Agency for Healthcare Research & Quality
Topic for a New Evidence Review

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Date:
January 12, 2026

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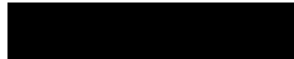

1. What is the decision or change (e.g. clinical topic, practice guideline, system design, delivery of care) you are facing or struggling with where a summary of the evidence would be helpful?

Estimates of the incidence of withdrawal following antidepressant cessation range from 27% to 86%, though studies of short-term use (typically 8–12 weeks) report lower rates.[1] This wide range reflects substantial heterogeneity in study design, duration of antidepressant exposure, drugs examined, and the criteria used to define and measure withdrawal symptoms. According to CDC data, 68% of antidepressant users aged 12 and older have taken an antidepressant for two years or more,[2] and recent research demonstrates that individuals with this duration of continuous use are significantly more likely to experience severe and longer-lasting withdrawal symptoms compared to those in shorter term studies[3] that have informed most guidelines. Despite the high incidence of withdrawal effects in real-world, longer-term use, representing approximately 25 million U.S. users,[4] and the substantial functional impairment withdrawal can cause, there remains no U.S. clinical guidance for safe discontinuation in long-term users. This gap persists even as systematic reviews have identified major limitations in the existing literature on how to safely stop antidepressants, including short follow-up periods, low-quality evidence, and a lack of data applicable to long-term antidepressant use.[5]

Evidence now supports that long-term antidepressant use leads to physiological adaptations that make standard tapering practices or linear dose reductions poorly tolerated or unsafe for many patients.[6] The American Psychiatric Association's 2010 guidance addressing antidepressant discontinuation consists of brief, non-specific recommendations [7] that are not supported by high-quality evidence for long-term users. This guidance is based on expert consensus from the early 2000s, premised on the understanding that withdrawal effects are "mild and brief," a conclusion drawn from studies in which antidepressant exposure lasted only 8 to 12 weeks.[8] Recent studies have found that this approach is unsuccessful for most long-term antidepressant users.[9] In the absence of robust official guidelines, clinicians often follow such short, conventional tapering schedules based on previously mentioned expert consensus and long-standing clinical convention, rather than from evidence applicable to long-term antidepressant use.[10] This gap has resulted in substantial variation in clinical practice, preventable patient harm, and ongoing confusion among healthcare providers.

Compounding this problem is diagnostic overshadowing and bias. Because patients carry a mental health diagnosis, reports of withdrawal symptoms are frequently discounted or misattributed. Withdrawal is commonly misdiagnosed as relapse of the original condition, leading to unnecessary or inappropriate treatment.[11] This misclassification not only worsens patient outcomes but also distorts data collection and obscures the true prevalence and burden of antidepressant withdrawal.

Due to healthcare systems inadequately addressing the withdrawal problem, a significant cohort of patients have turned to online peer-support forums for tapering and withdrawal advice.[12]

These communities have effectively functioned as informal sources of clinical guidance for patients who are unable to obtain adequate support within the healthcare system, highlighting a systemic failure.

Notably, many tapering approaches now described in the literature as hyperbolic[13] were first developed and disseminated within patient-led communities,[14] as long-term users attempted to reduce withdrawal symptoms following unsuccessful conventional tapers. These practices emerged through iterative, real-world experience and were later supported by pharmacodynamic research demonstrating non-linear relationships between antidepressant dose and receptor or transporter occupancy.[10,13] Several studies now show that patients unable to discontinue antidepressants with conventional tapering schedules of a few weeks were able to do so successfully, with significantly less withdrawal effects, using gradual hyperbolic tapering approaches.[15] Despite this convergence of patient-generated knowledge, biological rationale, and emerging empirical evidence, formal studies remain limited to a small number of researchers, and U.S. clinicians lack an authoritative, unbiased synthesis to guide implementation in clinical practice. By contrast, guidance from the United Kingdom, including recommendations from the National Institute for Health and Care Excellence, the Royal College of Psychiatrists, and the Maudsley Deprescribing Guidelines, reflects growing recognition of withdrawal risk and the need for individualized, hyperbolic tapering, particularly for long-term users. The absence of comparable U.S. guidance highlights an emerging gap in clinical practice.

An evidence review from AHRQ would help clarify the strength and limitations of this evidence, identify remaining research gaps, and support the development of best practices for deprescribing antidepressants in long-term users.

- Question(s):
    - What are best practices for deprescribing antidepressants in long-term users? What is the comparative effectiveness and safety of hyperbolic tapering versus conventional tapering strategies for those who have taken antidepressants for 12 months or longer?

- Population:
    - Users who have taken antidepressant medication for 12 months or longer.

