertension, smoking, dyslipidemia, sleep apnea, and coronary artery disease. [3]

### OBESITY

Obesity is one of the most important risk factors of a stroke [9]. Although the importance of healthy diet, exercise and healthy habits is the cornerstone of every stroke prevention recommendations, the significance of screening and properly treating depression as a factor increasing the chance of becoming obese is often overlooked. According to Milaneschi Y et al. (2019) [10], there are many biological mechanisms shared by obesity and depression in their pathogenesis. In their analysis of six metanalyses combining up to 26 cross-sectional studies every single one of them confirmed a positive association between depression and obesity. Other studies they reference, like Luppino FS et al.(2010) [11], confirm that the relationship between obesity and depression is bilateral- obesity longitudinally increases the risk of developing depression, and vice versa, depression increases the risk of subsequent obesity. The conclusion drawn from these information is that there is no holistic treatment of obesity without screening for depression and treating its symptoms. These two diseases increase bilaterally the risk of one causing the other in a patient and need to be treated simultaneously in order to achieve optimal results.

*Figure 1. Results of Milaneschi Y et al. (2019) analysis of different studies on association between depression and obesity.*

Study	Nr studies (sample size)	Depression definition	Obesity definition	Pooled effect size/Odds ratio (95% CI)	Specific details
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De Wit et al. (2010)	N = 8 [166,865]	Symptoms	BMI ≥ 30 or WC ≥ 88 (♀)/102 (♂)	1.23 (1.03–1.47)	
De Wit et al. (2010)	N = 9 [37,638]	Clin Diag	BMI ≥ 30 or WC ≥ 88 (♀)/102 (♂)	1.14 (0.90–1.44)	
Xu et al. (2011)	N = 12 [27,445]	Symptoms	WHR > 1 or WC ≥ 88 (♀)/102 (♂)	1.41 (1.22–1.64)	Only abdominal obesity indices
Xu et al. (2011)	N = 3 [7387]	Clin Diag	WHR > 1 or WC ≥ 88 (♀)/102 (♂)	1.30 (0.96–1.75)	
Abou Abbas et al. (2015)	N = 8 [12,641]	Combined sympt. or SR disease or Clin Diag	BMI ≥ 30 or WHR ≥ 0.84	1.27 (1.11–1.44)	Only studies from the Middle-East
Pereira-Miranda et al. (2015)	N = 9 [171,701]	Combined sympt. or Clin Diag	BMI ≥ 30	1.32 (1.26–1.38)	
Quek et al. (2017)	N = 7 [22,896]	Clin Diag	BMI > 95th p. or > age-specific cut-offs	1.34 (1.10–1.64)	Only childhood or adolescent samples
Jung et al. (2017)	N = 18 [371,897]	Symptoms	BMI ≥ 30	1.29 (1.18–1.42)	
Jung et al. (2017)	N = 8 [176,510]	Clin Diag	BMI ≥ 30	1.16 (1.02–1.32)	
Blaine (2008)	N = 23 [33,690]	Combined sympt. or Clin Diag	BMI weight change or onset of BMI ≥ 30	1.19 (1.14–1.24)	
Luppino et al. (2010)	N = 5 [52,421]	Symptoms	BMI ≥ 30	1.36 (1.03–1.80)	Adolescent and adult samples
Luppino et al. (2010)	N = 3 [2966]	Clin Diag	BMI ≥ 30	2.15 (1.48–3.12)	
Luppino et al. (2010)	N = 5 [3643]	Symptoms	BMI ≥ 30	1.48 (1.17–1.87)	
Luppino et al. (2010)	N = 4 [2991]	Clin Diag	BMI ≥ 30	1.71 (1.33–2.19)	

Mannan et al. (2016)	N = 12 [126,594]	Combined sympt. or Clin Diag	BMI ≥ 30	1.18 (1.04-1.35)	Adult samples only
Mannan et al. (2016)	N = 9 [85,358]	Combined sympt. or Clin Diag	BMI ≥ 30	1.37 (1.17-1.48)	
Mannan et al. (2016)	N = 6 [20,855]	Combined sympt. or Clin Diag	BMI ≥ 30	1.40 (1.16-1.70)	Adolescent samples only
Mannan et al. (2016)	N = 7 [16,373]	Combined sympt. or Clin Diag	BMI ≥ 30	1.70 (1.40-2.07)	

### PHYSICAL INACTIVITY

Physical activity is one of the most vital practices that should be encouraged by health practitioners in nearly every scenario. Due to the strong positive connection between physical inactivity and the increased risk of stroke[12], it is absolutely crucial that some kind of physical activity is implemented in patients with heightened risk of stroke, for example patients with atrial fibrillation. Although the link between physical inactivity and subsequent depression is well known[13] and mental health recommendations address this issue, there is not a lot of data showing the influence of depression on physical activity. Roshanaei-Moghaddam B et al. 2009[14] in their systemic review of eleven studies described that eight of these studies had evidence, that depression at baseline assesment was significantly associated with decline in the level of physical activity

