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ORIGINAL RESEARCH

Economic Evaluation of Extended-Release Amphetamine (Dyanavel XR) Among Individuals with Attention-Deficit/Hyperactivity Disorder From a United States Societal Perspective

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Introduction: In the treatment of attention-deficit/hyperactivity disorder (ADHD), supplemental use of immediate-release (IR) stimulants can lead to fluctuating plasma levels that impede symptom control and are more prone to diversion. The negative implications of IR stimulant supplementation are broad, leading to extra costs and harm to individuals and society. To quantify the economic impact of IR supplementation from a United States societal perspective, this study evaluated the incremental cost difference between Dyanavel XR and other extended-release (ER) stimulants over a one-year base-case horizon and summarized value using a benefit-cost ratio.

Methods: As a hypothesis-generating approach, a decision-tree model compared these interventions across direct medical, non-medical, and indirect costs. Analysis was conducted for the general ADHD population and stratified by age group to account for differences in medication use, adherence, and costs. Suboptimal response combined IR supplementation and patient-reported end-of-dose crash, with all inputs drawn from the published literature.

Results: The average per-person cost for Dyanavel XR was $43,219 versus $51,071 for other ER stimulants, resulting in savings of $7,852 per person over one year. Nationally, Dyanavel XR resulted in $44.6 billion in aggregate savings. The benefit-cost ratio of Dyanavel XR was 12.59, indicating that benefits outweighed the treatment cost; 16.89 in young adults and 0.89 in children. In one-way deterministic sensitivity analysis, Dyanavel XR remained cost-saving, highlighting the robustness of the economic benefit.

Conclusion: From a United States societal perspective, Dyanavel XR demonstrates an economic advantage over other ER stimulants, with value most pronounced in young adults and lower in children. Dyanavel XR's potential to reduce IR supplementation and end-of-dose crash, thereby mitigating downstream costs, makes it a compelling ADHD treatment option. The model's operational definition of suboptimal response is intended as a pragmatic framework for future research to test its predictive validity for clinical outcomes and quality-of-life measures.

Keywords: ADHD, amphetamine, attention-deficit/hyperactivity disorder, cost-benefit analysis, Dyanavel XR, economic evaluation, extended-release, immediate-release, societal perspective

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental condition characterized by inattention, hyperactivity, and impulsivity, affecting individuals across the lifespan. The prevalence of adult ADHD is estimated at 6%, while childhood ADHD prevalence was reported to be 11.4% in 2022 in the United States (US).[1,2] ADHD is heterogeneous in its course and is associated with functional impairment impacting educational and occupational attainment, social functioning, financial stability, and overall well-being.[3] Together, these impairments translate into substantial healthcare and non-healthcare costs.[4,5]

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Pharmacological intervention, particularly stimulants (methylphenidates and amphetamines), remains the gold standard in ADHD treatment. Stimulants are available as immediate-release (IR) or extended-release (ER) formulations. IR preparations have a rapid onset and short duration of action, necessitating frequent dosing, which may result in variable plasma concentrations, increased risk of adverse effects, reduced efficacy, and a chance for diversion.[6] The development of ER formulations that combine both IR and ER components within a single dosage form aims to mitigate these limitations.[6] ER stimulants currently represent 60% of all stimulant use, while IR stimulants represent the remaining 40% (based on the IQVIA Xponent data, June 2024 to May 2025). Guidelines have recommended ER stimulants as first-line treatments for ADHD.[7] However, clinicians may still find a role for IR stimulants due to their short duration, flexible dosing or titration, or additional coverage when the efficacy of an ER stimulant wanes towards the end of a patient's day.[8,9]

Classified as Drug Enforcement Administration (DEA) Schedule II medications, IR and ER stimulants carry a high risk of misuse and diversion. IR stimulants may be preferred for misuse by individuals due to faster onset, greater likeability, and easier extraction.[10] Reducing IR dispensing may therefore lessen diversion-related harms and downstream societal costs.

