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Review

Risk Factors and Early Warning Signs of Suicide Attempt for Patients on Sedatives and Antidepressants

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Abstract

Suicide remains a significant global health concern, often linked to psychiatric conditions such as depression and anxiety. Sedative-hypnotic and antidepressant medications are widely prescribed to manage these conditions, yet their relationship with suicide attempts is complex and controversial. This narrative review explores the risk of suicide attempts associated with sedative-hypnotics, such as benzodiazepines and non-benzodiazepine sleep aids, and antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs). Evidence suggests that both classes of medications may elevate suicide risk in certain populations, especially during treatment initiation or abrupt discontinuation. Sedative-hypnotics are implicated in increased impulsivity and withdrawal symptoms, while antidepressants are associated with heightened suicidal ideation, particularly in youth under 25 years. The benefit-risk profile of these medications varies significantly with factors like dosage, treatment duration, and individual patient characteristics. Effective mitigation strategies include cautious prescribing, close monitoring, and integration of non-pharmacologic interventions. Future research should focus on longitudinal and controlled studies to better understand the mechanisms underlying these risks and to inform personalized treatment approaches.

Keywords: *Suicide, risk factors, antidepressant, sedatives*

Introduction

Suicide remains a significant public health concern worldwide, with millions of individuals affected by suicidal ideation and attempts each year. The complexities of mental health disorders, particularly depression and anxiety, often lead to the prescription of pharmacological treatments such as sedative hypnotics and antidepressants. These medications are designed to alleviate symptoms and improve the quality of life for individuals struggling with mental health issues. However, their relationship with suicidal behavior is a topic of ongoing debate and research (1).

Sedative hypnotics, which encompass a variety of medications such as benzodiazepines and non-benzodiazepine sleep aids, are frequently prescribed by healthcare professionals for the purpose of managing conditions like insomnia and anxiety disorders over a short-term period. While it is true that these medications can offer rapid relief from such troubling symptoms, there have been growing concerns and discussions within the medical community regarding their potential to not only exacerbate but also amplify suicidal thoughts and behaviors in susceptible individuals (2).

The sedative effects produced by these drugs may effectively obscure or conceal any underlying mood disorders, creating a deceptive sense of security for the individuals taking them, which can ultimately lead to an increased risk of self-harm, especially when the medication is either discontinued or when the patient develops a tolerance to the drug effects. This complex interplay between medication and mental health necessitates a careful assessment by healthcare providers, who must weigh the immediate benefits against the long-term risks to ensure that patients receive appropriate support and monitoring throughout their treatment journey (3).

Antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), along with various other classes of antidepressant drugs, have gained widespread acceptance and utilization in the clinical practice as a primary approach for managing and treating major depressive disorder as well as anxiety disorders. While it is true that these medications can demonstrate considerable effectiveness in alleviating the symptoms associated with depression and in diminishing the presence of suicidal ideation, it is important to recognize that their overall influence on the risk of suicide presents a multifaceted and complex picture that requires careful consideration (4).

Several research studies have indicated that there may be a paradoxical increase in the prevalence of suicidal thoughts and behaviors, particularly among younger populations, during the early stages of treatment with antidepressants, which can lead to alarming and unintended consequences. This phenomenon underscores the critical importance of engaging in thorough and vigilant monitoring of patients, as well as fostering a more nuanced and sophisticated understanding of the ways in which these medications exert their effects on individuals who are at various points throughout their treatment period (5).

The interplay between sedative hypnotics, antidepressants, and the risk of suicide attempts is multifaceted. Factors such as dosage, duration of use, patient demographics, and the presence of co-occurring mental health disorders all contribute to the overall risk profile. Moreover, the potential for drug interactions and the impact of withdrawal symptoms must also be considered when evaluating the safety of these medications in vulnerable populations (5, 6).

Understanding the mechanisms of these medications is essential, as it can help clinicians to better tailor treatment plans and provide appropriate support for those who may be at heightened suicide risk during their initial phases of therapy (7).

