





Comorbid Adolescent Substance Use and Major Depressive Disorders: A Review

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ABSTRACT: Psychiatric comorbidity is the rule rather than the exception in adolescents diagnosed with substance use disorders (SUD). The aim of this evidence-based review is to enhance practitioners' understanding of the relationship between the commonly concomitant SUD and comorbid unipolar depression as well as increase the knowledge of treatment of adolescents with these comorbid disorders.

KEY WORDS: adolescent substance use disorders, depression, treatment

INTRODUCTION

The availability and quality of treatment for adolescents with substance use disorders remains a major public health concern in the United States. It is estimated that only 10 to 15 percent of substance abusing adolescents in need of therapeutic intervention actually enroll in treatment.¹ Eighty percent of adolescents with SUD who do seek treatment receive services in outpatient treatment settings.² The population of adolescents with SUD is heterogeneous, and one of the largest subgroups is composed of those with one or more comorbid psychiatric disorders, also known as dual diagnosis (DD). Dual diagnosis is the rule rather than the exception and amounts to 70 to 80 percent in clinical samples.¹

...depression, dysthymia, and depressive disorder, not otherwise specified, affect up to 8.3 percent of adolescents.³ Between 1993 and 2003, the number of adolescents presenting to publicly funded substance abuse treatment facilities increased 61 percent.⁴

Although the majority of youth with SUD manifest psychiatric comorbidity, little research pertaining to treatment of dual diagnosis has been reported. Only recently have reports on treatment of depression and SUD started to trickle into the scientific literature.¹ The comorbidity of SUD with depression in adolescents is well established. Developmentally, adolescence is a time when the prevalence of both depression and substance use increases in non-referred community samples. For example, depression, dysthymia, and depressive disorder, not otherwise specified, affect up to 8.3 percent of adolescents.³

Between 1993 and 2003, the number of adolescents presenting to publicly funded substance abuse treatment facilities increased 61 percent.⁴ Thus, it is not surprising that adolescents may suffer from both a mood disorder and substance misuse. In clinical samples, this comorbidity may be especially prevalent, with the prevalence of comorbid unipolar depressive disorders in clinical samples of adolescents with SUD ranging from 24 to 50 percent.^{5,6}

There exist a number of possible relationships between mood disorders and SUDs.⁷ For example, depression may precede substance use disorders, may develop as a consequence of preexisting substance use disorders, may moderate the

severity of substance use disorders, or may originate from a common vulnerability. The etiological mechanisms for dual diagnosis of SUD and depression may have important therapeutic and prognostic implications.⁸ However, to date they have not been systematically researched. However, there appears to be little scientific support for the popular self-medication hypothesis of depression/SUD dual diagnosis.⁹

Among youth in treatment for SUD, the presence of comorbid depression has important clinical implications. Depression and SUD comorbidity raise the risk of treatment dropout, poorer treatment response, and earlier

relapse.^{10,11} SUDs among depressed youths are a risk factor for suicidal behaviors, including ideation, attempts, and completed suicide.¹² Adolescents with combined depression and SUD have higher rates of perceived service needs and receive more treatment services as compared with non-comorbid adolescents.¹³

Clinically, there exists a need for a coordinated intervention toward both SUD and depressive disorders.¹ Piecemeal treatments targeting depression in the absence of treatment for SUD (or vice versa) have a higher risk of failure than treatments that simultaneously target both disorders.¹² Barriers for integrating treatment services for the dually diagnosed include: 1) the historical separation of substance abuse and mental health services; 2) a limited number of clinicians and researchers who focus on dually diagnosed youth; and 3) the tendency to exclude youth with SUD from medication clinical trials of psychiatric disorder.^{14,15}

ASSESSMENT AND TREATMENT OF SUD IN YOUTH

Screening youth for alcohol, tobacco and other drug use (ATOD) followed when necessary by a comprehensive assessment of drug use severity at the physician's office are necessary sequential steps before developing a treatment plan or making a referral. Unfortunately, one of the barriers to treatment for adolescents with substance use disorders (SUD) in general and those with comorbid psychiatric disorders in particular has been a lack of training in medical school and residency training programs for both pediatricians and child and adolescent psychiatrists. Fewer than half of the pediatricians surveyed reported screening adolescents for use of ATOD, and fewer than a quarter acknowledged feeling comfortable conducting a comprehensive assessment or offering or making