Lower reliance on IR stimulant supplementation could also benefit the patients receiving ADHD treatment by reducing variability in blood levels and improving adherence. Supplementing ER stimulants with an IR may represent suboptimal ADHD treatment as patients requiring a booster dose presumably do not experience sufficient duration of symptom control from their ER. Furthermore, since stimulant pharmacokinetics are tightly linked to therapeutic effect, the addition of an IR medication can cause fluctuating peaks in blood levels, potentially increasing the risk of adverse events and reducing efficacy.[6] Moreover, taking an additional IR dose during the school or work day may pose an additional barrier to adequate treatment. Inconvenience or social stigma associated with taking multiple doses a day contributes to treatment nonadherence.[11]

Dyanavel® XR is an extended-release amphetamine using a proprietary drug delivery technology, Liqui*XR*®, that utilizes ion exchange and diffusion through non-dissolving coatings of varying thicknesses to allow the gradual release of amphetamine over time.[12] A recent retrospective study, using pre-specified analyses, showed that Dyanavel XR is associated with a reduced tendency to supplement daily ER stimulant treatment with IR medications at 90 days.[13,14] Reducing the amount of IR stimulants used could benefit both individuals and society by reducing harm through misuse and diversion, improving ADHD treatment effectiveness, and reducing societal costs.

Prior ADHD economic evaluations have largely centered on healthcare-sector costs or formulation/adherence comparisons. Few adopt a full societal perspective, and to our knowledge, none quantify the economic implications of suboptimal treatment characterized by IR supplementation and end-of-dose crash. To fill this knowledge gap, the present analysis evaluates the incremental cost difference between Dyanavel XR and other ER stimulants and summarizes value via benefit-cost ratio over a one-year base-case horizon (with projections to five years) from a US societal perspective, estimating the economic impact of reduced IR supplementation. Because this is a decision-analytic synthesis of secondary evidence, the model is hypothesis-generating and not intended to establish causal relationships.

Methods

Model Structure

Economic evaluation was conducted using a decision tree framework to evaluate the cost outcomes associated with Dyanavel XR compared to other ER stimulants for ADHD (Figure 1). Since the objective was to synthesize cross-sector costs from heterogeneous secondary sources rather than estimate causal pathways in individual-level data, a decision-analytic model was selected as the appropriate framework. Other ER stimulants were specified as treatment-as-usual, a market-basket reflecting the prevailing real-world mix of ER stimulant products (including branded and generic). ER stimulants can vary in onset and duration due to differences in their technology. This market-basket comparator aligns with economic evaluation guidance to benchmark against established care and the current treatment mix, providing a relevant comparison for payers and policymakers. Parameter values (eg, IR-supplementation, adherence, and pharmacy costs) were derived from routinely collected data and applied as weighted averages to mirror current practice.

The analysis was conducted for the general ADHD population and stratified by age group (children, adolescents, and adults) to account for differences in medication use patterns, adherence, and costs. This approach allowed comprehensive coverage of

