

Spreading the Word: Comorbidity of Asthma and Depression Is Not Just the Product of a Vulnerable Personality



Perla A. Vargas, PhD *Glendale, Ariz*

Although the functional association between asthma, anxiety, and depression has been known for decades, the increasing prevalence of these comorbid conditions has furthered the interest of the health care community. Comorbidity between medical and mental conditions is the rule rather than the exception.¹ The prevalence of chronic diseases doubled between 1985 and 2005. Consequentially, the prevalence of multiple morbidities also increased significantly, with the prevalence of individuals with 2, 3, and 4 or more diseases rising by 20%, 60%, and 300%, respectively.² Increasing age, female sex, and low socioeconomic status are associated with higher multimorbidity.² By 2010, 31.5% of all Americans had multiple chronic conditions. In addition, the presence of a mental health disorder, particularly depression, appears to increase as the number of medical morbidities increases.¹ On the basis of the 2001-2003 National Comorbidity Survey Replication, 34 million American adults, or 17% of the adult population, had comorbid mental and medical conditions.³ Specifically, individuals with asthma have a higher prevalence of anxiety and depression than does the general population.^{3,4} Compared with those without asthma, individuals with asthma are approximately twice as likely to suffer from depressive disorders,⁴ and 3 times more likely to suffer from anxiety disorders.^{4,5} In turn, suffering from depression and/or anxiety increases the risk for poor adherence to preventive medications and lifestyle changes (eg, allergen avoidance), impairs functioning, and increases health care utilization,⁴ which can further worsen asthma control.⁶ The similarity and overlap of symptoms of anxiety and uncontrolled asthma, in particular, make managing severe asthma more challenging, and might lead to underdiagnosis and undertreatment of the comorbid mental condition.³ This complex pattern of symptoms in patients with multimorbidity has been found to worsen the prognosis and lead to increasing complications of both physical and mental disorders. For example, in this issue of the journal, González-Freire et al⁷ evaluate the impact of psychological

factors (ie, anxiety, depression, and coping strategies) and degree of asthma control on health-related quality of life. The prevalence of depression and anxiety among adults with asthma in their sample was comparable to estimates reported previously (14% and 35%, respectively), and most importantly, they found that poorly controlled asthma in combination with anxiety and depression significantly worsens the patients' quality of life. Specifically, González-Freire et al observed significant limitations in daily living activities (physical functioning, role physical, and role emotional), lack of energy (vitality), and severe limiting bodily pain. Furthermore, patients using avoidance coping strategies (ie, efforts to ignore or avoid the source of stress) to deal with their health problems had worse health-related quality of life. These findings are consistent with reports regarding the impact of using avoidance coping strategies in other medical conditions. Furthermore, the use of avoidance coping strategies has been associated with poor medication adherence, a likely contributor to poor long-term outcomes.

The functional relationship of anxiety, depression, and asthma is well documented, but it is still unknown whether the relationship is causal and whether asthma precedes, succeeds, or just presents concurrently with anxiety and depression.^{8,9} Although several mechanisms have been proposed, a full explanation of the relationship remains elusive. Recently, investigators posit that asthma and depression share pathophysiological pathways relevant to both disorders. The hygiene hypothesis, renamed as the "old friends" mechanism, suggests that transformations in the environment in industrialized societies limit bacterial exposure and produce changes in the microbiota that alter immunoregulation and heighten the inflammatory response, increasing the risk for both allergic disorders, including asthma,^{10,11} and many psychiatric disorders, including anxiety and affective disorders.¹¹ Ongoing research on commensal microbe interactions has contributed significantly to the understanding of asthma pathogenesis, comorbidity, and disease endotyping.¹²

On the clinical side, there is a notable paucity of research examining whether successful asthma management improves depressive symptoms, or whether treating depression in people with asthma improves their asthma outcomes, but 2 recent studies show promising results. In a study with 3182 patients with moderate to severe uncontrolled asthma, Sastre et al¹³ found that after 6 months of guideline-driven standardized asthma treatment delivered by specialists, both asthma outcomes (asthma control test score and mean FEV₁) and psychological outcomes (anxiety and depression) improved

School of Social and Behavioral Sciences, Arizona State University, Glendale, Ariz
Conflicts of interest: The author declares no relevant conflict of interest.

Received for publication July 22, 2019; accepted for publication July 23, 2019.

Corresponding author: Perla A. Vargas, PhD, School of Social and Behavioral Sciences, Arizona State University, 4701 W Thunderbird Rd, MC 3051, Glendale, AZ 85306. E-mail: Perla.Vargas@asu.edu.

J Allergy Clin Immunol Pract 2020;8:208-9.
2213-2198

© 2019 American Academy of Allergy, Asthma & Immunology
<https://doi.org/10.1016/j.jaip.2019.07.023>

significantly. Then, a study treating major depressive disorder with a selective serotonin reuptake inhibitor in patients with comorbid severe asthma showed that, among 77 completers, a 12-week treatment with 10 mg/d of escitalopram significantly improved asthma outcomes (asthma control test score and rescue oral corticosteroids), and had a modest reduction in depressive symptoms.¹⁴ These findings support the use of a coordinated treatment for the management of comorbid asthma and depression.

