SZEROCKI, Jan, MILEWSKA-PLIS, Katarzyna, WINKOWSKA, Alicja, GRUDINA, Alina, KŁAK, Igor, GRODZICKA , Joanna, BARTNIK, Katarzyna, HERIAN, Mariola, KARALUS, Monika and CURYŁO, Weronika. Gastroesophageal Reflux Disease and Its Associations with Depression, Other Psychiatric Disorders and Patient Quality of Life: A Literature Review. Quality in Sport. 2025;43:62331. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.43.62331
https://apcz.umk.pl/QS/article/view/62331

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a 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 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 interest regarding the publication of this paper.
Received: 15.06.2025. Revised: 11.07.2025. Accepted: 11.07.2025. Published: 14.07.2025.

Gastroesophageal Reflux Disease and Its Associations with Depression, Other Psychiatric Disorders and Patient Quality of Life: A Literature Review

Jan Szerocki
Independent Public Health Care Center Of the Ministry of Internal Affairs and Administration in Cracow; Kronikarza Galla 25, 30-053 Kraków, Poland
https://orcid.org/0009-0002-2107-9777
jasias99@interia.pl

Katarzyna Milewska-Plis
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Medyków 12, 40-055 Katowice, Poland
https://orcid.org/0009-0008-9931-5294
milewska.k26@gmail.com

Alicja Winkowska
Independent Public Health Care Center Of the Ministry of Internal Affairs and Administration in Cracow; Kronikarza Galla 25, 30-053 Kraków, Poland
https://orcid.org/0009-0005-2050-0031
alawinkowska@gmail.com

Alina Grudina
University Hospital in Cracow, Jakubowskiego 2, 30-688 Kraków, Poland
https://orcid.org/0009-0006-1280-7006
grudinaalina@gmai.com

Igor Kłak
Independent Public Health Care Center Of the Ministry of Internal Affairs and Administration in Cracow; Kronikarza Galla 25, 30-053 Kraków, Poland
https://orcid.org/0009-0005-3654-6755
igor.klak98@gmail.com

Joanna Grodzicka
Independent Public Healthcare Institution of the Ministry of the Interior and Administration in Lodz, Północna 42, 91-425 Łódź, Poland
joannagrodzicka2@gmail.com
https://orcid.org/0009-0008-3513-9607

Katarzyna Bartnik
5th Military Hospital with Polyclinic in Cracow: Cracow, Wrocławska 1-3 Street 30-901 Kraków, Małopolska, Poland
https://orcid.org/0009-0005-9095-5875
kasiabartnik08@gmail.com

Mariola Herian
University Hospital in Cracow, Jakubowskiego 2, 30-688 Kraków, Poland
https://orcid.org/0009-0005-4958-1410
mariola.herian@gmail.com

Monika Karalus
Independent Public Clinical Hospital named after Prof. W. Orłowski, Center of Postgraduate Medical Education, Czerniakowska 231, 00-416 Warsaw, Poland
https://orcid.org/0009-0005-9355-4698
m.karalus@protonmail.com

Weronika Curyło
Faculty of Medical Sciences in Katowice, Medical University of Silesia, 40-055 Katowice, Poland
https://orcid.org/0009-0007-0254-3569
weronikaccurylo@gmail.com

Corresponding Author: Jan Szerocki; jasias99@interia.pl

Abstract
Gastroesophageal reflux disease (GERD) is a prevalent gastrointestinal disorder whose incidence has been increasing in recent years. Due to its potential extraesophageal manifestations, diagnosing GERD can be challenging. Emerging evidence suggests that GERD may have significant implications not only in the digestive tract, including effects on mental health. This review investigates the potential associations between GERD and psychiatric disorders such as depression, anxiety, bipolar disorder and sleep disturbances, as well as its impact on quality of life and productivity. Relevant literature was found through databases including PubMed, ResearchGate and Google Scholar with a focus on meta-analyses and systematic reviews. The findings indicate that GERD is associated with a higher risk of mental health disorders, particularly depression and sleep disorders. These relationships may be

bidirectional. Additionally, recent studies highlight promising non-pharmacological interventions that may alleviate GERD symptoms.
Understanding the psychological consequences of GERD and integrating mental health screening into gastroenterological practice could potentially improve patient outcomes. However, further research is needed to clarify the mechanisms linking GERD and mental health.