Figure 2. Results of Roshanaei-Moghaddam B et al. 2009 study on influence of depression on physical inactivity

Study	Number of participants	Population characteristics	Specific details	Results
Van Gool et al.	1280	Dutch middle - aged and elderly	6-year gap between baseline assesment and follow-up	No significant relationship between baseline depression and changes in physical activity. Emerging depression patients between baseline and follow-up had 62% increased risk of becoming sedentary.
Katon et al.	2759	Primary care patients with diabetes	5-year gap between baseline assesment and followup	3 groups - depressed at baseline and followup, depressed at baseline but improved depression symptoms at followup, No symptoms of depression at baseline but signs of depression during followup- had greater chance of

				becoming sedentary compared to the group that was never depressed
Juarbe et al.	232	premenopausal Latina and White women.	1-year gap between baseline and follow-up	Pearson moment correlation coefficient did not show a significant association between baseline depression and the subsequent level of physical activity
Allan et al	388	individuals hospitalized for an acute coronary syndrome event	1-year gap between baseline and follow-up	depression during the hospitalization was significantly associated with decreased leisure activities
Brummett et al.	983	middle-aged patients with significant coronary artery disease who were admitted for their first cardiac catheterization	15- year gap between baseline and follow-up	baseline depressive symptoms were positively associated with a pattern of subsequent sedentary behavior.
Mayou et al.	224	Subjects after hospitalization for MI.	After baseline assessment follow-ups after 3 and 12 months	Compared to nondistressed individuals, a higher percentage of those with anxiety and depression during hospitalization had a significant decrease in exercise at 3 months and 1 year.
Harris et al.	424	Depressed patients	10- year gap between baseline assessment and follow-up	There was no evidence that baseline depression influenced the trajectory of physical exercise over time.
Ziegelstein et al.	204	patients who were hospitalized for acute myocardial infarction	4-month gap between baseline assessment and follow-up	In comparison to patients without mood disorder, patients with baseline major depressive disorder and/or dysthymia were significantly less likely to follow the prescribed physical activity

				regimens.
Guiry et al.	264	patients who were hospitalized for an acute coronary event	1- year gap between baseline assessment and follow-up	Depression at baseline was significantly associated with decreased adherence to exercise recommendations
Kaplan et al.	4025	community-dwelling respondents	9-year longitudinal epidemiologic study	Baseline depression was significantly associated with a future decline in physical activity in women with a similar but nonsignificant trend for men
Panagiotakos et al.	1955	community dwellers.	5- year gap between baseline assessment and follow-up	depression and anxiety were strong predictors of those who were sedentary at both baseline and follow-up and also of those who became more sedentary over time.

### ALCOHOLISM

Alcoholism is a well-known risk factor of stroke[15]. Generally, population as a whole is discouraged from drinking, especially population with heightened risk of stroke. However, health professionals tend to not look for factors, that may increase the possibility of a patient being non complainant with these kind of recommendations. Puddephatt JA et al. (2021) [16] in their analysis found that individuals with a common mental health disorders like depression and anxiety had a twofold increase in the odds of reporting an alcohol use disorder. That means that in order to heighten the likelihood of abstinence in patients, mental screening and adequate treatment of depression are essential.

### DIABETES

Diabetes is one of most commonly diagnosed diseases in developed countries. According to WHO (2023) [17] [In 2022](#), 14% of adults aged 18 years and older were living with diabetes. It also a well-known risk factor of stroke [18]. Considering this, it is imperative to consider multiple different factors influencing the risk of developing diabetes. In their work, Khawagi WY et al. (2024) [19] explain probable relationship between increased probability of developing diabetes in patients with depression. Moreover, they suggest that use of specific antidepressants, like fluoxetine, should be encouraged, due to their ability to increase glucose homeostasis. Suitable management of depression has been shown to reduce the risk of developing type 2 diabetes, which in turn may lower the subsequent risk of stroke.

### HIGH BLOOD PRESSURE

High blood pressure plays a part in around half of strokes [20]. It is one of the most common factors that are addressed when dealing with stroke risk. It also is one of the most prevalent diseases[21]. According to WHO (2023), it affects an estimated 1.28 billion adults aged 30–79 years worldwide. Holistic, non-invasive treatment and prevention of this ailment is one of the most important tasks of nearly every healthcare professional. This is why it is important to look for different factors that may influence the risk of hypertension incidence. According to Meng L. et al (2012) [22] depression increases risk of hypertension incidence with adjusted relative risk being 1.42. Their meta- analysis supports that depression can be treated as independent risk factor of hypertension, therefore it should be taken into consideration when approaching patients with higher stroke risk.

