

Anxiety in Major Depressive Disorder

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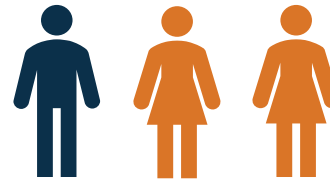
Objectives

- Share the prevalence of anxiety in Major Depressive Disorder (MDD)
- Discuss the clinical prognosis of comorbid anxiety with MDD
- Share the diagnostic criteria for anxiety in MDD
- Identify rating scales that assess anxiety and MDD
- Describe the neurotransmitter systems thought to be involved in depression and anxiety

Prevalence of Anxiety in Major Depressive Disorder



Nearly half of all patients diagnosed with depression also have symptoms of anxiety²



Depression is approximately twice as common in women than in men^{1,3}

1. Brody et al 2018 *NCHS Data Brief* No 303
2. Anxiety and Depression Association of America (ADAA) Facts and Statistics Sheet 2019
3. Bogren et al 2018 *Eur Arch Psychiatry Clin Neurosci* 268: 179-189.

Anxious Depression Can Worsen Prognosis^{1,2}

Anxious depression predicts greater morbidity and has been associated with^{2,3}:

Increased
Suicidality

Greater
Functional
Impairment

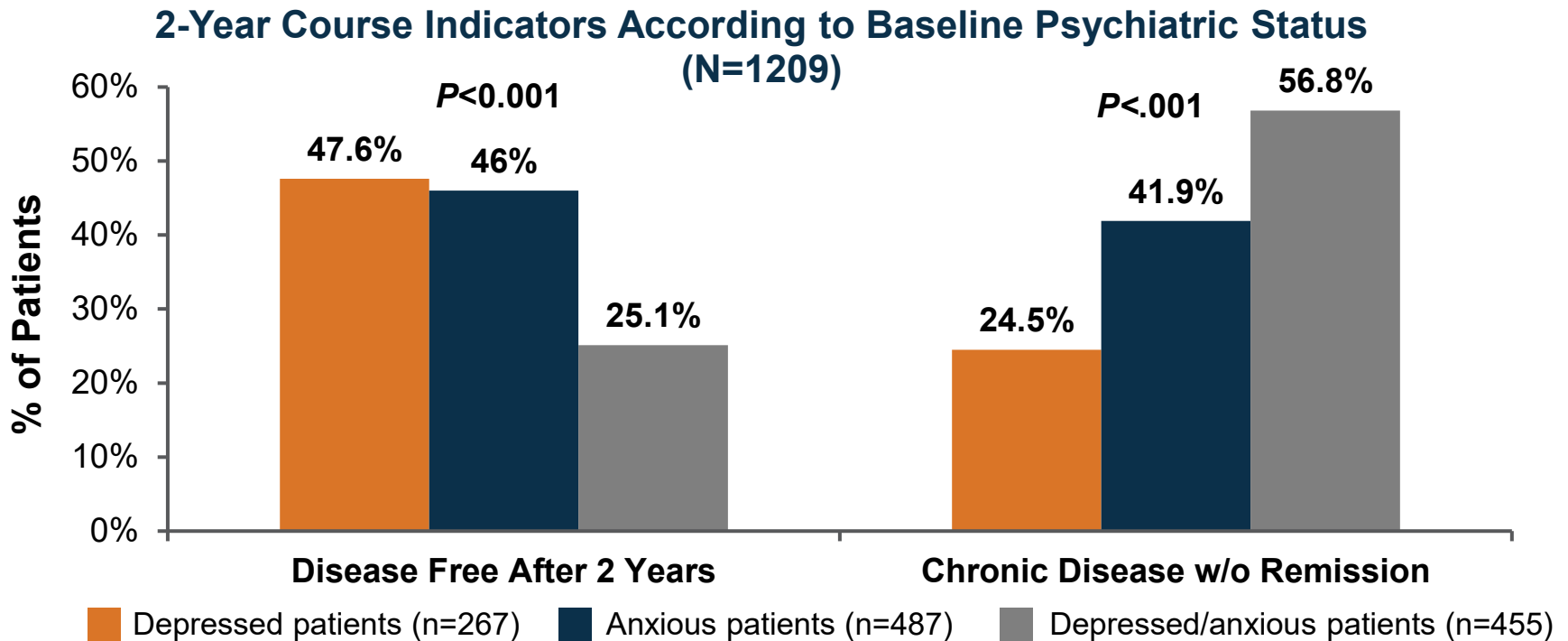
Worse
Health-
Related
QoL

Depressed
Episodes of
Longer
Duration

Poorer
Response to
Treatment

1. Trivedi MH, et al. *Am J Psychiatry*. 2006;163:28-40.
2. Fava M, et al. *Can J Psychiatry*. 2006;51:823-835.
3. Zimmerman M, et al. *J Clin Psychiatry*. 2014;75:601-607.

Patients With Anxiety and MDD Have Worse Prognosis

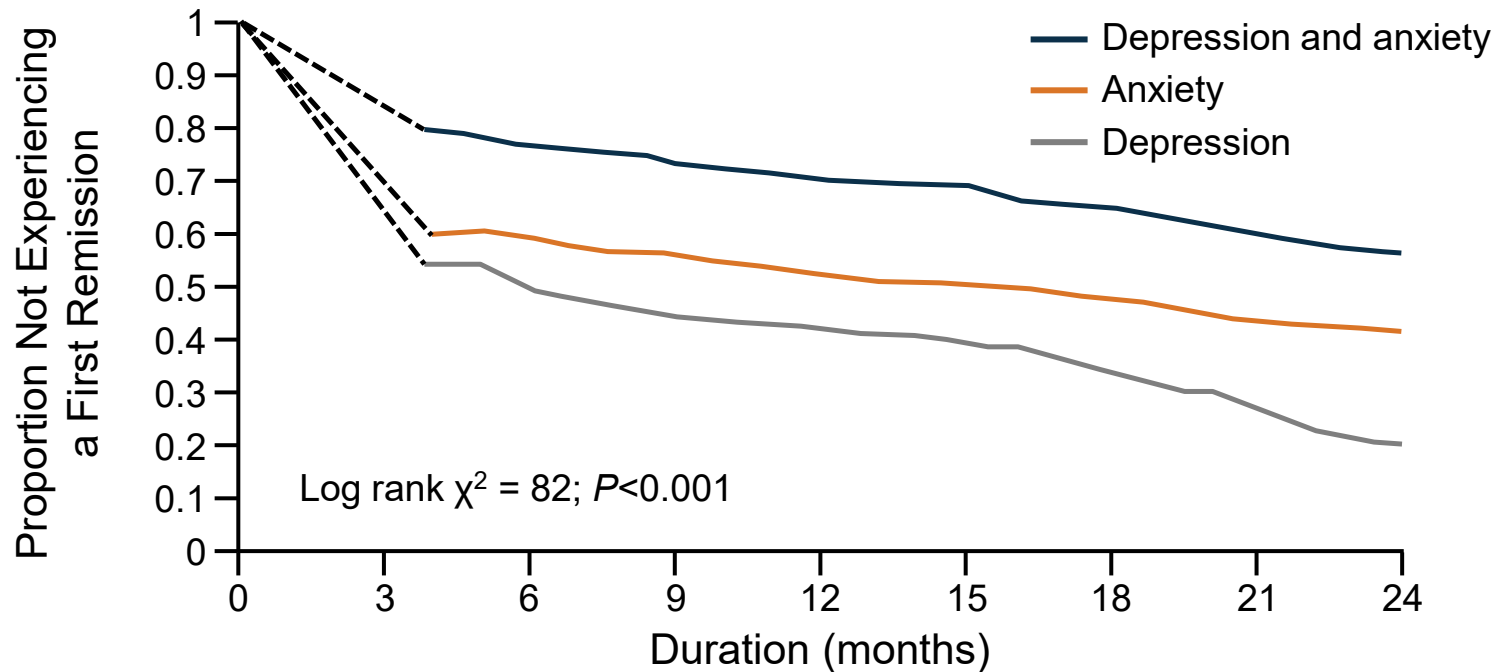


- After 2 years, only 25.1% of patients with comorbid depression/anxiety were disease free, compared with 47.6% and 46%, respectively, of patients with depression only and anxiety only ($P < 0.001$)
- 56.8% of depressed and anxious patients never achieved remission, whereas 24.5% of depressed patients and 41.9% of anxious patients never achieved remission

P value based on chi-square statistics for categorical variables and Mann Whitney nonparametric statistics for continuous variables.