Keywords: Gastroesophageal Reflux; Depressive Disorder; Mental Health; Quality of Life

Introduction

Gastroesophageal reflux disease (GERD) is a seemingly benign yet insidious condition affecting the upper gastrointestinal tract. Its pathophysiology is complex, but several key factors are believed to play a major role in its development. These include lower esophageal sphincter (LES) insufficiency, transient LES relaxations (TLESR), which are suspected to be the predominant mechanism in many patients, hiatal hernia, esophageal dysmotility and visceral hypersensitivity (Tack & Pandolfino, 2018).
Gastroesophageal reflux disease symptoms can be broadly categorized into gastrointestinal and extraesophageal manifestations. The most typical gastrointestinal symptoms are heartburn and regurgitation of gastric contents into the esophagus, which may affect up to 13.3% of the general population (Eusebi, Ratnakumaran, Yuan, et al., 2018). Dyspepsia is also noteworthy, occurring in as many as 43.9% of individuals with gastroesophageal reflux disease. Furthermore, those with gastroesophageal reflux disease symptoms are approximately seven times more likely to experience dyspepsia compared to individuals without gastroesophageal reflux disease (Eusebi, Ratnakumaran, Bazzoli, et al., 2018).
There is growing recognition of GERD's extraesophageal symptoms, such as chronic cough, asthma, laryngopharyngeal reflux (LPR) and frequent throat clearing. These symptoms can pose significant challenges in routine diagnostic procedures for gastroesophageal reflux disease (Sidhwa et al., 2017).
The global prevalence of gastroesophageal reflux disease is estimated at 13.98%, although this figure varies considerably by region and country; for example: 4.16% in China and 22.4% in Turkey (Nirwan et al., 2020) . Identified risk factors include tobacco smoking, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and obesity (Nirwan et al., 2020).
Importantly, the burden of gastroesophageal reflux disease has changed over the past few decades. A study comparing its prevalence between 1990 and 2019 revealed shifts in disease frequency associated with levels of socioeconomic development and geographic location (Nirwan et al., 2020) .
Given the global prevalence of gastroesophageal reflux disease and the diagnostic complexity (especially in cases involving extraesophageal symptoms) (Nirwan et al., 2020) this review aims to explore the co-occurrence of gastroesophageal reflux disease and psychiatric disorders. This perspective may shed new light on possible contributors to the rising incidence of depression and other mental health conditions.

Diagnosis of Gastroesophageal Reflux Disease

The diagnostic process for gastroesophageal reflux disease (GERD) should ideally begin in the primary care setting. In cases without clinical uncertainty and in the absence of alarm symptoms, a presumptive diagnosis may be made based on a thorough medical history and physical examination. In patients presenting with typical symptoms, an 8-week trial of empiric proton pump inhibitor (PPI) therapy (administered once daily before meals) is recommended. If the patient responds well to this treatment, continuation is not advised, and the positive response supports the clinical diagnosis of gastroesophageal reflux disease, indicating that further diagnostic evaluation such as endoscopy is not immediately necessary(Katz et al., 2022).

Physicians should be familiar with the alarm symptoms associated with gastroesophageal reflux disease. These include dysphagia, odynophagia, anemia, unintentional weight loss, gastrointestinal bleeding, persistent vomiting and the new onset of symptoms after the age of 50 (Katz et al., 2022). The presence of any of these alarm features warrants prompt upper endoscopy.