In this narrative review, we aim to explore the risk of suicide attempts in patients taking sedative hypnotics and antidepressant drugs. We will analyze the evidence surrounding the relationship between these medications and suicidal behavior, focusing on the underlying mechanisms that may contribute to increased risk. By examining the nuances of this relationship, we hope to provide insights for clinicians and researchers that can inform treatment decisions and improve patient outcomes.

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Methodology

This narrative review is based on a comprehensive literature search conducted on 21 November 2024 in the Medline and Cochrane databases. Utilizing medical subject headings (MeSH) and relevant keywords, the search aimed to identify studies examining the risk of suicide attempts associated with the use of sedative-hypnotics and antidepressant drugs. To ensure thoroughness, a manual search was also conducted using Google Scholar, and the reference lists of identified papers were reviewed to locate additional relevant studies. The review focused on articles addressing the incidence, mechanisms, risk factors, and mitigation strategies related to suicidal behavior in patients using these medications. No restrictions were applied regarding publication date, language, participant age, or type of publication, ensuring a broad and inclusive exploration of the available literature.

Discussion

Suicide risk and sedative hypnotics

The relationship between sedative-hypnotic medications and suicide risk is complex, shaped by a combination of pharmacological effects, patient-specific factors, and underlying psychiatric conditions. Current evidence suggests an association between these medications and suicidal behaviors, but confounding factors make it difficult to draw definitive conclusions about causation (3).

Studies investigating benzodiazepines and suicide highlight their potential to elevate risk, especially in high doses or among vulnerable populations. For instance, naturalistic studies report a twofold increase in suicide risk associated with high-dose benzodiazepine use, even after adjusting for illness severity and adherence (8). Laboratory research further suggests that benzodiazepines may exacerbate impulsivity, a key mediator of suicidal behavior. In one controlled study, individuals who received a 10 mg dose of diazepam were significantly more likely to exhibit self-aggressive behaviors compared to those given placebo (9). This disinhibition effect could explain why benzodiazepines are disproportionately implicated in suicidal events across various clinical and demographic groups.

Benzodiazepines may also contribute to suicidality through withdrawal or rebound symptoms, particularly anxiety and insomnia, which are well-established risk factors for suicide. Sudden dose reductions or discontinuation can lead to heightened psychological distress, compounding pre-existing vulnerabilities in at-risk patients. Additionally, the sedative properties of benzodiazepines make them a common agent in intentional overdoses, further increasing their association with suicide attempts and deaths. This pharmacological toxicity underscores the need for cautious prescribing practices, particularly in patients with a history of suicidal ideation or behaviors (10).

Hypnotics, including benzodiazepine receptor agonists and "Z-drugs," show similar associations with suicide. Epidemiological studies have reported increased odds of suicide among users of these medications, even after controlling confounding factors such as insomnia and psychiatric comorbidities. For example, a Taiwanese study found a significant association between zolpidem use and suicide attempts, with an adjusted odds ratio of 2.08 (11). This risk appears to extend beyond benzodiazepines, as newer hypnotics, such as suvorexant, have also been linked to dose-dependent suicidal ideation in clinical trials (12). Mechanistically, these agents may induce disinhibition, parasomnias, or states of confusion, potentially triggering self-harm behaviors in susceptible individuals (10).

However, not all findings are consistent, and some studies point to protective effects of sedative-hypnotics in specific contexts. By alleviating insomnia and anxiety, these medications can reduce psychological distress, potentially lowering suicide risk in some patients. This duality—where sedative-hypnotics can both increase and decrease suicide risk depending on the context—emphasizes the importance of patient-specific risk assessments (1).

Regulatory actions reflect the uncertain risk-benefit profile of sedative-hypnotics. The U.S. Food and Drug Administration (FDA) mandates suicide risk

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warnings on hypnotic labels, citing evidence of dose-dependent associations with suicidal ideation. Despite these precautions, the lack of large-scale trials explicitly designed to assess suicide outcomes leaves gaps in understanding. Available data often rely on observational designs, which, while valuable, are prone to confounding factors. Patients prescribed sedative-hypnotics are more likely to have severe psychiatric conditions or substance use disorders, both of which independently increase suicide risk. These limitations highlight the need for controlled studies to disentangle the effects of the medications from those of the underlying disorders they are prescribed to treat (6).