Penninx B, et al. *J Affect Disord.* 2011;133:76-85.

Time to First Remission Found to Be Longer in Patients With Co-occurring MDD and Anxiety^a



- Median time to remission in the depression group was 6 months for depression versus 12 months for comorbid depression and anxiety
- Median time to remission in the anxiety group was 16 months for anxiety and 24 months for comorbid depression and anxiety

^aSurvival curve illustrating time until first remission across baseline psychiatric status (n=1209). The dotted lines (----) are projected lines since by definition no remission could have occurred within the first 3-month period.

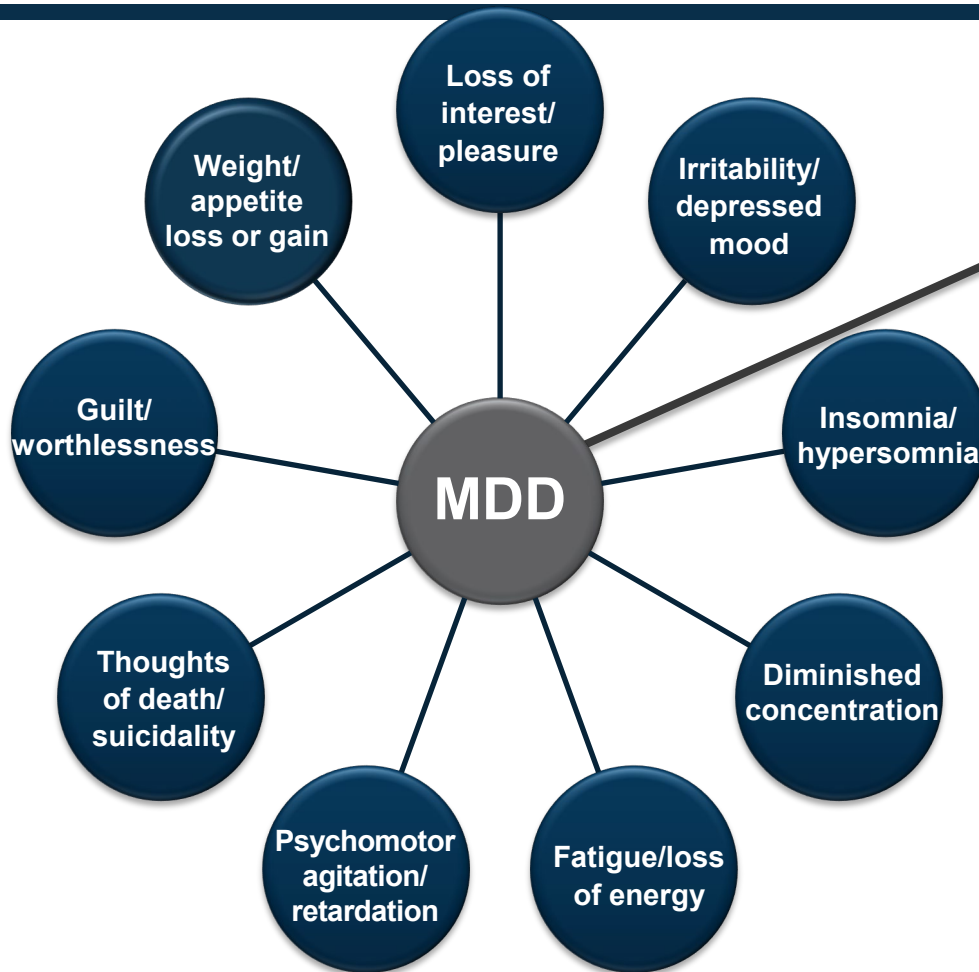
Penninx B, et al. *J Affect Disord.* 2011;133:76-85.