There are instances where PPI therapy is either unavailable or contraindicated. In such cases, diagnostic tools such as the GerdQ questionnaire may be useful. The GerdQ consists of six questions evaluating the frequency of gastroesophageal reflux disease symptoms, their impact on the patient's quality of life, and the need for medications (Velanovich, 2007). Despite its moderate sensitivity and specificity, the GerdQ remains a practical diagnostic aid, particularly when empirical PPI testing is not feasible (Simadibrata et al., 2023).

A number of studies have compared the diagnostic accuracy of upper endoscopy with esophageal pH monitoring and pH impedance monitoring. These modalities have demonstrated high sensitivity and specificity, especially in cases of gastroesophageal reflux disease with extraesophageal symptoms (M. Zhang et al., 2019). Of particular interest are findings on esophageal mucosal impedance and baseline impedance, which have shown diagnostic accuracy comparable to that of pH/pH impedance monitoring and endoscopy.

Treatment of Gastroesophageal Reflux Disease

The treatment of gastroesophageal reflux disease (GERD) is a critical issue, not only because of its potential complications but also due to its significant impact on patients' quality of life (both of which will be discussed in subsequent sections) This section focuses on well-established therapeutic interventions, although recent literature increasingly highlights promising non-pharmacological strategies that may alleviate gastroesophageal reflux disease symptoms.

Proton pump inhibitors (PPIs) remain an important part of pharmacological therapy. One study suggests that a full/standard dose of esomeprazole may be recommended as first-line therapy in adults without alarm symptoms for a duration of 4-8 weeks (C. Zhang et al., 2017). This regimen was associated with symptom relief and was generally well tolerated. However, other

studies have reported some differences: for example, twice-daily PPI therapy showed superior endoscopic healing rates compared to once-daily dosing, though no significant differences were observed in symptom relief or 24-hour pH monitoring outcomes (H. Zhang et al., 2017).

It is important to note that PPIs should not be regarded as an ideal long-term solution. Prolonged use has been associated with a range of complications, including micronutrient deficiencies (e.g. hypomagnesemia, anemia, vitamin B12 deficiency, hypocalcemia) and a potential increased risk of various cancers (gastric, pancreatic, colorectal, hepatic). Additionally, an elevated risk of dementia has been suggested, although some studies have failed to confirm a definitive link (Maideen, 2023).

Interestingly, certain sources have reported less obvious associations between long-term PPI use and adverse outcomes, such as an increased risk of pneumonia and hip fractures (Islam et al., 2018). The latter may be a secondary consequence of PPI-induced micronutrient deficiencies, such as hypocalcemia (Maideen, 2023).

Given these potential risks (Islam et al., 2018; Maideen, 2023) , lifestyle modifications remain a vital component of GERD management. Key recommendations include weight normalization in overweight or obese patients and avoiding food intake 2-3 hours before bedtime. Head-of-bed elevation during sleep is also advised. Smoking cessation and the avoidance of tobacco products are strongly encouraged (Kahrilas et al., 2008), as these measures not only alleviate gastroesophageal reflux disease symptoms but also provide broader health benefits. Patients should also identify and eliminate specific dietary “trigger foods” that exacerbate their individual symptoms (Kahrilas et al., 2008).

Surgical treatment - antireflux surgery - may be considered in patients with a confirmed gastroesophageal reflux disease diagnosis who do not respond to PPI therapy or in those for whom long-term PPI use poses unacceptable risks (McKinley et al., 2021). These procedures aim to mechanically enhance the function of the lower esophageal sphincter, thereby preventing gastric content from refluxing into the esophagus. Evidence suggests that surgical interventions may outperform pharmacological treatment in terms of symptom control and improvements in quality of life. However, it is noteworthy that some patients continue to require PPI therapy postoperatively (McKinley et al., 2021). Various surgical techniques exist - such as posterior partial fundoplication, total posterior fundoplication, and anterior 90° fundoplication - with differing efficacy profiles (Markar et al., 2022).

