

## Dosage-Form and Drug Delivery Strategies for Adolescent Psychotropic Treatment: Current Solutions and Implementation Gaps

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### ABSTRACT

Adolescent psychotropic treatment is shaped not only by pharmacological efficacy but also by whether formulations can be initiated, tolerated, and sustained in daily life. This narrative review examines dosage-form and drug delivery strategies relevant to adolescent psychotropic treatment and discusses implementation gaps affecting acceptability, feasibility, and treatment continuity. The review focuses on four practical domains: long-acting injectable strategies in adolescent psychopharmacology, extended-release and alternative delivery strategies in attention-deficit/hyperactivity disorder, acceptability of oral dosage forms, and dose-flexible or manipulation-based approaches used when age-appropriate formulations are limited. Across the literature, long-acting and extended-release formulations are consistently presented as adherence-supportive strategies because they may reduce dosing burden and better fit school-day routines, whereas manipulation-based strategies are described mainly as pragmatic responses to formulation shortages rather than optimized solutions. Evidence specific to adolescents remains uneven, with extensive reliance on off-label use, extrapolation from adult data, and broader paediatric literature. Data from resource-constrained settings are especially sparse. Overall, the literature suggests that dosage-form strategy is materially relevant to treatment continuity in adolescent psychopharmacology, but current implementation remains limited by narrow formulation diversity, scarce adolescent-specific evidence, and insufficient integration between pharmaceutical design and real-world care delivery.

**Keywords:** adolescent psychopharmacology; dosage form; drug delivery; long-acting injectable; extended-release; medication adherence

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### INTRODUCTION

Adolescent psychotropic treatment represents an important area of clinical and pharmacotherapeutic concern because treatment continuity during this developmental stage may influence both short-term symptom control and longer-term clinical stability. Although psychotropic medications are used across a range of adolescent psychiatric conditions, their effectiveness in practice depends not only on pharmacological efficacy but also on whether treatment can be initiated, maintained, and integrated into everyday life. In adolescents, this process may be complicated by developmental transitions, school-based routines, family dynamics, and varying levels of autonomy in medication use.<sup>1</sup>

Within this context, dosage form and route of administration are highly relevant to the practical management of psychotropic treatment. Factors such as dosing frequency, swallowability, regimen complexity, flexibility of dose adjustment, and the physical burden of administration may shape whether treatment is

feasible and acceptable over time. These considerations are particularly important in adolescent psychopharmacology, where medication-taking may be influenced by preferences, stigma, caregiver involvement, and the challenge of sustaining treatment within changing daily routines.<sup>2,3</sup>

The available literature suggests that several dosage-form and drug delivery strategies may be relevant to adolescent psychotropic treatment. These include long-acting injectable formulations, which may reduce reliance on daily oral administration; extended-release formulations, which may simplify dosing schedules and support symptom coverage across the day; and dose-flexible or manipulation-based approaches used when age-appropriate formulations are lacking. The literature also points to the importance of oral dosage-form acceptability, including the practical suitability of solid, liquid, or alternative formulations for younger patients and adolescents.<sup>2-4</sup>

Despite these developments, important implementation gaps remain. Much of the literature is fragmented

across diagnostic categories, medication classes, and age groups, and relatively little work has examined these strategies through the combined lens of acceptability, feasibility, continuity of care, and contextual applicability. This limitation may be especially relevant for resource-constrained settings, where infrastructure, access, workforce capacity, and continuity of medication supply may affect how psychotropic treatments are delivered and sustained. This narrative review therefore examines dosage-form and drug delivery strategies relevant to adolescent psychotropic treatment and discusses current implementation gaps affecting acceptability, feasibility, treatment continuity, and applicability in resource-constrained settings.

### APPROACH TO THE NARRATIVE REVIEW

This article is presented as a narrative review rather than a systematic or scoping review. It synthesizes peer-reviewed literature that is directly relevant to dosage-form and drug delivery issues in adolescent psychotropic treatment, prioritizing studies and reviews that inform acceptability, feasibility, treatment continuity, or implementation challenges.

Literature was identified through structured searches centered on adolescent psychopharmacology, dosage forms, long-acting and extended-release formulations, route-of-administration alternatives, oral acceptability, dose manipulation, and implementation considerations. Priority was given to publications from 2017 to 2025 that contributed directly to at least one of the analytic domains developed for this review: long-acting injectable strategies, extended-release and alternative delivery strategies in ADHD, oral dosage-form

acceptability, dose-flexible and manipulation-based strategies, and implementation gaps.