Anxiety Distinguisher in DSM-IV and DSM-5^{1,2,3}

DSM-IV (Anxious Depression) ²	DSM-5 (Anxious Distress) ³
HAMD anxiety/somatization factor ≥ 7	MADRS, IDS-SR, HAMD
Psychic anxiety	Tension – MADRS item 3 (inner tension) ≥ 3
Somatic anxiety	Restlessness – IDS-SR item 24 (feeling restless) ≥ 2
Gastrointestinal symptoms	Concentration - MADRS item 6 (concentration difficulties) ≥ 3
General somatic symptoms	Apprehension - HAM-D item 10 (anxiety – psychic) ≥ 3
Hypochondriasis	
Insight	

1. Weiller E, et al. *ASCP*. 2017
2. Fava M, et al. *Psychol Med*. 2004;34(7):1299-1308
3. Thase M, et al. *Neuropsych Dis Tx*. 2019;15:37-45.

Anxious Distress Specifier in DSM-5



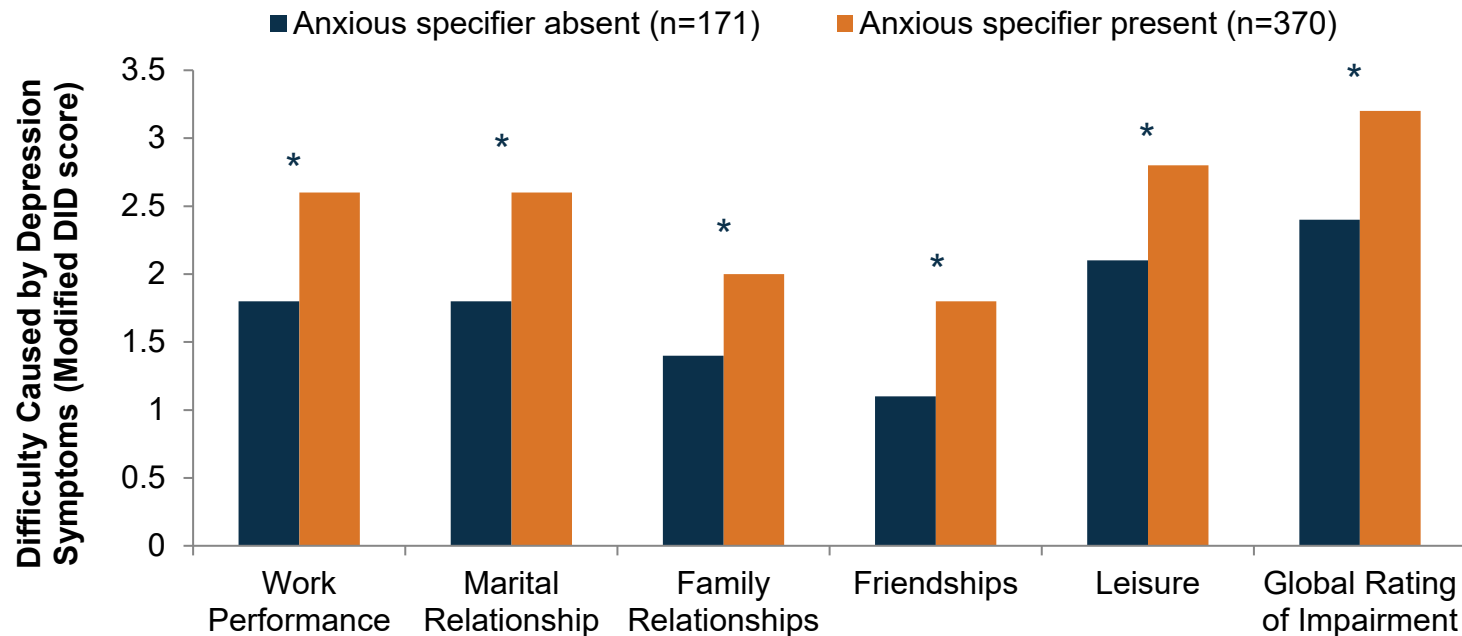
Anxious distress specifier:

- Feeling keyed up or tense
- Feeling unusually restless
- Difficulty concentrating because of worry
- Fear that something awful may happen
- Feeling that the individual might lose control of himself or herself

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

Anxious Distress Decreases Functioning in Patients With MDD

Patient-reported Psychosocial Function Impairment Based on *DSM-5* Anxious Distress Specifier



- Patients who met the anxious distress specifier had greater impairment of QoL and greater functional impairment compared with those who did not

* $P < 0.001$.

CUDOS-A=Clinically Useful Depression Outcome Scale–Anxious Distress Specifier Subscale; DID=Diagnostic Inventory for Depression
Zimmerman M, et al. *J Clin Psychiatry*. 2014;75:601-607.

Somatic Symptoms That Can Occur with Depression and Anxiety^{1,2}

- Muscle aches and pains
- Headaches
- Dry mouth
- Choking sensation
- “Churning stomach” sensation
- Nausea and/or vomiting
- Diarrhea
- Palpitations
- Chest pain
- Sudden redness of the skin
- Shortness of breath
- Dizziness
- Blurred vision
- Loss of sex drive
- Difficulties with urination

1. Tiller JW. *Med J Aust.* 2013;199(6):S28-S31

2. <https://www.psychguides.com/anxiety>.

How Can Anxiety and Depression Be Measured in Depression Trials

- Clinician rated Depression
 - MADRS¹
 - Line item 3 (inner tension), Line item 6 (concentration difficulties)²
 - HAM-D³
 - anxiety/somatization factor - 6 items⁴
 - IDS – C⁵
 - KSQ⁶
 - anxiety subscale, 17 items
- Clinician rated Anxiety
 - HAM-A⁷
 - GAD-7⁸
- Patient rated Depression
 - IDS-SR⁵
 - Line item 24 (feeling restless)²
- Patient rated Anxiety
 - CUXOS⁹

1. Montgomery SA Asberg M *Brit J Psych.* 1979;134 (4):382–89 2. Thase M, et al. *Neuropsychiatr Dis Tx* 2019; 15:37-45 (page 38 and 39). 3. Hamilton M, et al. *J Neurol Neurosurg Psychiatry* 1960;23:56–62 4. Fava M, et al. *Psychol Med* 2004;34(7):1299-1308 5. Rush AJ, et al. *Int J Methods Psychiatr Res* 2000;9:45–59 6. Kellner R, et al. *J Clin Psych* 1987;48:268-274 7. Hamilton Anxiety Rating Scale (HAM-A). <file:///M:/Special%20Projects/anxiety%20resources%202019/Rating%20scales/HAMILTON-ANXIETY.pdf> 8. Spitzer RL et al. *Arch Intern Med* 2006;166(10):1092-1097 9. Zimmerman M et al. *J Clin Psych.* 2010; 71:534– 542.

MADRS – Montgomery-Asberg Depression Rating Scale; HAMD – Hamilton Rating Scale for Depression; IDS-C – Inventory of Depression Symptoms Clinician Rated; KSQ –Kellner’s Symptom Questionnaire; HAM-A - Hamilton Rating Scale for Anxiety; GAD-7 - Generalised Anxiety Disorder Assessment; IDS-SR – IDS Self Rated; CUXOS – Clinically Useful Anxiety Outcome Scale

Clinician-rated Scale for Anxiety

- The Hamilton Anxiety Rating Scale, HAM-A, is a widely used and well-validated tool for measuring the severity of a patient's anxiety^{1,2}
- The scale consists of 14 items, each defined by a series of symptoms, and measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety)²
- Each item is scored on a 5-point scale, ranging from 0 (not present) to 4 (severe)²
- Total score range is 0 to 56, where²:
 - <17 is considered mild severity
 - 18 to 24 is considered mild to moderate severity
 - 25 to 30 is considered moderate to severe severity