Importantly, certain subgroups may face heightened risks. Older adults, for example, show increased rates of suicide following hypnotic use, potentially due to age-related changes in pharmacokinetics and pharmacodynamics (13). In contrast, younger individuals may be more vulnerable to disinhibitory effects, particularly when using high-potency agents like alprazolam (14). These findings suggest that the safety profile of sedative-hypnotics varies significantly across populations, necessitating tailored prescribing practices.

Mitigating the suicide risk associated with sedative-hypnotics requires multifaceted strategies. Clinicians should prioritize the lowest effective doses, avoid abrupt discontinuation, and carefully monitor patients during treatment initiation and tapering phases. Non-pharmacologic interventions, such as cognitive-behavioral therapy for insomnia (CBT-I), offer safer alternatives for managing sleep disturbances and should be considered as first-line treatments where appropriate. Additionally, integrating suicide prevention measures, such as safety planning and restriction of access to means, into routine care for patients receiving sedative-hypnotics is essential (10).

Future research should focus on clarifying the mechanisms by which sedative-hypnotics influence suicidality. Longitudinal studies with rigorous adjustment for confounding variables are needed to establish causal relationships. Comparative trials assessing the safety profiles of different agents within this drug class could also guide clinical decision-making. Finally, exploring biomarkers of vulnerability to adverse effects may enable personalized treatment approaches, reducing risks while preserving therapeutic benefits.

In conclusion, sedative-hypnotics are associated with an elevated risk of suicidal behaviors, but the nature of this relationship remains complex and context-dependent. While these medications may exacerbate suicidality in some patients, they can also provide relief from insomnia and anxiety, reducing distress in others. Optimizing their use requires careful patient selection, close monitoring, and an emphasis on non-pharmacologic alternatives wherever possible. Balancing these considerations will be critical to improving outcomes for patients at risk of both insomnia and suicide.

Suicide risk and antidepressants

Antidepressants play a critical role in the treatment of depressive disorders but are associated with an increased risk of suicidal events, particularly in younger individuals. This relationship has been extensively investigated through clinical trials and observational studies, producing mixed findings. While antidepressants provide significant benefits to many patients, understanding and mitigating the associated risks remains a priority in clinical practice (5).

The link between antidepressant uses and suicidal behavior has been most clearly demonstrated in youth and adults under 25. A meta-analysis of 24 randomized clinical trials (RCTs) found that antidepressant use increased the risk of suicidal events in depressed youth with an odds ratio (OR) of 1.66 and across all indications (OR = 1.95) (15). An FDA meta-analysis showed a higher risk for individuals under 25 (OR = 1.62), reduced risk for those aged 25–64 (OR = 0.87), and a protective effect in adults over 65 (OR = 0.37) (16). Another meta-analysis of 27 RCTs reported a 0.7% absolute increase in suicidal events in the antidepressant group compared to placebo, with a 1.7-fold increased risk. However, the benefit-risk balance remained favorable, with 11 times more adolescents responding positively to antidepressants than

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experiencing a suicidal event (17). A Cochrane review also reported increased risk (OR = 1.6) but noted 4.5 times more clinical remissions than suicidal events (18). These findings underscore the importance of contextualizing the risks of antidepressant treatment within the broader framework of clinical benefits. While there is a measurable increase in suicidal events among youth, the overall therapeutic advantages for the majority of treated individuals highlight the need for careful patient selection, monitoring, and risk communication

Youth-specific vulnerabilities may explain their heightened risk. Developmental factors, including immature prefrontal cortical development and altered serotonergic receptor densities, contribute to impulsivity and emotional dysregulation, which may amplify the risk of suicidality during antidepressant treatment (19). Additionally, younger individuals metabolize antidepressants more rapidly, which can lead to suboptimal drug levels at standard doses or withdrawal symptoms at lower doses (20). Pharmacologically induced mania or mixed depressive states, which are more prevalent in adolescents and young adults, are also linked to increased suicide risk (21). Sleep disturbances, a common side effect of many antidepressants, further compound this risk, given the well-established association between insomnia and suicidal behavior (22). These findings suggest the need for cautious dosing and close monitoring in younger populations to manage these unique risks effectively.