TABLE 1. Rating scales that screen for depression in adolescents

MEASURE	AGE APPROPRIATENESS (APPROXIMATE YEARS)	READING LEVEL (GRADE)	SPANISH VERSION	NUMBER OF ITEMS	TIME TO COMPLETE (APPROXIMATE MINUTES)
Children's Depression Inventory (CDI) ³	7–17	1st	Yes	27	10–15
Center for Epidemiological Studies-Depression Scale for Children (CES-DC) ⁴	12–18	6th	Yes	20	5–10
Center for Epidemiological Studies-Depression Scale (CES-D) ⁵	14 and older	6th	No	20	5–10
Reynolds Child Depression Scale ¹	8–12	2nd	Yes	30	10–15
Reynolds Adolescent Depression Scale ²	13–18	3rd	No	30	10–15
Beck Depression Inventory (BDI) ^{6,7}	14 and older	6th	Yes	21	5–10

1. Reynolds WM. *Reynolds Child Depression Scale*. Odessa, FL: Psychological Assessment Resources, 1989.

2. Reynolds WM. *Reynolds Adolescent Depression Scale*. Odessa, FL: Psychological Assessment Resources, 1986.

3. Kovacs M. *Children's Depression Inventory*. North Tonawanda, NY: Multi-Health System, 1992.

4. Fendrich M, Weissman MM, Warner V. Screening for depressive disorder in children and adolescents: Validating the Center for Epidemiologic Studies Depression Scale for Children. *Am J Epidemiol* 1990;131:538–51.

5. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychological Measurement* 1977;1:385–401.

6. Beck AT. *Beck Depression Inventory*. Philadelphia, PA: Center for Cognitive Therapy, 1961.

7. Beck AT, Steer RA, Brown GK. *BDI-II, Beck Depression Inventory Manual, Second Edition*. Boston: Harcourt Brace, 1996.

referral for treatment.^{16,17} Barriers to screening of ATOD use and treatment of SUD reported by pediatricians include insufficient time, lack of training to manage positive screens for ATOD use, unfamiliarity with screening tools, lack of treatment resources, and need to triage for other problems.¹⁸ No such reports are available for child and adolescent psychiatrists.

There is, however, no compelling reason to believe that their level of knowledge is any different.

Most treatment programs advocate a goal of abstinence, although it is not attainable for a significant segment of youth in treatment who respond with partial or no improvement at all. Psychosocial treatment strategies that have shown promise in

reducing SUD among adolescents include family therapies, such as multisystemic therapy (MST), functional family therapy (FFT), and multidimensional family therapy (MDFT).¹⁹ Other interventions with an evidence base include behavioral therapy, cognitive-behavioral therapy (CBT), motivational interviewing known also as motivational

enhancement therapy (MMI/MET), contingency management reinforcement, Minnesota 12-step model, integrative models of treatment, such as MET/CBT, and the community reinforcement approach utilized in the multicenter Cannabis Youth Treatment study (CYT).^{6,20-24} Despite some prominent differences in design and methodology, the most recent studies employing different treatment modalities in youth with SUD have reported only minor differences in outcomes across conditions in terms of days of substance use at three months.^{6,17,24} For a comprehensive review, please see Little and Rowe.²⁵

Pathways to recovery from SUD are complicated and often involve intermittent and episodic periods of improvement, followed by relapse, and evolving changes in symptom severity. The variable clinical course of adolescent SUD often leads to premature termination from treatment and then later re-entry into the

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treatment system.²⁶ Maintaining and sustaining treatment gains in the post-treatment period is challenging in that many youth with SUD have yet to attain their peak level of substance use and yet to experience marked adverse consequences from use. A considerable number of adolescents in treatment are actually “continuing users” at the end of the designated treatment period because they did not abstain during treatment and/or had no motivation to do so later.²⁷

Rates of dropout from treatment as well as partial or no reduction in

use may range between 20 and 50 percent.²⁸ Maintenance of treatment gains in the months after treatment ends is another focus of concern. Brown, et al., reported 60-percent and 80-percent relapse rate at three months and one year, respectively, after completing treatment.²⁹ Williams and Chang’s comprehensive and comparative review of adolescent treatment outcome reported that the average rate of sustained abstinence is 38 percent at six months and 32 percent at 12 months.³⁰ The best predictor of long-term outcomes is initial level of change with clinical intervention. Treatment specificity appears not to be correlated with outcome.