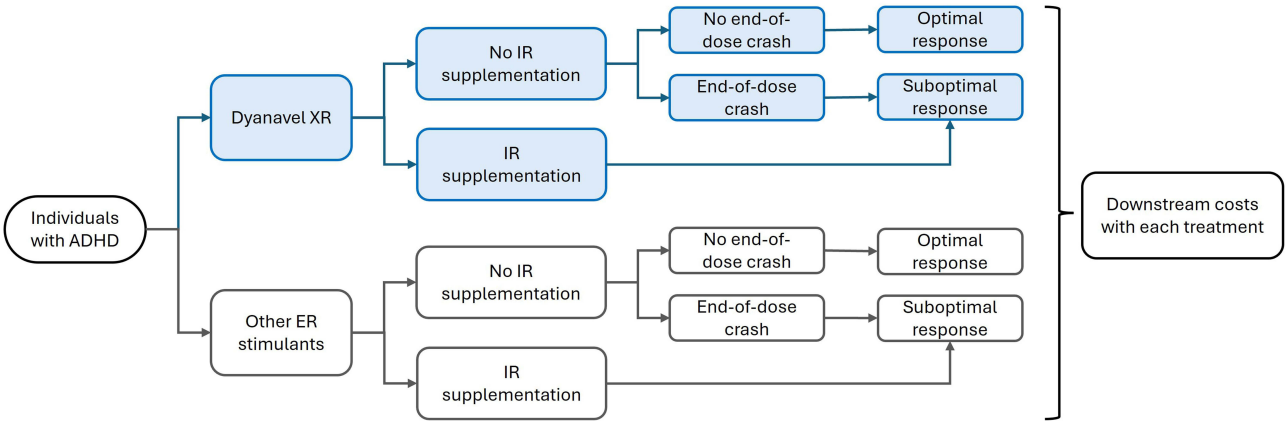

Figure 1 Schematic of the model.
Notes: 1. Optimal or suboptimal response classification based on a combination of IR supplementation and end-of-dose crash, ie, any IR supplementation or patient-reported end-of-dose crash is classified as suboptimal response. 2. Across pooled age groups, 6.1% of patients on Dyanavel XR and 15.4% of patients in the other ER stimulants group received IR supplementation. 3. Across pooled age groups, 23.6% of patients on Dyanavel XR and 30.5% of patients in the other ER stimulants group were predicted to have end-of-dose crash.
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ER, extended-release; IR, immediate-release.

outcomes (healthcare, education, productivity, crime, injuries, and motor vehicle incidents) that cannot feasibly be captured in a single primary dataset while maintaining transparency and reproducibility. This study used Microsoft® Excel 2024 to construct and execute the analytical model.

Individuals with ADHD entered the decision tree and initiated either Dyanavel XR or other ER stimulants. Within each treatment arm, individuals were first split by IR supplementation; any need for IR supplementation was considered a suboptimal response, reflecting insufficient ER coverage in routine care. Those with no IR supplementation were then stratified by patient-reported end-of-dose crash (a transient rebound of symptoms as ER levels waned). Patient-reported end-of-dose crash was treated as a binary variable; this pragmatic operationalization enabled consistent risk and cost assignment across branches. Individuals with a reported end-of-dose crash were also classified as suboptimal responders, whereas those with no end-of-dose crash comprised the optimal response group. Consequently, optimal response was restricted to the subgroup with no IR supplementation and no patient-reported end-of-dose crash ($P_{optimal} = P_{no\ IR} \times P_{no\ crash}$); all others were suboptimal responders ($P_{suboptimal} = 1 - P_{optimal}$). In conceptual terms, the model's definition of suboptimal response functions as a framework to explore how IR supplementation and patient-reported end-of-dose crash may relate to downstream events and associated costs. This operationalization was intended to be hypothesis-generating rather than a validated causal marker for patient outcomes. Suboptimal response is therefore represented here as a societal-cost construct. These events were, thus, treated as proxies for discontinuous all-day coverage. This structure, applied in parallel for Dyanavel XR and other ER stimulants, ensured the model captured every instance of discontinuous symptom control and linked each response category to downstream costs with each treatment arm. Both costs and benefits, monetized and expressed as cost offsets, were assigned to each treatment arm. The model allowed for a comparison of the overall net economic impact of Dyanavel XR with that of other ER stimulants across varying time horizons and age segments.

Model Population

The model's target population was defined using the total US population as of December 31, 2024 and the population was further stratified into standard age bands (6–12, 13–17, 18–24, 25–34, 35–44, 45–54, 55–64, and ≥65) to capture differences in resource utilization across groups, based on estimates from the US Census Bureau.[15] ADHD prevalence of 11.5% for ages 6–12 years,[1] 15.5% for 13–17 years,[1] and 6.0% for ≥18 years[2] was applied to estimate the number of individuals with ADHD in the US. For analyses encompassing all ages, the average ADHD prevalence of 7.2% was applied to the full US population, reflecting the combined age-adjusted burden.

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Treatment and Response

The analysis was limited to the treated ADHD population, with a stimulant prescription rate of 8.0% applied for children,[16] and the same rate was assumed for adolescents in the absence of adolescent-specific estimates. Adults were assigned a rate of 33.4%.[2] Pooled across all age groups, the weighted average probability of prescription stimulant use was 24.9%.

Within the Dyanavel XR or other ER treatment arms, the need for supplemental IR stimulants was informed by IQVIA Formulary Impact Analyzer (FIA) data for individuals starting between August 2022 and August 2023, which included the percentage of individuals who had at least one claim for an IR product during the period they were also on an ER product. IR-supplementation rates from IQVIA FIA (August 2022–August 2023) were applied to the 2024 target population, assuming year-to-year stability in clinical practice patterns. Rates were calculated by age and treatment group. These real-world estimates reflect routine practice, including formulary coverage, access, and prescriber behavior. They are used here as utilization parameters for a societal decision model rather than causal effects. The percentage of individuals on Dyanavel XR with IR supplementation was 6.1% for all age groups, 4.3% for the 6–12 years age group, 4.4% for the 13–17 years age group, and 8.0% for those aged 18 years and older. The percentage of individuals on other ER stimulants with IR supplementation was 15.4% for all age groups, 10.2% for the 6–12 years age group, 10.0% for the 13–17 years age group, and 17.2% for those aged 18 years and older.