The aim of this review is descriptive rather than quantitative. Accordingly, the synthesis does not attempt to generate pooled effect estimates. Instead, it integrates the literature to clarify how formulation and delivery strategies are being used, what problems they are intended to solve, and where the evidence remains incomplete for adolescent psychotropic care.

### RESULTS

The results of this narrative review map the range of dosage-form and drug delivery strategies currently reported in the literature for adolescent psychotropic treatment. The evidence base includes clinical studies, observational studies, review-level evidence, and implementation-relevant literature, reflecting both established formulation strategies and practical approaches to treatment delivery. Rather than estimating pooled effectiveness, the present synthesis organizes the literature according to the main dosage-form and delivery approaches described, their clinical relevance, and their reported implications for acceptability, feasibility, and treatment continuity.

Across the mapped evidence, recurring themes include long-acting and extended-release strategies, oral dosage-form acceptability, dose-flexible approaches used when age-appropriate formulations are limited, and adjunctive adherence-support interventions. The general characteristics of the included literature are summarized in Table 1. For transparency and consistency, all studies included in Table 1 are also represented in the reference list.

**Table 1. General characteristics of the literature included in this narrative review (n = 26)**

Study	Setting / population	Psychotropic treatment context	Dosage-form or delivery strategy	Design	Main finding	Implementation relevance
Correll et al., 2021 [1]	International; child and adolescent mental disorders	Broad psychiatric treatment landscape in youth	Pharmacological, psychosocial, and brain-stimulation interventions	Umbrella review	Maps pharmacological options across youth mental disorders.	Provides high-level context on efficacy and acceptability across youth mental-health treatments.
Khan et al., 2022 [2]	International; paediatric pharmaceuticals	Paediatric chronic treatment with relevance to psychotropics	Acceptability-related dosage-form design	Narrative review	Discusses formulation features linked to paediatric acceptability.	Summarizes how swallowability, size, taste, and dose flexibility shape paediatric acceptability.
Jayasree et al., 2024 [3]	International; mental health disorders	Adults and adolescents in broader mental-health adherence	Medication non-adherence typology and adherence-enhancing strategies	Narrative review	Classifies non-adherence and summarizes corrective strategies.	Frames intentional and unintentional non-adherence and highlights regimen

Dosage-Form and Drug Delivery Strategies for Adolescent Psychotropic Treatment: Current Solutions and Implementation Gaps

Study	Setting / population	Psychotropic treatment context	Dosage-form or delivery strategy	Design	Main finding	Implementation relevance
		literature				simplification and long-acting strategies.
Smogur et al., 2022 [4]	Europe and United States	Children and adolescents	Approved psychotropic medications in youth	Regulatory/scoping review	Catalogues approved psychotropics and available dosage forms.	Maps approved psychotropics, ages, dosage forms, and dose ranges, highlighting limited formulation diversity.
Baeza et al., 2023 [5]	Multinational	Adolescents with schizophrenia-spectrum disorders	Antipsychotic treatment	Long-acting injectable antipsychotics	Systematic review	Synthesizes available adolescent LAI evidence and reports generally favorable effectiveness and tolerability.
Sun et al., 2025 [6]	United States; acute psychiatric hospital	Patients younger than 18 years	Antipsychotic treatment	Long-acting injectable antipsychotics	Retrospective chart review	Describes real-world initiation patterns, off-label dosing variability, and continuity issues during hospitalization.
Parikh et al., 2025 [7]	United States; inpatient and outpatient psychiatry	Adolescents with bipolar disorder or schizoaffective disorder	Antipsychotic treatment	Long-acting injectable antipsychotics	Prospective observational cohort	Reports sustained clinical improvement and strong treatment continuity in a high-risk adolescent sample.
Levy et al., 2025 [8]	Israel; psychiatric hospital	Children and adolescents compared with young adults	Antipsychotic treatment	Long-acting injectable antipsychotics	Retrospective comparative cohort	Suggests similar efficacy and tolerability patterns in younger and adult groups, supporting feasibility.
Ward et al., 2025 [9]	United States; multistate Medicaid claims	Children and adolescents with schizophrenia	Antipsychotic treatment	Second-generation LAI antipsychotics	Claims-based cohort study	Examines prescribing and discontinuation patterns and identifies persistence challenges and racial inequities.
Lytle et al., 2017 [10]	United States; mixed psychiatric settings	Youth younger than 18 years	Severe psychiatric disorders	Long-acting injectable antipsychotics	Narrative literature review	Provides early support for LAI use in youth when oral adherence is