ASSESSMENT OF UNIPOLAR DEPRESSION IN YOUTH

The psychiatric assessment of adolescents with substance use disorders should routinely include screening questions about depressive symptoms. Symptoms include depressive or sad mood, irritability, anhedonia, and

suicidality. Symptoms should be considered clinically significant if they are present most of the time, affect the teenagers daily psychosocial or academic functioning, and are above and beyond what is expected for the adolescent’s chronological and psychological age. Validated rating scales that screen for depression utilizing either a parent- or self-report are used to quantify depressive symptoms. If screening suggests significant depressive symptoms, a thorough clinical evaluation should be completed to determine the presence of a

depressive disorder and other comorbid psychiatric and medical conditions. Table 1 presents some of these rating scales.

TREATMENT OF UNIPOLAR DEPRESSION IN YOUTH

Psychosocial therapies for depression in youth include cognitive-behavioral, interpersonal, cognitive, and to a lesser extent, family-based interventions. All have some evidence for effectiveness in treating adolescent depressive disorders.³¹⁻³⁵ A recent meta-analysis of youth depression psychotherapy trials showed a small but positive effect size of 0.34.³⁶ A component profiles analysis revealed that effective psychosocial therapies for adolescent depression all share some common therapeutic foci. These components include a focus on having youths achieve measurable goals or increase their competence in at least one self-identified area, providing psychoeducation about depression and its treatment, teaching some form of individual self-monitoring skill, addressing social relationship issues, addressing communication skills, teaching cognitive restructuring to help modify unrealistic, negative thoughts about oneself, others, and events, teaching general problem-solving skills, and using behavioral activation techniques to help the adolescent engage in behaviors that are pleasurable and can elevate their mood.³³ Process elements common to effective youth depression therapies include the therapist’s indication that there is hope for change, that depression is a treatable illness, and providing exercises for the adolescent to practice skills learned in therapy outside of the treatment session.³³

Given high placebo response rates between 35 and 60 percent in clinical antidepressant trials for youth depression, it is advisable to initiate treatment for youth depression with psychotherapy for mild to moderate depression and assess outcome over 4 to 8 weeks

before consideration of adding antidepressant medication.³⁷ For more severe and impairing depression, antidepressants may be initiated with the start of psychotherapy. Extant psychopharmacological research supports using an algorithmic approach to adolescent antidepressant treatment beginning with SSRIs, including either fluoxetine, citalopram, or sertraline. Fluoxetine has the most empirical support, with three large, positive studies indicating superiority to placebo.⁴⁰ Recent reports of increased suicidality in pediatric patients treated with antidepressant medications have resulted in the FDA placing a black box warning in the prescribing literature for antidepressants.⁴¹ This warning has resulted in diminished prescribing rates of antidepressant medications for early-onset depression.⁴² However, a more recent and complete meta-analysis of clinical response and risk for suicidality finds a very favorable risk/benefit profile for antidepressant therapy in pediatric depression.⁴³ When initiating antidepressant therapy, clinicians should have frequent contact with patients to assess any increase in suicidality.

Despite a number of efficacious psychosocial and medical treatments, however, full remission of MDD with acute treatment is not the norm, and five-year relapse rates may be as high as 50 to 70 percent.⁴⁴ In the recent Treatment for Adolescents with Depression study, 12 weeks of cognitive behavior therapy (CBT) plus fluoxetine was most efficacious for moderate to severe MDD, but full remission from episode at Week 12 was attained by only 37 percent with combined treatment.^{40,45} All treatments led to a decrease in suicidal ideation, with combination therapy also having the best results on this outcome. Of the monotherapies, fluoxetine was a more effective acute intervention than CBT.