Observational pharmacoepidemiologic studies provide a contrasting perspective to RCTs by analyzing large, real-world datasets. Most of these studies demonstrate a protective relationship between regional antidepressant use and suicide rates. This was observed exclusively with SSRI prescriptions, while a greater proportion of tricyclic antidepressants correlated with higher suicide rates (23). Between 1990 and 2000, it was revealed that a 1% increase in antidepressant prescriptions has been associated with a 0.23 per 100,000 reductions in suicide rates, especially in youth (24). Furthermore, prolonged treatment durations exceeding six months are associated with lower suicide attempt rates compared to shorter treatment courses (25). However, these findings are not universal. A Finnish study reported a significant relation between the rate of suicide attempts and SSRI administration (26). Another report pointed to increased suicide risks immediately following the initiation of antidepressant therapy, particularly within the first week and during dose escalations (27). These early risks may indicate underlying disease severity or the time lag before therapeutic effects emerge.

The association between antidepressant use and suicide attempts in cross-sectional studies may be influenced by confounding factors, such as the severity of underlying conditions. In a previous study, suicide attempts often preceded antidepressant initiation, and attempt rates declined after treatment began (28). A large propensity-matched study showed the association between antidepressant use and suicide attempts disappeared after accounting for confounders (29). However, some case-control studies have linked antidepressants to increased suicide risk in youth (30), a finding inconsistent with low rates of antidepressant toxicology in postmortem samples (31). Higher antidepressant doses have been associated with suicidal behavior, potentially reflecting more severe or refractory conditions in those patients (32).

The introduction of the U.S. Food and Drug Administration's (FDA) "Black Box Warning" in 2004 marked a turning point in the perception and management of antidepressant-associated suicidality. The warning highlighted the increased risk of suicidal events in youth, leading to a significant reduction in antidepressant prescriptions in adolescents and young adults. This decline in prescribing was paralleled by decreases in depression diagnoses and mental health care visits, as well as an increase in youth suicide rates in several countries (33-36). These unintended consequences emphasize the importance of balancing risk communication with continued access to effective treatments. Restricting antidepressant use without offering alternative

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interventions may leave many young people untreated, heightening their vulnerability to depressive symptoms and suicidality.

Suicidal events are not evenly distributed across all patients taking antidepressants. Certain subgroups are at significantly higher risk, including individuals with pre-existing suicidal ideation, nonsuicidal self-injury, family conflict, substance use disorders, or treatment resistance (37). Moreover, higher initial doses of antidepressants are associated with an increased risk of self-harm, particularly in adolescents and young adults (38). Differences in suicidal event rates across antidepressant classes and agents have also been reported, with SSRIs generally posing lower risks compared to tricyclic antidepressants or certain atypical agents. For example, studies have identified venlafaxine and mirtazapine as having higher associated risks of suicidal behavior than citalopram or fluoxetine (4, 39). These findings underscore the need for personalized treatment plans that account for individual risk factors and medication profiles.

Discrepancies between RCTs and observational studies highlight the need for further research. While RCTs offer rigorous experimental control, they often exclude high-risk individuals and focus on short-term outcomes. In contrast, observational studies capture real-world data from diverse populations but are prone to confounding by indication. Longitudinal studies examining the long-term safety and efficacy of antidepressants in youth, as well as head-to-head comparisons of different agents, are critical to addressing these gaps. Research into biological markers and genetic predispositions could also improve risk stratification and guide personalized treatment approaches.

Clinicians should have several strategies to minimize the risk of suicidal attempts when prescribing antidepressants, especially in younger populations. Close monitoring during the initial weeks of treatment and after dose adjustments is critical, as suicidal behavior is most likely to occur during these periods. Weekly follow-ups, even if conducted by telephone, can help identify emerging risks early (40). Starting at lower doses and titrating slowly reduces the likelihood of side effects such as agitation, akathisia or insomnia that may contribute to suicidal ideation (5). Patients and caregivers should be educated about potential adverse effects, including mania, insomnia and withdrawal symptoms, to encourage adherence and timely reporting of concerns. Addressing comorbid conditions such as substance use, or family discord is also essential in reducing overall risk (41).