1. Maier W et al. *J Affect Disord.* 1988;14(1):61-68.

2. Hamilton Anxiety Rating Scale (HAM-A). file:///M:/Special%20Projects/anxiety%20resources%202019/Rating%20scales/HAMILTON-ANXIETY.pdf

Patient-rated Outcome Scale for Anxiety

- Clinically Useful Anxiety Outcome Scale (CUXOS)
- 20-Item scale not disorder specific
- Psychic anxiety (6 items), somatic anxiety (14 items)
- Discriminates between different levels of severity
 - Empirically derived cutoff points
 - 91.4% completed in < 2 minutes

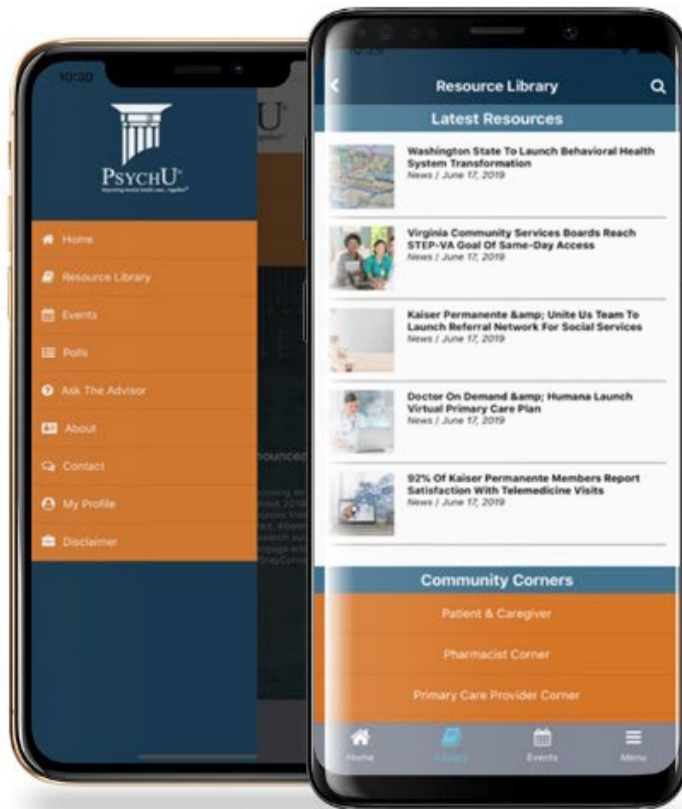
Zimmerman M et al. *J Clin Psychiatry*. 2010;71(5):534-542.

Receptors Thought to Play a Role in Depression and Anxiety

	Depression	Anxiety
D ₂ agonism	X ¹	
D ₃ agonism	X ²	
5HT _{1A} agonism	X ^{3,4}	X ⁴
5HT _{2A} antagonism	X ¹	
5HT ₇ antagonism	X ⁵	
α ₁ antagonism		X ⁷
α ₂ antagonism	X ^{4,6}	
H ₁ antagonism		X ⁴

1. Chermoloz O et al. *Psychopharmacol (Berl)* 2009;206(2):335-344 2. Leggio GM et al. *Pharmacol Therap* 2016;165:164-177 3. Blier P *Biol Psychiatry* 2003;53:193–203. 4. Correll CU. *Eur Psych* 2010;25:S12-S21 5. Matthys A et al. *Molecul Neurobiol* 2011; 43:228-253 6. Uys M et al. *Front Psychiatry* 2017;8(144):1-23 7. Goddard AW et al. *Depression and Anxiety* 2010;27:339-350

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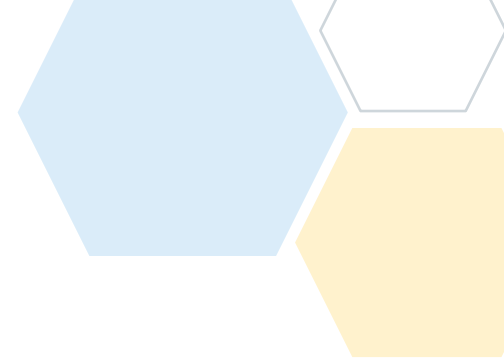


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