TABLE 2. General clinical guidelines in the treatment of depression in dually diagnosed adolescents

TREATMENT INTERVENTION	PARTICIPANTS	DETAILS
Psychoeducation	Parents, adolescent, and clinician	<i>Causes of depression</i>
		Depression is an illness; not a weakness
		Emphasize chronic and recurring nature of depression
		<i>Symptoms</i>
		Course of illness with/without treatment
		Review of evidence based practice in the treatment of adolescent depression
		Risks associated with depression, including risk for suicide
		Risks associated with various treatments, including risks associated with no treatment
Family involvement	Parents, adolescent, and clinician	Provide parenting guidance
		Help family manage conflict
		Reduce family dysfunction
Supportive management	Adolescent and clinician	Active listening
		Restoration of hope
		Problem solving
		Coping skills
		Monitor for any high risk behaviors including risk for suicidality
School	Parents, adolescent, clinician, and appropriate school personnel	Advocate for educational supports until recovery achieved
		Adolescent students with MDD may qualify for school-based educational supports in the Emotional Disturbance Disability category under the Individuals with Educational Disabilities Act

SUD teens have been excluded from all adolescent treatment studies for MDD, thus making it impossible to develop a rational empirically based clinical approach to the substance abusing adolescent with major depressive disorder. Similarly, although depressed youths have been included in some samples in treatment studies for SUD, in general, results have not been analyzed separately for this dual diagnostic group. There exists a great need to scientifically develop and test interventions for SUD youths with depression in future studies.

TREATMENT OF SUD AND COMORBID DEPRESSION

Evidence-based research of the treatment of SUD and depression in youth includes either psychosocial interventions or psychosocial interventions integrated with SSRI pharmacotherapy (when indicated). The guidelines for the treatment of depression in dually diagnosed adolescents are the same as the guidelines for the treatment of depression not complicated by alcohol or substance abuse. However, since substance misuse may impair judgment and increase impulsivity, close and frequent

monitoring of the depressed teenager who is dually diagnosed is mandatory. Since depression in adolescents is often a chronic and intermittently recurring illness that predicts increased risk for depression in the adult years and since comorbid substance use disorders may increase depression severity, the treatment of depression should always include

treatment, regardless of the specific type(s) of intervention used (antidepressants, psychosocial interventions, or both).

Maintenance treatment is used to avoid depressive episode recurrences in adolescents who have had a more recurrent, severe, and chronic disorder. Maintenance treatment may last several years or more.⁴⁶

General interventions [that include] family involvement, supportive therapy, psychoeducational supports, and supportive therapy may be sufficient treatment for the dually diagnosed adolescent with uncomplicated, brief, or mild depression.

acute and continuation phases. The main goal of the acute phase is to develop a treatment plan that is acceptable to the adolescent and parents and addresses the substance abuse issues, to provide education about the nature of depression, including how ongoing substance abuse can worsen depressive symptoms, and the risks and benefits of various treatments, including the risk accruing from a decision not to seek treatment, to introduce an intervention(s), and to achieve a response to treatment. The acute phase generally takes from several weeks to up to three months. Continuation treatment is required for all depressed youths to consolidate the response during the acute phase and to avoid depressive relapse. The consolidation phase generally lasts 6 to 12 months. Thus, the total length of time to treat a single episode of adolescent depression including the acute and continuation phase may last between 9 and 15 months. Table 2 presents general elements in the treatment of adolescent depression that should be present in both the acute and continuation phases of

Psychosocial treatment. An important question is whether psychosocial treatment that targets both SUD and depression is more efficacious for substance use outcomes in depressed SUD teens than treatment targeting only SUD. Studies have demonstrated that treatments sometimes have beneficial effects for non-targeted, yet comorbid conditions. For example, Kendall, et al., showed

...in adolescents with more severe depression, chronic or recurrent depressive episodes, functional impairment, suicidality, and/or agitation, the addition of antidepressant therapy and specific types of empirically supported psychotherapy...may be necessary.

that anxiety-focused treatment alleviated comorbid oppositional defiant and attention deficit disorders.⁴⁷ Also, Kaminer, et al., reported that treatment and aftercare for SUD adolescents reduced suicidal ideations.⁴⁸ As

noted above, youth with depression have been included in some studies of psychotherapy for SUD, but analyses have not always investigated comparative efficacy for this sub-group. In some studies, comorbidity, including depression, has been associated with poorer outcome of SUD treatment.^{11,13,49}