Current guidelines for the treatment of severe asthma emphasize the importance to address all potential aggravating factors, specifically comorbidities, in patients who are not well controlled. However, there is currently a glaring gap in evidence-based programs for assessment, treatment, and follow-up of comorbid asthma and depression. Although the studies by Sastre et al¹³ and Brown et al¹⁴ provide initial evidence of how to best deliver care to people with these overlapping disorders, there is a need for further research to develop evidence-based standardized algorithms to guide clinical practice. Clearly, regardless of the underlying cause of the association, the evidence suggests an intricate interdependence between symptoms of asthma, anxiety, and depression that worsens the burden of each condition alone, creating a vicious cycle that leads to lower quality of life.^{3,7}

Asthma is a complex heterogeneous disease, which makes it difficult to manage. Despite evidence that asthma control is achievable, 82% of patients with moderate to severe asthma fail to achieve adequate control of their symptoms.¹⁵ The presence of common asthma comorbidities such as allergic rhinitis, gastroesophageal reflux, sleep disorders, anxiety, and depression may increase inflammation, affect the airways, complicate disease management, and increase the risk of treatment failure.¹⁶ We know that the relationship between asthma, allergic disorders, and mental health disorders is complex, probably involving multiple biological and social modulating factors including sex, body weight, sleep quality, and chronic pain.¹⁷ Moreover, it is becoming clear that having multiple chronic conditions is the new norm for patients with asthma and allergic disease. The current single-disease framework on which the health care system, medical education, clinical evidence, and treatment guidelines are based lacks the breadth to effectively manage overlapping and interrelated medical and mental conditions impacting patients with asthma. As these trends in asthma-related morbidity persist, appropriate management of multiple morbidities will require new strategies and commitment to patient-centered, multidisciplinary,

collaborative research, and care management to address the needs of the ever more prevalent complex cases.^{1,3}

Acknowledgment

Special thanks to Elias Robles for his helpful editorial comments.

REFERENCES

1. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380:37-43.
2. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur J Gen Pract* 2008;14:28-32.
3. Druss BG, Walker ER. Mental disorders and medical comorbidity. *Synth Proj Res Synth Rep* 2011;1-26.
4. Katon W, Lozano P, Russo J, McCauley E, Richardson L, Bush T. The prevalence of DSM-IV anxiety and depressive disorders in youth with asthma compared with controls. *J Adolesc Health* 2007;41:455-63.
5. Weiser EB. The prevalence of anxiety disorders among adults with asthma: a meta-analytic review. *J Clin Psychol Med Settings* 2007;14:297-307.
6. Richardson LP, Lozano P, Russo J, McCauley E, Bush T, Katon W. Asthma symptom burden: relationship to asthma severity and anxiety and depression symptoms. *Pediatrics* 2006;118:1042-51.
7. González-Freire B, Vázquez I, Pértaga-Díaz S. The relationship of psychological factors and asthma control to health-related quality of life. *J Allergy Clin Immunol Pract* 2020;8:197-207.
8. Hasler G, Gergen PJ, Kleinbaum DG, Ajdacic V, Gamma A, Eich D, et al. Asthma and panic in young adults: a 20-year prospective community study. *Am J Respir Crit Care Med* 2005;171:1224-30.
9. To T, Ryckman K, Zhu J, Williams D, Feldman LY, Larsen K, et al. Mental health services claims and adult onset asthma in Ontario, Canada. *J Allergy Clin Immunol Pract* 2017;5:1388-1393.e3.
10. Umetsu DT, McIntire JJ, Akbari O, Macaubas C, DeKruyff RH. Asthma: an epidemic of dysregulated immunity. *Nat Immunol* 2002;3:715.
11. Rook GA, Raison CL, Lowry CA. Microbiota, immunoregulatory old friends and psychiatric disorders. *Adv Exp Med Biol* 2014;817:319-56.
12. Agache I, Akdis CA. Precision medicine and phenotypes, endotypes, genotypes, regiotypes, and theratypes of allergic diseases. *J Clin Invest* 2019;129:1493-503.
13. Sastre J, Crespo A, Fernandez-Sanchez A, Rial M, Plaza V, Investigators of the CONCORD Study Group. Anxiety, depression, and asthma control: changes after standardized treatment. *J Allergy Clin Immunol Pract* 2018;6:1953-9.
14. Brown ES, Sayed N, Van Enkevort E, Kulikova A, Nakamura A, Khan DA, et al. A randomized, double-blind, placebo-controlled trial of escitalopram in patients with asthma and major depressive disorder. *J Allergy Clin Immunol Pract* 2018;6:1604-12.
15. Marcus P, Arnold RJ, Ekins S, Sacco P, Massanari M, Stanley Young S, et al, CHARIOT Study Investigators. A retrospective randomized study of asthma control in the US: results of the CHARIOT study. *Curr Med Res Opin* 2008;24:3443-52.
16. Gershon AS, Wang C, Guan J, To T. Burden of comorbidity in individuals with asthma. *Thorax* 2010;65:612-8.
17. Vargas PA, Robles E. Asthma and allergy as risk factors for suicidal behavior among young adults. *J Am Coll Health* 2019;67:97-112.