In conclusion, each therapeutic approach carries its own unique set of benefits and limitations and treatment strategies must be carefully tailored to the individual needs and circumstances of the patient. What works well for one person may not be as effective for another, making a personalized approach essential for optimizing outcomes. Lifestyle modifications play an essential role and should not be underestimated. Regular education of the patients regarding the impact of lifestyle factors on gastroesophageal reflux disease is especially valuable in achieving long-term symptom control.

Epidemiology of Depression

Depression has become a major public health concern in contemporary society. Notably, there has been a substantial upward trend in its global incidence over the past two decades. For instance, the global number of individuals affected by depression increased from 182,183,358 in 1990 to 290,185,742 in 2019 (Liu et al., 2024). Significant variation in depression rates has been observed depending on the country of residence; however, a decline in incidence was noted in only 23 countries, including Lithuania and Bosnia and Herzegovina (Liu et al., 2024).

Numerous studies have documented the prevalence of depression across different demographic and social groups over specific time periods. Of particular concern is the increase in depressive disorders among women of reproductive age, where prevalence rose by 67.6% between 1990 and 2021. Notably, 42.2% of this increase occurred between 1990 and 2019, with an additional 17.9% between 2019 and 2021, suggesting a significant impact of the COVID-19 pandemic (Dai et al., 2025) . When examining depression in men, one study focusing on Iranian males aged 15 to 87 years found that 13.9% had experienced Major Depressive Disorder (MDD) (Hajebi et al., 2025).

Given the alarming number of individuals currently affected by depression and the persistent increase in incidence over the last two decades, it is crucial to investigate the potential comorbidity of depression with other highly prevalent disorders.

In the following sections, this review will explore evidence supporting the co-occurrence of gastroesophageal reflux disease (GERD) and depression. Additionally, it will examine the broader health consequences of gastroesophageal reflux disease that may indirectly contribute to an increased risk of developing depressive symptoms.

Gastroesophageal Reflux Disease and Depression

In my view one of the most interesting aspects to consider when examining gastroesophageal reflux disease (GERD) is the high prevalence of anxiety and depressive symptoms among affected individuals. Both anxiety and depression are significantly more common in patients with gastroesophageal reflux disease compared to healthy control groups (Zamani et al., 2023) . In fact, studies have reported that as many as one in three individuals with gastroesophageal reflux disease may experience symptoms of anxiety or depression (Zamani et al., 2023).

Cohort studies have demonstrated an increased risk of developing anxiety and depressive symptoms in patients diagnosed with gastroesophageal reflux disease, and conversely, individuals with pre-existing anxiety or depressive disorders also show an elevated risk of developing gastroesophageal reflux disease (Zamani et al., 2023). Moreover, evidence from genetic studies suggests that genetically predicted major depressive disorder may contribute to an increased risk of several gastrointestinal conditions, including GERD (Chen et al., 2023). These findings indicate a bidirectional association between gastroesophageal reflux disease and depressive symptoms, emphasizing the importance of recognizing this overlap in clinical practice.

From a broader perspective, both gastroesophageal reflux disease and depression have shown increasing prevalence over the past two decades (N. Li et al., 2023; Liu et al., 2024). Considering the mutual reinforcement of risk between these two conditions, one could speculate

about the presence of a vicious cycle: a rising incidence of gastroesophageal reflux disease contributing to higher rates of depression, and vice versa. While this hypothesis is supported by current data trends, it remains speculative and would require further epidemiological and analytical studies to be substantiated.

Additionally, it is important to note the established association between gastroesophageal reflux disease and other psychiatric disorders. A noteworthy example is the bidirectional relationship observed between gastroesophageal reflux disease and bipolar disorder. Individuals with gastroesophageal reflux disease have been shown to have a 2.29-fold increased risk of developing bipolar disorder, whereas those with bipolar disorder exhibit a 2.8-fold higher risk of developing gastroesophageal reflux disease. Interestingly, modifiable risk factors have been identified that influence this relationship, including alcohol misuse among patients with gastroesophageal reflux disease and the use of multiple psychoactive drugs in those with bipolar disorder (Nurita et al., 2025).