Another important question is whether psychosocial treatment that targets both SUD and depression is more efficacious on depression outcomes in teens than similar treatment targeting only SUD. It may seem evident that the answer should be positive, but there are conflicting data. Investigators have distinguished between primary and secondary depression in SUD adolescents, with secondary depression following the onset of SUD.⁵⁰ Although successful treatment of SUD could hypothetically reduce secondary depression, two studies did not find this outcome, suggesting a need to target depression even in secondary cases.^{6,51}

Hawke and her colleagues indicated that although comorbidity is a key correlate of treatment outcome among adolescents in treatment for SUD, most studies examine comorbidity as a static patient characteristic that affects

drug use severity and outcomes.⁵² The stability or change of psychiatric diagnostic status among substance-abusing adolescents has not been systematically examined. Findings by Hawke, et al.,⁵² indicate that diagnostic status changes

considerably over time, among a substantial percentage of depressed youths in treatment for SUD only. However, the investigators did not assess whether reduced substance use mediated reduced depression. In addition, the one-year follow-up period was long enough to allow for depression remission based on natural course. In summary, it remains to be seen whether targeting comorbid conditions during SUD treatment improves substance-related outcomes. Similarly, the question remains whether effective SUD treatment alone can lead to reduced severity of depression.

Psychosocial treatment for adolescents with SUD and depression ideally should arise from a theoretical model with demonstrated efficacy in the treatment of both SUD and depression. Cognitive behavior therapy (CBT), broadly construed, provides such a foundation. Family systems, behavioral, and cognitive behavioral therapy models have all shown promise in treating adolescent SUD. Family therapy models have been particularly efficacious for teen SUD, and have some emerging evidence of efficacy for adolescent depression.³³ Only one study utilizing a psychosocial approach to the treatment of SUD and depression in youth is reported. Curry, et al., developed Family and Coping Skills (FACS) therapy as an integrated family and peer group CBT intervention for SUD adolescents with depression.⁵³ It combines adolescent group skills training with cognitive behavioral family therapy, using modalities and components from effective interventions for either problem. Adolescents also complete periodic urine drug screens. Adolescents attend two group and one family therapy sessions per week. Thus the treatment approximates an intensive outpatient intervention. Pilot testing indicates considerable promise. A larger scale randomized, controlled study is

necessary to replicate and expand upon this preliminary study.

Pharmacotherapy treatment.

When should the clinician consider the addition of an antidepressant to the treatment plan for a dually diagnosed adolescent? General interventions as noted in Table 2, including family involvement, supportive therapy, psychoeducational supports, and

Heavy, sustained substance use or poor adherence with or refusal of medication may preclude pharmacotherapy. Once abstinence or a reduction in substance use has occurred, physicians may proceed with a trial of antidepressant medications.⁵⁹

supportive therapy, may be sufficient treatment for the dually diagnosed adolescent with uncomplicated, brief, or mild depression. However, in adolescents with more severe depression, chronic or recurrent depressive episodes, functional impairment, suicidality, and/or agitation the addition of antidepressant therapy and specific types of empirically supported psychotherapy (see earlier discussion) may be necessary. Adolescents with substance use disorders have higher rates of depression than teenagers in the general population. Comorbid depression is associated with more severe substance abuse, poorer antidepressant treatment outcomes, and higher relapse rates. Thus, the dually diagnosed adolescent requires close clinical evaluation and monitoring of treatment. For depressed adolescents with complications such as those noted above, consideration to prescribing an antidepressant as well as psychosocial treatment is warranted. Although the extant literature is limited, most studies

have examined fluoxetine in the treatment of dually diagnosed teenagers.

Only three studies have evaluated the efficacy of SSRI antidepressants in depressed adolescents with SUD. Riggs, et al., reported that of eight adolescents treated with fluoxetine, seven demonstrated marked improvement in depressive symptoms.⁵⁴ The

study was conducted in a residential treatment center, so the subjects could not drink or use substances. Consequently, drug and alcohol consumption were not measured as part of the study. No subject was discontinued from the medication because of side effects. The authors of that study concluded that fluoxetine appears to be safe and effective in treating depression in adolescents with MDD and SUD.