## SMOKING

Nicotine consumption is one of the most prevalent addictions in the world. According to WHO (2023) [23], there are around 1.3 billion tobacco users worldwide. Smoking is linked to more than 20 types of cancer and it kills up to half of its users if they don't quit. One of the consequences of smoking is increased risk of stroke [24]. Addressing issues that may increase risk of a patient becoming a tobacco user seems to be imperative to adequate control of stroke risk. In their systemic review Fluharty M et al.(2017) [25] analysed associations between smoking, depression and anxiety. They reported that in 14 studies investigating the association of baseline depression with subsequent smoking onset, 10 found evidence to support this association, while four found no evidence of an association. Furthermore, they found out that out of 37 studies that measured smoking status, 33 found evidence that supported the association between baseline depression and smoking status. In other categories investigated, most of the studies had results suggesting that depression leads to greater smoking heaviness, tobacco dependence but surprisingly not to increasing smoking trajectory. Conclusion drawn from this study is that health practitioners, in order to help with smoking cessation or to prevent smoking onset, need to screen for depression in patients.

Figure 3. Studies investigating association between baseline depression and different smoking categories from Fluharty M et al.

Category	Depression into smoking association investigated	Bidirectional association investigated	Number of studies with results showing positive association
Smoking onset	13	1	10 (71%)
Smoking status	29	8	33 (89%)
Smoking heaviness	9	2	8 (73%)
Tobacco dependence	12	1	12 (92%)
Smoking trajectory	7	0	1 (14%)

## DYSLIPIDAEMIA

Dyslipidaemia is associated with high risk of stroke, especially high LDL and non HDL lipid levels [26]. Management of lipid levels is one of more important and common practices in healthcare systems worldwide. Therefore, it is important to look at the factors that may increase risk of dyslipidaemia. In their study Guan J et al. (2024) [27] found that serum levels of triglycerides, LDL and total cholesterol, were higher in congenital heart disease patients with depression compared to those without depression, while HDL levels were lower in the depressed group. However, it is difficult to conclude whether dyslipidaemia increases the risk factor of depression, the opposite association or if the relationship between two conditions is bilateral. Further research is required in this topic, however, available data urges us to always consider holistic approach when taking care of patients with unbalanced lipid levels

## SLEEP APNEA

Sleep apnea is a well-documented independent risk factor of a stroke [28]. It is also widely known as a risk factor of depression[29]. It also important to point out that these two conditions have very similar symptoms, often masking each other's presence. However, there is little data available whether depression can lead to sleep apnea. Study conducted by Chen G et al (2021) [30] suggests that depression slightly increases the risk of sleep apnea, however more data is required. Regardless, when dealing with high risk of stroke patients with symptoms suggesting depression, health professionals should rule out sleep apnea, and treat depression adequately to decrease risk of developing sleep apnea and subsequently decrease the risk of stroke.

## CORONARY ARTERY DISEASE

One of the most well known risk factors of stroke is coronary artery disease [31]. There is also a growing amount of research correlating mental health issues and coronary artery disease. In their study, De Hert M

et al (2018) [32]. analysed available literature to review their influence on each other. They reported that relationship between the two diseases is bidirectional, with each increasing the risk of the other. According to their analysis depression is up to four times more prevalent in patients with coronary artery disease and on the other hand, risk of developing coronary heart disease is 30% greater in population affected by depression. Additionally, depression is also reported as a risk factor for mortality in patients with coronary heart disease [33]. This implies that there is no adequate medical care for patients at risk of developing coronary artery disease, without screening for and treating potential depression.

## DISCUSSION

Available data suggest that depression influences risk factors of stroke. However, there seems to be lack of protocols for adequate screening of patients. Potential pharmaceutical therapies of depression may also put patients in danger of side effects of drugs. Consequently it may be beneficial to try non-pharmaceutical treatment. Nevertheless, lack of treatment algorithms in this area means that the most precise and beneficial approach for high stroke risk patients remains to be specified. Each case must be treated holistically, and every treatment should be considered carefully, especially if care-giver decides that a treatment needs to include pharmaceuticals. Every patient is different and the responsibility for adequate choice remains on the health practitioner.

## CONCLUSIONS

1. Depression is positively associated with very single stroke risk factor. For some of the, like for example for smoking, the association seems to be bilateral.
2. Even though some organisations list is as one of the risk factors, this approach is not as widely spread as purely somatic risk factors.
3. Whether it is a considered a risk factor by itself or not, due to influence that it has over somatic risk factors, it is impossible to properly asses and treat somatic risk factors without diligent screening for symptoms of depression

Healthcare professionals should recognize depression as a crucial part of stroke risk assessment. Screening for mental health issues, early diagnosis and treatment in patients with heightened stroke risk, such as those with atrial fibrillation, should be treated with due diligence, in order to provide patient with holistic approach.

## AUTHORS CONTRIBUTIONS

Conceptualization, MB, and AB; methodology, WK; software, AZ; check, MS, MK and KK; formal analysis, MB; investigation, MB; resources, AB; data curation, AZ; writing - rough preparation, KK; writing - review and editing, WK; visualization, WK; supervision, KK; project administration, KK; receiving funding, does not apply All authors have read and agreed with the published version of the manuscript.

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## CONFLICT OF INTEREST

The authors declare no competing interests.

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