The baseline patient-reported end-of-dose crash probability was set at 30.5%, the complement of the overall stimulant response probability (69.5%). The probability of stimulant response was informed by a meta-analysis of stimulant response rates among children, reporting 68% for amphetamine and 71% for methylphenidate.[17] This 30.5% end-of-dose crash probability for stimulants is consistent with the literature, noting ~30% rebound symptoms with stimulants.[18] Because age-specific estimates were scarce, these rates were applied across all age groups. To estimate the absolute probability of an end-of-dose crash for Dyanavel XR, the published logistic-regression coefficient, $\beta = -0.35$,[13,14] was applied to the calculated baseline crash probability (30.5%). This yielded an estimated end-of-dose crash probability of ~23.6% for Dyanavel XR and a corresponding probability of no end-of-dose crash of ~76.4%.

Aggregating across ages and accounting for both IR supplementation and patient-reported end-of-dose crash, the overall mean probability of a suboptimal response was 28.3% for Dyanavel XR versus 41.2% for other ER stimulants.

Healthcare Resource Utilization and Cost Inputs

The costs considered in the present model included stimulant medication, direct medical, direct non-healthcare, and indirect costs (Table 1). Costs and utilization parameters were sourced from peer-reviewed publications or administrative claims datasets and harmonized to the model population. Where data were sparse, conservative assumptions were made and explicitly documented. All unit costs were inflated to 2025 US dollars (USD), utilizing the historical Consumer Price Index for medical care from the US Bureau of Labor Statistics,[19] where applicable.

Table 1 Healthcare Resource Utilization and Cost Inputs

Parameter	Input Value		Source
Trainings & Special Education			
Annual utilization, % (no. of contacts)			
Optimal response	**6–12 years**	**13–17 years**	
Social skills training	18.5% (9.2)	7.1% (9.2)	[20, 21]
Home training	4.3% (10.0)	0.0% (0.0)	[20, 21]
Special education	1.5% (–)	0.1% (–)	[20, 21]
Disciplinary action (school)	1.5% (–)	0.1% (–)	Assumption[a]
Suboptimal response	**6–12 years**	**13–17 years**	
Social skills training	28.5% (9.8)	26.3% (11.4)	[20, 21]
Home training	12.9% (11.2)	10.1% (10.0)	[20, 21]
Special education	12.2% (–)	8.6% (–)	[20, 21]
Disciplinary action (school)	12.2% (–)	8.6% (–)	Assumption[a]

(*Continued*)

Table 1 (Continued).

Parameter	Input Value		Source
Average costs			
Social skills training	$50 / contact		[22]
Home training	$175 / contact		[23]
Disciplinary action (school)	$889 / year		[24]
Special education	$6,157 / year		[24]
Productivity Loss			
Average costs			
Absenteeism and presenteeism, 12–17 years	$312 / year		[25]
Unemployment, 12–17 years	$57 / year		[25]
Premature mortality, 12–17 years	$221 / year		[25]
Caregiving, 6–17 years	$1,133 / year		[25]
Grade retention, 6–17 years	$327 / year		[24]
Absenteeism and presenteeism; low ADHD symptoms, 18+ years	$12,296 / year		[26]
Absenteeism and presenteeism; high ADHD symptoms, 18+ years	$17,572 / year		[26]
Unemployment, 18–65 years	$9,041 / year		[4]
Premature mortality, 18–65 years	$439 / year		[4]
Caregiving, 18–65 years	$900 / year		[4]
Substance Use Disorder			
Prevalence			
Alcohol use disorder, 12–18 years	5.3%		Assumption[b]
Alcohol use disorder, 18–69 years	5.3%		[27]
Drug use disorder, 12–18 years	13.7%		Assumption[b]
Drug use disorder, 18–69 years	13.7%		[27]
Average healthcare costs			
Alcohol use disorder, 18–44 years	$11,345 / year		[28]
Alcohol use disorder, 45–64 years	$18,599 / year		[28]
Alcohol use disorder, ≥65 years	$15,247 / year		[28]
Drug use disorder, all ages	$10,841 / year		[29]
Treatment probability			
Alcohol use disorder, all ages	7.6%		[30]
Drug use disorder, all ages	13.1%		[30]
Average treatment costs, all ages	$3,956 / year		[31]
Motor Vehicle Accidents			
Average accident-related cost, treated ADHD	$25,791 / year		[32]
Average accident-related cost, untreated ADHD	$47,074 / year		[32]
Crime and Offenses			
Incidence rate ratio of criminality in untreated vs treated ADHD	1.15		[33]
Probability of committing an offense by an individual with ADHD in untreated vs treated	7.3%		[33]
Number of offenses in the general population (2019)[c]	**Violent**	**Non-violent**	
6–12 years	46	155	Calculation[d]
13–17 years	736	2,522	Calculation[d]
18–24 years	682	2,016	Calculation[d]
25–34 years	1,006	3,059	Calculation[d]
35–44 years	629	2,009	Calculation[d]