The role of psychotherapeutic interventions alongside pharmacologic treatment deserves particular attention. Cognitive-behavioral therapy (CBT) has shown efficacy in reducing depressive symptoms and suicidal ideation in youth and can enhance the effectiveness of antidepressants. Combining medication with CBT may result in faster and more sustained improvements, particularly in patients with treatment-resistant depression. Incorporating safety planning and distress tolerance strategies into care can further support individuals during the vulnerable early stages of treatment (42).

In conclusion, the relationship between antidepressants and suicidality is complex and influenced by age, individual risk factors, and treatment context. While antidepressants are linked to a modest increase in suicidal events in youth, the overall benefit-risk profile supports their use in managing depressive disorders when appropriately monitored. Tailored treatment strategies, including cautious dosing, regular follow-ups, and integration of psychotherapeutic approaches, are essential in mitigating risks. Future research and thoughtful risk communication will be pivotal in optimizing the safe and effective use of antidepressants across all age groups.

Conclusion

The risk of suicide attempts associated with sedative-hypnotics and antidepressant drugs highlights the complexity of treating mental health conditions in vulnerable populations. While these medications play a crucial role in alleviating symptoms of insomnia, anxiety, and depression,

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their potential to exacerbate suicidality necessitates a careful, individualized approach to treatment.

Sedative-hypnotics, particularly benzodiazepines, pose unique challenges due to their disinhibitory effects, withdrawal syndromes, and use in intentional overdoses. Similarly, antidepressants, especially in younger populations, carry a risk of early treatment-emergent suicidality that underscores the importance of vigilant monitoring. The nuanced interplay of pharmacological effects, patient-specific factors, and co-occurring conditions demands tailored strategies to balance therapeutic benefits against potential harms.

To optimize outcomes, clinicians should adopt cautious dosing, avoid abrupt discontinuation, and prioritize close monitoring during critical treatment phases. Non-pharmacologic interventions, such as cognitive-behavioral therapy, offer safer alternatives or complements to medication. Regulatory guidelines, while helpful in raising awareness, must evolve to reflect nuanced insights into population-specific risks and benefits.

Disclosure

Conflict of interest

There is no conflict of interest.

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Ethical Consideration

Not applicable.

Data availability

Data that supports the findings of this study are embedded within the manuscript which is based on a comprehensive literature search conducted on November 2024, in the Medline and Cochrane databases.

Author Contribution

The authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

References

1. Yerevanian BI, Choi YM. Impact of psychotropic drugs on suicide and suicidal behaviors. Bipolar Disord. 2013;15(5):594-621.

2. Ybanez L, Spiller HA, Badeti J, Casavant MJ, Rine N, Michaels NL, et al. Suspected suicides and suicide attempts involving antipsychotic or sedative-hypnotic medications reported to America's Poison Centers, 2000-2021. Clin Toxicol (Phila). 2023;61(4):294-304.

3. Tournier M, Benard-Laribiere A, Jollant F, Hucteau E, Diop PY, Jarne-Munoz A, et al. Risk of suicide attempt and suicide associated with benzodiazepine: A nationwide case crossover study. Acta Psychiatr Scand. 2023;148(3):233-41.

4. Coupland C, Hill T, Morriss R, Arthur A, Moore M, Hippisley-Cox J. Antidepressant use and risk of suicide and attempted suicide or self harm in people aged 20 to 64: cohort study using a primary care database. BMJ. 2015;350:h517.

5. Brent DA. Antidepressants and suicidality. Psychiatr Clin North Am. 2016;39(3):503-12.

6. Dodds TJ. Prescribed benzodiazepines and suicide risk: A review of the literature. Prim Care Companion CNS Disord. 2017;19(2).

7. Pfeifer P, Greusing S, Kupferschmidt H, Bartsch C, Reisch T. A comprehensive analysis of attempted and fatal suicide cases involving frequently used psychotropic medications. Gen Hosp Psychiatry. 2020;63:16-20.