Gastroesophageal Reflux Disease and Sleep Disorders

As widely recognized, mental health is influenced by a complex interplay of psychological, physical and genetic factors. A particularly insidious contributor to poor mental health may be gastroesophageal reflux disease (GERD) which has been shown to negatively affect sleep quality. Gastroesophageal reflux disease has been associated with an increased risk of poor sleep quality, sleep disturbances and short sleep duration (Tan et al., 2024). Intriguingly, this relationship appears to be bidirectional: not only can gastroesophageal reflux disease impair sleep but sleep disturbances such as insomnia or short sleep duration have also been shown to significantly increase the risk of gastroesophageal reflux disease (Tan et al., 2024).

The inclusion of sleep disturbances in this discussion is not incidental, because sleep dysfunction represents a major risk factor for the development of depressive disorders. Insomnia has been consistently associated with a higher risk of depression and evidence suggests that the prevention of insomnia in non-depressed individuals may reduce the likelihood of future depressive episodes (L. Li et al., 2016). Similarly, chronically reduced sleep duration has been linked to increased vulnerability to depression (Gao & Gao, 2025).

Gastroesophageal reflux disease (GERD) increases the risk of insomnia and short sleep duration (Tan et al., 2024), both of which are associated with an elevated risk of developing depression (Gao & Gao, 2025; L. Li et al., 2016). Given these associations, an important question arises: Could gastroesophageal reflux disease contribute to an elevated risk of depression via its impact on sleep? This hypothesis is plausible, though it requires further investigation through robust studies and research. However, the existing data support the need for clinical awareness of this potential pathway.

Both gastroesophageal reflux disease and sleep disorders are highly prevalent conditions within the general population (Nirwan et al., 2020; San & Arranz, 2024), affecting a substantial number

of individuals worldwide. Given this widespread occurrence, routine screening for sleep disturbances in patients diagnosed with gastroesophageal reflux disease could be a valuable addition to everyday clinical practice. Such early identification of sleep-related problems in these patients may facilitate timely and targeted intervention, potentially mitigating the risk of sleep-related mental health deterioration and preventing the progression to more severe psychiatric conditions such as major depressive disorder.

Gastroesophageal Reflux Disease and Quality of Life

In modern medicine, there is a growing emphasis not only on extending life expectancy but also on enhancing quality of life (QoL). This shift is reflected in the increasing use of metrics such as the Quality-Adjusted Life Year (QALY) in public health assessments (Touré et al., 2021). Quality of life is a complex, subjective construct, influenced not only by physical health but also by individual values, cultural or religious factors and personal goals. Nonetheless, an important finding is the demonstrated association between higher QoL and reduced mortality risk, supporting the potential prognostic value of QoL measurements (Phyo et al., 2020).

When evaluating the burden of gastroesophageal reflux disease (GERD), research indicates a significant negative impact on patients' quality of life (Fuchs et al., 2022). One interesting study assessed this using the Gastrointestinal Quality of Life Index (GIQLI). Results showed that patients with gastroesophageal reflux disease had a GIQLI score reduced to 55 - 75% of the maximum possible value. The physical domain was most affected, dropping to 55% of the maximum score, while the emotional domain was reduced to 60% (Fuchs et al., 2022).

Among the various manifestations of gastroesophageal reflux disease, nocturnal symptoms appear to be particularly detrimental to daily functioning and overall well-being (Wiklund, 2004) . These nighttime symptoms are often associated with poor sleep quality which in turn disrupts both personal and professional life. Data from European populations show that gastroesophageal reflux disease can lead to a 26% reduction in daily productivity. Additionally, the condition contributes to workplace absenteeism with reported weekly work absences ranging from 0.5 to 3.2 hours depending on the country (Gisbert et al., 2009).