(*Continued*)

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Table 1 (Continued).

Parameter	Input Value		Source
45–54 years	337	1,056	Calculation[d]
55–64 years	176	492	Calculation[d]
65+ years	48	103	Calculation[d]
Average cost of offense			
Violent offense	$75,243 / year		[34]
Non-violent offense	$7,612 / year		[34]
Healthcare			
Annual utilization, % (no. of contacts)			
Optimal response, 6–17 years	**6–12 years**	**13–17 years**	
Clinician visit	100.0% (2.3)	100.0% (2.4)	[20, 21]
Crisis contact	100.0% (0.6)	100.0% (0.4)	[20, 21]
Psycho-education	89.4% (2.6)	94.3% (2.8)	[20, 21]
Parent/family counseling	48.5% (8.3)	30.6% (5.9)	[20, 21]
Behavior therapy	7.1% (13.2)	9.3% (10.0)	[20, 21]
Suboptimal response, 6–17 years	**6–12 years**	**13–17 years**	
Clinician visit	100.0% (3.4)	100.0% (3.9)	[20, 21]
Crisis contact	100.0% (1.5)	100.0% (1.3)	[20, 21]
Psycho-education	92.9% (3.6)	90.1% (3.6)	[20, 21]
Parent/family counseling	75.8% (7.9)	44.2% (8.2)	[20, 21]
Behavior therapy	22.8% (11.8)	27.7% (11.4)	[20, 21]
Optimal response, 18+ years			
Clinician visit	100.0% (4.0)		[3, 35, 36]
Crisis contact	100.0% (0.4)		Assumption[e]
Behavior therapy	11.7% (1.0)		Assumption[f]
Suboptimal response, 18+ years			
Clinician visit	100.0% (12.0)		[3, 35, 36]
Crisis contact	100.0% (1.3)		Assumption[e]
Behavior therapy	35.2% (1.0)		[2]
Average costs			
Clinician visit	$85 / contact		[37]
Crisis contact	$130 / contact		[37]
Psycho-education	$93 / contact		[38]
Parent/family counseling	$160 / contact		[39]
Behavior therapy (Children/adolescents)	$175 / contact		[23]
Behavior therapy (Adults)	$1,100 / year		[40]
Outpatient, inpatient, and ED-related			
Children	$1,525 / year		[25]
Adolescents	$2,438 / year		[25]
Adults	$2,290 / year		[4]
Stimulant abuse, misuse, and diversion			
Probability of stimulant abuse			
18–64 years	9.0%		[41]
Probability of stimulant misuse			
13–17 years	6.5%		[42]
18–25 years	36.5%		[41]
26–34 years	30.7%		[41]
35–64 years	17.9%		[41]

(*Continued*)

Table 1 (Continued).