Another small double-blind pilot study involving ten adolescents made a preliminary assessment of the efficacy of the SSRI antidepressant sertraline- versus placebo in treating adolescents with alcohol use disorders plus comorbid depression.⁵⁵ Five of the subjects received sertraline, and five received placebo. Results from this study demonstrated that both treatment groups showed an improvement in drinking and in depressive symptoms, but there were no significant between-group differences in either drinking or depression with their very small study groups. The authors of that study concluded that they were unable to generalize about the

results of their pilot study because of its very limited sample size.

A pilot study involving 13 adolescents with comorbid depression suggested fluoxetine efficacy for decreasing significantly within-group depressive symptoms, and alcohol use depression.⁵⁶ Data from one-, three-, and five-year follow-up studies from that pilot study suggested that continued treatment is often needed to prevent recurrences of major depression.⁵⁷ The promising results of these preliminary studies involving comorbid adolescents are consistent with the results of double-blind, placebo-controlled trials of fluoxetine in comorbid adults reported by Cornelius' team.

Riggs and colleagues completed a 16-week double-blind, placebo-controlled study involving 126 adolescents with MDD, SUDs and behavior problems.⁵⁸ All subjects

fluoxetine from placebo occurred further along in treatment of these dually diagnosed youths than in studies of non-SUD children and adolescents, suggesting that a longer treatment period may be necessary for substance abusing adolescents with MDD.^{38,40}

LIMITATIONS AND CONCLUSION

The American Academy of Child and Adolescent Psychiatry's *Practice Parameters for the Assessment and Treatment of Children and Adolescents with Substance Use Disorders* concluded that it is essential to treat psychiatric disorders that are comorbid with substance use disorders among adolescents, and that integration of psychotherapy and medication therapy is currently thought to be the best treatment of that population.¹² The *Practice Parameters* also suggest that SSRI

abuse; 3) poor adherence with treatment in general and with medications in particular, making close clinical monitoring a requirement; and 4) increased risk for side effects of the antidepressants, including potential increased suicidality. It is essential to be aware of the state of the ongoing debate regarding whether and to what degree the use or lack of use of SSRIs for the treatment of depression in individuals under the age of 25 years of age contributes to increased suicidality.⁵⁹⁻⁶¹ The Food and Drug Administration recommends that depressed youth should be seen every week for the first four weeks and biweekly thereafter following the administration of a SSRI.⁵⁹

Heavy, sustained substance use or poor adherence with or refusal of medication may preclude pharmacotherapy. Once abstinence or a reduction in substance use has occurred, physicians may proceed with a trial of antidepressant medications.⁵⁹ Treatment may need to be long-term. For example, in the TADS study, continuation and maintenance treatment out to 36 weeks was included, and continued response and improved rates of remission were noted over this period.⁶²

It is noteworthy that even when the desired level of care according to the American Society of Addiction Medicine⁶³ is achieved, there are variations in the treatment menu of SUD treatment programs within the same level.⁶⁴ The treatment pivotal components that are recommended here include personal or group psychotherapy focused on drug refusal skills and management of high-risk situations for use integrated with pharmacotherapy for depression complemented by periodic drug urinalysis.

Finally, given the relapsing and remitting nature of SUD, continuity of care should be already considered at the onset rather than at the end of treatment given potential dropout.^{65,66}

The treatment pivotal components that are recommended here include personal or group psychotherapy focused on drug refusal skills and management of high-risk situations for use integrated with pharmacotherapy for depression complemented by periodic drug urinalysis.

also received CBT for SUD concurrent with the medication trial. Fluoxetine had superior efficacy to placebo from Week 13 ($p=0.05$) through Week 17 ($p=0.01$) and higher rates of complete remission of depression ($p=0.05$). Those adolescents whose depressions remitted, regardless of medication group assignment, significantly reduced their drug use whereas non-remitters showed no change in drug use. Overall, fluoxetine was well tolerated and demonstrated a good safety profile, despite non-abstinence in the majority of participants. It is notable that the separation of

antidepressants are a promising form of therapy for depressive disorders in combination with substance use disorders among adolescents.

As summarized by Volkow, treatment of dually diagnosed adolescents should include interventions for both disorders because lack of adequate treatment of one of the disorders might interfere with recovery.⁸ However, treatment of the comorbid disorder creates potential concerns for both undesirable drug interactions, such as 1) drugs of abuse interfering with the effectiveness of antidepressants; 2) enhanced toxicity of the drug of

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