8. Tiihonen J, Mittendorfer-Rutz E, Torniainen M, Alexanderson K, Tanskanen A. Mortality and cumulative exposure to antipsychotics, antidepressants, and benzodiazepines in patients with schizophrenia: An observational follow-up study. Am J Psychiatry. 2016;173(6):600-6.

9. Berman ME, Jones GD, McCloskey MS. The effects of diazepam on human self-aggressive behavior. Psychopharmacology (Berl). 2005;178(1):100-6.

10. McCall WV, Benca RM, Rosenquist PB, Riley MA, McCloud L, Newman JC, et al. Hypnotic medications and suicide: Risk, mechanisms,

http://dx.doi.org/10.52533/JOHS.2024.41206

mitigation, and the FDA. Am J Psychiatry. 2017;174(1):18-25.

11. Sun Y, Lin CC, Lu CJ, Hsu CY, Kao CH. Association between zolpidem and suicide: A nationwide population-based case-control study. Mayo Clin Proc. 2016;91(3):308-15.

12. Petrous J, Furmaga K. Adverse reaction with suvorexant for insomnia: acute worsening of depression with emergence of suicidal thoughts. BMJ Case Rep. 2017;2017.

13. Thomas P. Psychotropic drugs in the elderly. Soins Gerontol. 2023;28(163):27-9.

14. Giorgetti A, Sommer MJ, Wilde M, Perdekamp MG, Auwarter V. A case of fatal multidrug intoxication involving flualprazolam: distribution in body fluids and solid tissues. Forensic Toxicol. 2022;40(1):180-8.

15. Hammad TA, Laughren T, Racoosin J. Suicidality in pediatric patients treated with antidepressant drugs. Arch Gen Psychiatry. 2006;63(3):332-9.

16. Stone M, Laughren T, Jones ML, Levenson M, Holland PC, Hughes A, et al. Risk of suicidality in clinical trials of antidepressants in adults: analysis of proprietary data submitted to US Food and Drug Administration. BMJ. 2009;339:b2880.

17. Bridge JA, Iyengar S, Salary CB, Barbe RP, Birmaher B, Pincus HA, et al. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. JAMA. 2007;297(15):1683-96.

18. Hetrick SE, McKenzie JE, Cox GR, Simmons MB, Merry SN. Newer generation antidepressants for depressive disorders in children and adolescents. Cochrane Database Syst Rev. 2012;11(11):CD004851.

19. Casey BJ, Jones RM, Levita L, Libby V, Pattwell SS, Ruberry EJ, et al. The storm and stress of adolescence: insights from human imaging and mouse genetics. Dev Psychobiol. 2010;52(3):225-35.

20. Sakolsky DJ, Perel JM, Emslie GJ, Clarke GN, Wagner KD, Vitiello B, et al. Antidepressant exposure as a predictor of clinical outcomes in the Treatment of Resistant Depression in Adolescents (TORDIA) study. J Clin Psychopharmacol. 2011;31(1):92-7.

21. Martin A, Young C, Leckman JF, Mukonoweshuro C, Rosenheck R, Leslie D. Age effects on antidepressant-induced manic conversion. Arch Pediatr Adolesc Med. 2004;158(8):773-80.

22. Pigeon WR, Pinquart M, Conner K. Meta-analysis of sleep disturbance and suicidal thoughts and behaviors. J Clin Psychiatry. 2012;73(9):e1160-7.

23. Gibbons RD, Hur K, Bhaumik DK, Mann JJ. The relationship between antidepressant medication use and rate of suicide. Arch Gen Psychiatry. 2005;62(2):165-72.

24. Olfson M, Shaffer D, Marcus SC, Greenberg T. Relationship between antidepressant medication treatment and suicide in adolescents. Arch Gen Psychiatry. 2003;60(10):978-82.

25. Valuck RJ, Libby AM, Sills MR, Giese AA, Allen RR. Antidepressant treatment and risk of suicide attempt by adolescents with major depressive disorder: a propensity-adjusted retrospective cohort study. CNS Drugs. 2004;18(15):1119-32.

26. Tiihonen J, Lonnqvist J, Wahlbeck K, Klaukka T, Tanskanen A, Haukka J. Antidepressants and the risk of suicide, attempted suicide, and overall mortality in a nationwide cohort. Arch Gen Psychiatry. 2006;63(12):1358-67.