Parameter	Input Value	Source
Probability of stimulant diversion		
≤17 years	12.0%	[43]
18–64 years	16.6%	[44]
Average ED visits per year (per ADHD individual from stimulant abuse or misuse)		
5–11 years	0.000	Calculation[g]
12–17 years	0.016	Calculation[g]
18–25 years	0.009	Calculation[g]
26–34 years	0.005	Calculation[g]
35+ years	0.003	Calculation[g]
Average hospitalizations per year (per ADHD individual from stimulant abuse or misuse)		
18–25 years	0.011	Calculation[h]
26–64 years	0.013	Calculation[h]
65+ years	0.001	Calculation[h]
Average costs		
Total prescription cost to payers from diversion	$253,742,749 / year	[44]
ED visit from stimulant abuse or misuse	$817 / visit	[45]
Hospitalization from stimulant abuse or misuse	$14,008 / hospitalization	[46]
Disability		
Average disability-related cost for 18–65 years	$20,877 / year	[47, 48]
Injury-related		
Average medical costs		
6–12 years	$262 / year	[49]
13–17 years	$370 / year	[49]
18–64 years	$3,575 / year	[50]

Notes: [a] Assumed the same probability as special education, only applicable to suboptimal response. [b] Assumed the same probability for adolescents as for adults. [c] Calculated based on the relative risk of offense in ADHD versus controls applied to the number of offenses per year in the general population. [d] Calculated based on the number of offenses from the Federal Bureau of Investigation report,[51] and applied to individuals with ADHD based on the probability of committing an offense (7.3%). [e] Assumed to have the same probability and number of contacts as for adolescents. [f] Assumed to have a ~3 times lower probability based on data trends observed in children/adolescents. [g] Calculated based on the number of ED visits in ADHD individuals, sourced from published literature,[52] and applied to individuals with abuse, misuse, or diversion. [h] Calculated based on the number of hospitalizations in ADHD individuals, sourced from published literature,[46] and applied to individuals with abuse, misuse, or diversion.
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ED, emergency department.

Stimulant Medication Costs

The cost of Dyanavel XR to patients was estimated at $75 to $173 per month. This data, provided directly by the manufacturer, encompasses all patient payment methods, including coupons, out-of-pocket expenses, and insurance coverage. Assuming daily single-pill doses, the annual cost per person for Dyanavel XR ranged from $890 to $2,072. To estimate the annual cost of other ER stimulants, pharmacy-related costs from 2024 IQVIA FIA data, as reported in a published claims analysis, were utilized. These data included all costs regardless of payment method. The average ADHD-related pharmacy cost was then weighted by insurance type, resulting in an average annual medication cost of $654.06 per person for other ER stimulants. This estimate considered both brand and generic versions available in the market and their respective market shares. For IR medication, the annual cost was estimated at $196.50 per person.

The cost of each ER regimen included the acquisition cost of Dyanavel XR or the comparator ER stimulant plus the cost of IR supplementation, which was applied only to the proportion of individuals who required a supplement.

Both ER and IR costs were then weighted by their respective real-world adherence rates. Adherence estimates for Dyanavel XR, other ER stimulants, and IR stimulants were derived from FIA data covering January 2024 through December 2024. Adherence was quantified using the proportion of days covered (PDC) metric, which was calculated for each individual as the total number of days' supply dispensed divided by the number of days in the observation period.

This was then averaged first across all individuals within each age-defined cohort and subsequently across Dyanavel XR, other ER stimulant, and IR stimulant groups to yield age group-specific PDC values. These PDC values were assumed to constrain both treatment efficacy and medication costs, on the basis that missed doses would postpone subsequent dispensing until the prior 30-day supply was exhausted. Pooled across all age groups, mean adherence rates were 43.1% for Dyanavel XR, 46.0% for other ER stimulants, and 54.5% for IR stimulants.

Direct Healthcare Costs

ADHD-Related Medical Care

Annual healthcare utilization patterns and associated costs were incorporated separately for children, adolescents, and adults. For children and adolescents, service categories included clinician visits, crisis contacts, psycho-education, parent/family counseling, and behavioral therapy, with utilization rates sourced from economic evaluation studies among children and adolescents with ADHD.[20,21] For adults, service categories included clinician visits, crisis contacts, and behavior therapy, which were estimated based on clinical recommendations[3,35,36] and from economic evaluation studies conducted among children and adolescents.[20,21] Unit costs for each service, including clinician visits and crisis contacts, were based on the Healthcare Common Procedure Coding System.[37] Unit costs for psycho-education[38] and parent/family counseling[39] were sourced from mental health treatment centers providing services for ADHD treatment. Costs for behavioral therapy were sourced from organization websites.[23,40] These inputs enabled the calculation of per-person annual direct medical costs, stratified by age and response status. These service- and response-specific costs were summed up to yield annual direct medical costs per person by age and response status. In addition, excess costs due to outpatient, inpatient, and emergency department (ED) visits related to ADHD for those with a suboptimal response were calculated as the sum of the primary payer's paid amount and the individual's out-of-pocket expenses, by using health insurance claims data from the IBM MarketScan Research Databases.[4,25]