Dosage-Form and Drug Delivery Strategies for Adolescent Psychotropic Treatment: Current Solutions and Implementation Gaps

Study	Setting / population	Psychotropic treatment context	Dosage-form or delivery strategy	Design	Main finding	Implementation relevance
						problematic.
Bertagnoli et al., 2025 [11]	Global	Paediatric, adolescent, and pregnancy populations	Long-acting therapies including psychiatric applications	Injectable and implantable long-acting systems	Systematic review	Highlights the limited paediatric evidence base for long-acting formulations, including psychotropic applications.
Cutler et al., 2023 [12]	Multicentre clinical trial	Children and adolescents with ADHD	ADHD pharmacotherapy	Transdermal d-amphetamine system	Pivotal clinical trial	Shows efficacy and tolerability of sustained transdermal stimulant delivery as an alternative to oral dosing.
Findling et al., 2025 [13]	Multicentre, international	Children and adolescents with ADHD	ADHD pharmacotherapy	Extended-release viloxazine	Long-term open-label extension study	Describes sustained symptom control and tolerability with once-daily non-stimulant extended-release therapy.
Childress et al., 2025 [14]	United States; specialized clinics	Children and adolescents with ADHD	ADHD pharmacotherapy	Extended-release viloxazine with psychostimulants	Open-label phase 4 study	Shows flexible morning or evening dosing and maintained tolerability in combination treatment.
Childress et al., 2020 [15]	International review context	Children and adolescents with ADHD	ADHD pharmacotherapy	Extended-release guanfacine	Narrative review	Summarizes a once-daily non-stimulant extended-release option relevant to regimen simplification.
Ferrin et al., 2025 [16]	International	Children and adolescents with ADHD	Routine ADHD medication use	Long-acting formulations and adherence-supportive approaches	Systematic review	Finds that long-acting formulations are associated with better adherence and persistence than shorter-acting regimens.
Nazarova et al., 2022 [17]	Global	Predominantly paediatric and adult ADHD trials	ADHD pharmacotherapy	Extended-release stimulant and non-stimulant formulations	Analytical review	Maps the expansion of long-acting ADHD formulations and other therapeutic options investigated in trials.

Dosage-Form and Drug Delivery Strategies for Adolescent Psychotropic Treatment: Current Solutions and Implementation Gaps

Study	Setting / population	Psychotropic treatment context	Dosage-form or delivery strategy	Design	Main finding	Implementation relevance
Kolari et al., 2025 [18]	Finland; nationwide registers	Children and adolescents receiving ADHD medication	ADHD pharmacotherapy	Real-world use of stimulant and related formulations	Population-based cohort	Shows that treatment duration in routine care extends for years but is shorter in adolescents than in younger children.
Alessandri et al., 2021 [19]	Seven European countries; community survey	Children and adolescents	Oral medication use including psychotropic relevance	Preference for solids, liquids, ODTs/films, and granules	Cross-sectional survey	Documents age-related dosage-form preferences and variable familiarity with alternative oral formulations.
O'Brien et al., 2025 [20]	International	Mainly adults, with relevance to youth adaptation	Antidepressant and benzodiazepine tapering	Splitting, dilution, and other manipulation strategies	Systematic review	Reviews manipulation-based psychotropic tapering methods and their implications for dose accuracy.
Paulsson et al., 2025 [21]	Europe; paediatric healthcare settings	Children and adolescents	Paediatric oral medicine administration with psychotropic relevance	Crushing, splitting, dispersion, and manipulation of oral dosage forms	Narrative review	Highlights how manipulation is common when child-appropriate formulations are unavailable and summarizes related risks.
Strawn et al., 2023 [22]	Clinical review context	Children and adolescents	SSRI/SNRI treatment for anxiety and depression	Flexible dose reduction and discontinuation approaches	Narrative review	Discusses tapering challenges and the role of pharmacokinetically informed dose reduction in youth.
Carvalho and Almeida, 2022 [23]	International	General populations with paediatric relevance	Personalized pharmacotherapy	Compounded and individualized formulations	Narrative review	Argues that tailored formulations may support treatment implementation and persistence when standard forms are poorly suited.
Valaei Sharif et al., 2024 [24]	International	Children and adolescents with ADHD	ADHD medication adherence	Educational, behavioral, digital, and professional support strategies	Scoping review	Synthesizes non-formulation adherence interventions relevant to implementation in youth treatment