27. Wijlaars LP, Nazareth I, Whitaker HJ, Evans SJ, Petersen I. Suicide-related events in young people following prescription of SSRIs and other antidepressants: a self-controlled case series analysis. BMJ Open. 2013;3(9):e003247.

28. Simon GE, Savarino J, Operskalski B, Wang PS. Suicide risk during antidepressant treatment. Am J Psychiatry. 2006;163(1):41-7.

29. Gibbons RD, Coca Perraillon M, Hur K, Conti RM, Valuck RJ, Brent DA. Antidepressant treatment and suicide attempts and self-inflicted injury in children and adolescents. Pharmacoepidemiol Drug Saf. 2015;24(2):208-14.

30. Olfson M, Marcus SC, Shaffer D. Antidepressant drug therapy and suicide in severely depressed

http://dx.doi.org/10.52533/JOHS.2024.41206

children and adults: A case-control study. Arch Gen Psychiatry. 2006;63(8):865-72.

31. Leon AC, Marzuk PM, Tardiff K, Teres JJ. Paroxetine, other antidepressants, and youth suicide in New York City: 1993 through 1998. J Clin Psychiatry. 2004;65(7):915-8.

32. Courtet P, Lopez-Castroman J, Jaussent I, Gorwood PA. Antidepressant dosage and suicidal ideation. JAMA Intern Med. 2014;174(11):1863-5.

33. Gibbons RD, Brown CH, Hur K, Marcus SM, Bhaumik DK, Erkens JA, et al. Early evidence on the effects of regulators' suicidality warnings on SSRI prescriptions and suicide in children and adolescents. Am J Psychiatry. 2007;164(9):1356-63.

34. Libby AM, Orton HD, Valuck RJ. Persisting decline in depression treatment after FDA warnings. Arch Gen Psychiatry. 2009;66(6):633-9.

35. Katz LY, Kozyrskyj AL, Prior HJ, Enns MW, Cox BJ, Sareen J. Effect of regulatory warnings on antidepressant prescription rates, use of health services and outcomes among children, adolescents and young adults. CMAJ. 2008;178(8):1005-11.

36. Wheeler BW, Gunnell D, Metcalfe C, Stephens P, Martin RM. The population impact on incidence of suicide and non-fatal self harm of regulatory action against the use of selective serotonin reuptake inhibitors in under 18s in the United Kingdom: ecological study. BMJ. 2008;336(7643):542-5.

37. Wilkinson P, Kelvin R, Roberts C, Dubicka B, Goodyer I. Clinical and psychosocial predictors of suicide attempts and nonsuicidal self-injury in the Adolescent Depression Antidepressants and Psychotherapy Trial (ADAPT). Am J Psychiatry. 2011;168(5):495-501.

38. Miller M, Swanson SA, Azrael D, Pate V, Sturmer T. Antidepressant dose, age, and the risk of deliberate self-harm. JAMA Intern Med. 2014;174(6):899-909.

39. Schneeweiss S, Patrick AR, Solomon DH, Mehta J, Dormuth C, Miller M, et al. Variation in the risk of suicide attempts and completed suicides by antidepressant agent in adults: a propensity score-adjusted analysis of 9 years' data. Arch Gen Psychiatry. 2010;67(5):497-506.

40. Woldu H, Porta G, Goldstein T, Sakolsky D, Perel J, Emslie G, et al. Pharmacokinetically and clinician-determined adherence to an antidepressant regimen and clinical outcome in the TORDIA trial. J Am Acad Child Adolesc Psychiatry. 2011;50(5):490-8.

41. Maalouf FT, Atwi M, Brent DA. Treatment-resistant depression in adolescents: review and updates on clinical management. Depress Anxiety. 2011;28(11):946-54.

42. Stanley B, Brown G, Brent DA, Wells K, Poling K, Curry J, et al. Cognitive-behavioral therapy for suicide prevention (CBT-SP): treatment model, feasibility, and acceptability. J Am Acad Child Adolesc Psychiatry. 2009;48(10):1005-13.

http://dx.doi.org/10.52533/JOHS.2024.41206