Given this evidence, it becomes clear that even seemingly mild gastroesophageal reflux disease symptoms should not be overlooked in clinical practice. Symptoms that may appear minor in terms of objective severity can still lead to substantial impairments in QoL. Moreover, considering the established relationship between higher QoL and reduced mortality, addressing gastroesophageal reflux disease symptoms proactively may offer benefits that extend beyond symptom control alone.

GERD: potentially effective interventions

Given the wide array of physical and psychological consequences caused by gastroesophageal reflux disease (GERD), it is important to conclude this review by highlighting promising, non-pharmacological strategies that offer hope for symptom alleviation. While lifestyle

modifications such as dietary changes, weight management and sleep positioning are long-standing elements of gastroesophageal reflux disease management guidelines (Kahrilas et al., 2008), newer approaches are emerging as valuable adjuncts.

One pathophysiological mechanism of gastroesophageal reflux disease involves decreased lower esophageal sphincter (LES) pressure. Recent studies suggest that breathing exercises may enhance LES pressure, potentially improving the anti-reflux barrier. The underlying mechanism is likely related to increased diaphragmatic tone (Qiu et al., 2020). Supporting this hypothesis, another study demonstrated that diaphragmatic breathing, particularly when performed in an upright position, significantly reduced the frequency of postprandial reflux events in gastroesophageal reflux disease patients (Halland et al., 2021) . This intervention stands out for its accessibility: patients can perform it anywhere, at any time, without the need for expensive equipment or clinical supervision.

Another intriguing non-pharmacological approach is osteopathic intervention as an adjunct therapy in gastroesophageal reflux disease management. In a small-scale study, a series of four osteopathic treatments over an eight-week period yielded promising outcomes, including reduced medication use and improved scores on the Quality of Life in Reflux and Dyspepsia (QUOLRAD) questionnaire (Lynen et al., 2022). While the sample size was limited and such therapies may not be covered by public health systems, thus posing financial barriers to access, these preliminary results are encouraging. The potential to decrease long-term pharmacological dependency and its associated side effects presents a compelling case for further research into osteopathic treatments in gastroesophageal reflux disease care.

Conclusion

Gastroesophageal reflux disease (GERD) is a common condition that can significantly impair patients' quality of life through a wide spectrum of symptoms. Despite its seemingly straightforward diagnosis and treatment, the clinical picture can be complex, as some patients may not exhibit the typical esophageal manifestations. The observed bidirectional relationship between gastroesophageal reflux disease and depression is a compelling area of inquiry that warrants deeper investigation. Moreover, gastroesophageal reflux disease appears to increase the risk of additional psychiatric conditions, including sleep disturbances, anxiety disorders, depression and bipolar affective disorder. Current evidence underscores the need for further large-scale studies to better understand these associations and their clinical implications. A more integrated approach to managing gastroesophageal reflux disease may contribute not only to improved symptom control but also to better mental health outcomes and overall patient well-being.

Disclosure:

Author Contributions

Conceptualization, Jan Szerocki and Katarzyna Milewska-Plis; methodology, Igor Kłak; software, Alicja Winkowska; check, Alina Grudina, Joanna Grodzicka and Katarzyna Bartnik; formal analysis, Mariola Herian; investigation, Weronika Curyło; resources, Katarzyna Milewska-Plis; data curation, Jan Szerocki; writing - rough preparation, Jan Szerocki; writing

- review and editing, Igor Kłak; visualization, Alina Grudina; supervision, Monika Karalus; project administration, Joanna Grodzicka.

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

Funding Statement:
The study did not receive any special funding.

Institutional Review Board Statement:
Not applicable.

Informed Consent Statement:
Not applicable.

Data Availability Statement:
Not applicable.

Acknowledgments:
Artificial intelligence (AI) was used only for language enhancement purposes, such as grammar correction and stylistic refinement.

Conflict of Interest:
All authors declare no conflict of interest.

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