Dosage-Form and Drug Delivery Strategies for Adolescent Psychotropic Treatment: Current Solutions and Implementation Gaps

Study	Setting / population	Psychotropic treatment context	Dosage-form or delivery strategy	Design	Main finding	Implementation relevance
						programs.
Vitija et al., 2022 [25]	International	Children and adolescents with ADHD, anxiety, or depression	Psychotropic adherence support	Digital adherence-support interventions	Rapid systematic review and meta-analysis	Suggests potential adherence benefits from digital tools that can complement dosage-form strategies.
Kloosterboer et al., 2020 [26]	International	Children and adolescents	Psychotropic treatment monitoring	Therapeutic drug monitoring relevance to psychopharmacology	Systematic review	Highlights the heterogeneity of concentration-response evidence and the need for individualized psychotropic management in youth.

### **Long-acting injectable strategies in adolescent psychopharmacology**

Long-acting injectable antipsychotics appear in the literature as a clinically relevant option for adolescents with severe psychiatric disorders when daily oral adherence is difficult to maintain. Existing reports describe LAIs as a way to reduce reliance on daily pill-taking and to provide more sustained treatment continuity, especially in patients with schizophrenia-spectrum disorders, bipolar disorder, or repeated instability on oral regimens.<sup>5-10</sup>

The currently available adolescent data are still limited and methodologically heterogeneous. Real-world studies describe off-label initiation in inpatient and outpatient care, substantial variability in dosing and product selection, and a continuing need for careful monitoring of tolerability, metabolic effects, and extrapyramidal symptoms. At the same time, prospective and comparative cohort data suggest that LAIs may help maintain continuity in selected high-risk adolescents.<sup>6-10</sup>

Broader work on long-acting therapies emphasizes how restricted the paediatric evidence base remains. A recent systematic review of long-acting formulations across paediatric and related populations found that psychotropic long-acting systems remain understudied, supporting the conclusion that adolescent LAI use is clinically relevant but still insufficiently standardized for routine implementation across settings.<sup>11</sup>

### **Extended-release and alternative delivery strategies in ADHD treatment**

The ADHD literature contains the clearest body of evidence linking dosage-form strategy to treatment continuity in children and adolescents. Once-daily extended-release stimulant and non-stimulant formulations are repeatedly described as a way to reduce midday dosing, limit school-time administration, and provide symptom coverage across the day. These features make delivery strategy directly relevant to adherence and persistence in everyday adolescent routines.<sup>13-18</sup>

Alternative delivery routes have also emerged. The dextroamphetamine transdermal system provides sustained stimulant delivery without oral administration and may be useful for young people who struggle with swallowing, school-time stigma, or fixed dosing schedules. Likewise, adjunctive or flexible-timing use of viloxazine extended-release has been reported as feasible in combination treatment plans.<sup>12-14</sup>

Even with these options, implementation challenges remain. Systematic review evidence indicates that adherence and persistence in paediatric ADHD are still generally suboptimal and that long-acting formulations help but do not fully resolve discontinuation, especially in adolescents. Real-world register data similarly suggest shorter treatment duration in adolescents than in younger children, reinforcing the need for adolescent-specific continuity strategies.<sup>16,18</sup>

### **Acceptability of oral dosage forms in adolescents**

Oral dosage-form acceptability remains a central issue in adolescent psychotropic treatment. Even when a medication is clinically appropriate, long-term continuation may be undermined if the formulation is difficult to swallow, unpleasant to taste, socially inconvenient, or poorly matched to daily routines. Paediatric formulation research consistently identifies swallowability, dosage-form size, taste, and flexibility as key determinants of acceptability.<sup>2,19</sup>

Survey-based evidence indicates that adolescents generally prefer conventional solid oral dosage forms more than younger children do, whereas familiarity with alternatives such as orally disintegrating tablets, films, or granules is more limited. In psychotropic treatment, these findings matter because available formulations are often narrow in scope and do not always align with developmental preferences or practical day-to-day use.<sup>4,19</sup>

The relevance of oral acceptability is reinforced by the limited diversity of approved psychotropic formulations in youth and by broader paediatric reviews showing that dosage-form design is closely tied to adherence. For adolescent psychopharmacology, this means that formulation usability should be considered part of treatment planning rather than an afterthought once a drug has been selected.<sup>2,4</sup>