- Intervention:
    - Hyperbolic tapering strategies, defined as non-linear dose reductions that become progressively smaller over time based on the pharmacodynamic principle of receptor or transporter occupancy. Approaches include exponential tapering schedules (e.g., fixed-percentage reductions), microtapering, use of liquid formulations, and compounded medications (e.g. tapering strips) to facilitate gradual dose reductions below the minimum doses achievable with standard commercially available tablets or capsules.

- Comparator:

    - Standard linear tapering schedules (e.g., fixed dose reductions over 0–8 weeks), which often involves halving the dose for 2–4 weeks, then halving again for 2–4 weeks before stopping the medication completely.

- Outcomes:
    - Successful discontinuation, withdrawal severity and duration, quality of life, functional impairment, misdiagnosis, healthcare utilization, relapses, reinstatement of medication, use of additional medication.

- Setting:
    - Primary care, psychiatry, ambulatory care, telehealth, integrated behavioral health settings.

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2. Why are you struggling with this issue?

The median duration of antidepressant use among real-world patients in the U.S. is five years,[1] yet no U.S. clinical guidelines exist to provide evidence-based instructions for tapering long-term users, resulting in wide practice variation and reliance on anecdotal and outdated guidance. Withdrawal is frequently misdiagnosed as relapse, leading to unnecessary treatment and sometimes hindering recovery. An evidence review is needed to resolve these uncertainties and inform safer tapering practices and future guidelines.

References

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3. What do you want to see changed? How will you know that your issue is improving or has been addressed?

We aim to obtain a comprehensive, neutral synthesis of the evidence on best practices for tapering antidepressants following long-term use (≥12 months), including a comparison between the effectiveness of hyperbolic tapering and conventional linear tapering. This would help close the current guidance gap that leaves prescribers without clear, evidence-based tapering strategies and reduce patient harm associated with conventional tapering, which include rapid (typically 2–8 weeks) and linear tapering schedules. Ultimately, the goal is to support the development of a U.S. clinical guideline on tapering antidepressants, particularly for long-term users. Indicators that the issue is improving would include implementation of safer, evidence-based tapering practices, greater clinician awareness of withdrawal effects, reduced reports of severe and protracted withdrawal syndromes, and improved patient outcomes during and after tapering attempts (e.g. decreased relapse, decreased misdiagnosis of relapse of mental health conditions).

4. When do you need the evidence report?

We request that the evidence report be completed January 12, 2027. This timeline balances the need for a rigorous and methodologically sound review with the urgency of addressing major public health and clinical concerns. With millions of Americans taking antidepressants long-term, and research demonstrating that prolonged use increases the risk of severe and functionally impairing withdrawal, timely evidence is critical to inform safe tapering practices. In addition, recent media coverage and growing public awareness may prompt more individuals to attempt discontinuation, making it imperative that prescribers and patients have access to evidence-based guidance. Completing the review within this period will also ensure that the findings can inform emerging policy discussions, clinical guideline development, healthcare provider education, and future research priorities, helping to reduce misdiagnosis, unnecessary treatment, and improve patient safety.

5. What will you do with the evidence report?

The evidence report would be used to inform the development of future U.S. clinical guidelines on antidepressant tapering and deprescribing by providing an authoritative, evidence-based synthesis of tapering strategies for long-term users. At present, no U.S. guideline offers evidence-based tapering recommendations for this population.

A relevant precedent is the development of benzodiazepine tapering guidance led by the American Society of Addiction Medicine (ASAM), which emerged through collaboration with the patient-led Benzodiazepine Information Coalition (BIC) after the FDA became overwhelmed with reports of withdrawal harm. The resulting guidance represented a meaningful step forward from the prior absence of formal guidelines and demonstrated how patient-reported harm, evidence review, and expert consensus can catalyze federal-adjacent clinical guidance.

A similar pathway could be pursued for antidepressants. By providing a neutral synthesis of the evidence on withdrawal risk, tapering strategies, and the comparative effectiveness of hyperbolic versus conventional tapering, the report would educate health systems and inform quality improvement initiatives aimed at reducing preventable harm associated with

antidepressant withdrawal, misdiagnosis of withdrawal as relapse or entirely new diagnoses, unnecessary healthcare utilization, and inappropriate treatment. It would also support medical education and training efforts through the incorporation of evidence-based deprescribing principles into continuing medical education, residency training, and integrated behavioral health programs. Finally, the evidence review would help identify critical research gaps and priorities, guiding funders and researchers toward high-quality studies most urgently needed to address the needs of long-term antidepressant users and real-world tapering strategies.

Eligibility Criteria

Inclusions: Patients taking antidepressants for more than 12 months for any indication.

Exclusions: Short-term users (<12 months), agomelatine, studies with follow-up too short to capture withdrawal symptoms (<14 days), studies in which withdrawal symptoms are not evaluated (risking confounding relapse with withdrawal).