### **Dose-flexible and manipulation-based psychotropic strategies**

When age-appropriate or tapering-friendly formulations are unavailable, clinicians and caregivers often rely on manipulation-based strategies to adapt psychotropic treatment for adolescent use. These approaches include tablet splitting, crushing, dispersing solid dosage forms, liquid dilution, and extemporaneous compounding to obtain non-standard strengths or more manageable administration forms.<sup>20-23</sup>

Recent evidence illustrates both the necessity and the limitations of these approaches. Manipulation may enable gradual dose reduction or individualized titration, but it can also affect dose accuracy, consistency of administration, and the integrity of modified-release products. These concerns are particularly important for psychotropics used in tapering or in formulations that were not designed to be altered outside controlled settings.<sup>20-22</sup>

These findings reinforce a broader problem: current formulation availability does not always match the clinical need for fine-grained dosing. Manipulation-based strategies therefore function mainly as pragmatic workarounds rather than optimized delivery solutions. The literature on compounding underscores the theoretical value of tailored formulations, but also shows how limited the direct evidence remains regarding adherence gains from personalized compounding itself.<sup>23,26</sup>

### **Implementation gaps and future directions**

Across domains, the literature reveals several cross-cutting implementation gaps. First, adolescent-specific

evidence remains uneven. Many delivery strategies that appear promising in principle, including LAIs, extended-release products, and manipulation-based dose-adjustment approaches, are still supported largely by off-label use, extrapolation from adult practice, or broader paediatric evidence rather than robust adolescent-specific trials.<sup>4-11,20-23</sup>

Second, formulation diversity remains limited and implementation is context-sensitive. Available psychotropic dosage forms do not always align with adolescent developmental needs, family capacity, or everyday treatment logistics. In ADHD, adherence-support interventions that combine educational, behavioral, digital, or professional support elements have shown promise, suggesting that dosage-form strategy alone is rarely enough.<sup>2,4,16,24,25</sup>

Finally, evidence from resource-constrained settings remains notably sparse. Although the issue is highly relevant for costlier long-acting formulations, specialist-dependent prescribing, and digital add-on supports, the literature still provides limited direct evidence on feasibility, continuity, and scalability in low-resource adolescent mental-health care. Future work should therefore integrate pharmaceutical design with implementation research and adolescent-centered usability considerations from the outset.<sup>11,16,18,23-26</sup>

## DISCUSSION

Viewed together, the literature suggests that dosage-form and delivery strategy are not peripheral issues in adolescent psychopharmacology. Rather, they are embedded in the practical mechanics of whether treatment can continue over time. Long-acting injectables may reduce the burden of daily oral adherence in selected severe disorders, extended-release ADHD formulations may fit school-day routines more effectively than immediate-release regimens, and oral acceptability remains a persistent determinant of whether a theoretically appropriate treatment is practically usable.<sup>5-19</sup>

The review also highlights a tension between clinical flexibility and pharmaceutical adequacy. Where commercially available formulations fail to support titration, tapering, or acceptable administration, clinicians and families improvise through manipulation-based strategies. These workarounds may solve immediate practical problems, but they also expose the limits of current formulation diversity and the lack of adolescent-specific psychotropic design. In this sense, delivery strategy should be understood as both a therapeutic and an implementation issue.<sup>20-23,26</sup>

A practical implication is that future development should move toward more patient-centered delivery systems rather than simply extending adult models downward into adolescent care. The most useful innovations are likely to be those that reduce regimen burden, preserve dosing accuracy, fit daily routines, and remain feasible across different health-system contexts. Equally important, implementation research should examine how formulation design interacts with

family capacity, service infrastructure, cost, and adherence-support programs, especially in settings where specialized resources are limited.<sup>11,16,18,24,25</sup>

## CONCLUSION

Current evidence indicates that dosage-form and drug delivery strategy meaningfully shape adolescent psychotropic treatment. Long-acting injectable antipsychotics may support continuity in selected severe psychiatric conditions, extended-release and alternative delivery systems play a particularly visible role in ADHD management, oral acceptability remains critical to sustained use, and manipulation-based strategies continue to fill gaps where age-appropriate formulations are lacking. At the same time, the field remains constrained by limited adolescent-specific evidence, narrow formulation diversity, and scarce implementation data from resource-constrained settings. Narrative review evidence therefore supports a more adolescent-centered and implementation-aware approach to psychotropic formulation development and clinical use.

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