Substance Use Disorder-Related Treatment

The model captured economic burden attributable to comorbid substance use disorders in adolescents and adults, distinguishing between alcohol use disorder (AUD) and drug use disorder (DUD), where applicable. Prevalence estimates for AUD and DUD were sourced from a cross-sectional clinical study that consisted of individuals admitted to a private psychiatric outpatient clinic (2014–2018).[27] Annual healthcare costs for each disorder[28,29] were then multiplied by the corresponding prevalence to estimate per-person costs. Additionally, treatment of substance use disorder[30] and related costs were considered, reflecting the standard expenses of a treatment program.[31] All substance abuse-related costs were applied exclusively to individuals with suboptimal ADHD response, under the assumption that uncontrolled ADHD exacerbates the risk of comorbid substance use.

Injury-Related Medical Care

Age-specific excess annual healthcare costs for injury events were applied to those with suboptimal ADHD control. The data on injuries for children and adolescents with ADHD were derived from the Medical Expenditure Panel Survey (2011–2020),[49] and for adults, were derived from the MarketScan healthcare claims databases (2002–2007).[50]

Stimulant Abuse, Misuse, and Diversion-Related Medical Expenses

Prevalence estimates for stimulant abuse, misuse, and diversion were drawn from observational studies or a systematic literature review. Stimulant abuse was defined as persistent maladaptive patterns of stimulant use resulting in clinically significant impairment or distress.[10,41] Stimulant abuse was only considered for adults.[41] Stimulant misuse was referred to as taking prescriptions not prescribed to the individual or taking prescriptions differently than prescribed.[10] Data were sourced from published literature.[41,42] Diversion was characterized by the transfer of legitimately prescribed medication to others for whom it was not prescribed.[43,44] To capture healthcare utilization, age-specific rates of ED visits were calculated using ADHD-population denominators and visit counts.[52] Hospitalization rates were obtained from a cross-sectional study that used hospital discharge data from the Healthcare Cost and Utilization Project National Inpatient Sample.[46] Unit costs for diverted medication prescriptions, ED visits, and hospital admissions were also sourced from

published literature.[44–46] Annual per-person costs were then estimated by multiplying each prevalence or per-person event rate by its corresponding unit cost, yielding the total stimulant-related economic burden.

Direct Non-Healthcare Costs

Education and Training

For children and adolescents (6–17 years), the model incorporated annual costs for special education and specialized training, applied separately to optimal and suboptimal responses. Service utilization rates (percentage of individuals and number of contacts per year) for social skills training, home training, and special education were sourced from economic evaluation studies among children and adolescents with ADHD.[20,21] Given the scarcity of data in the literature, the proportion of children and adolescents who may receive disciplinary action at school was assumed to be the same as the proportion of children/adolescents who may receive special education. These data were applied to those with suboptimal response. Unit costs were sourced from published literature or organization websites providing these services, as applicable.[22–24] Unit costs for each of these were reported on a per-contact basis for training services and a per-year basis for special education and disciplinary action. They were then multiplied by annual contact counts and service prevalence to yield total annual costs per person.

Motor Vehicle Accidents

Annual costs associated with motor vehicle accidents were applied to adolescents and adults in the decision model, distinguishing between those with optimal and suboptimal responses to ADHD. These costs were sourced from the economic evaluation of Dyanavel XR versus standard of care stimulant medications or the untreated ADHD population.[32] Cost components comprised human capital costs, medical care, emergency medical services, market productivity, household productivity, insurance administration, workplace costs, legal costs, congestion costs, property damage, value of statistical life, and quality of life.[32] In the model, individuals with an optimal response were assumed to incur accident-related costs similar to those of a treated population, and those with a suboptimal response were assumed to have costs similar to those of the untreated population (no ADHD medication use).[32] These values were assumed to capture the differential societal burden of crash-related healthcare and property damage costs across response statuses.

Crime and Offenses

The annual cost of violent and non-violent offenses among ADHD was calculated across all age groups to account for age-specific differences in risk of committing an offense. Total offense counts were extracted from the Federal Bureau of Investigation's 2019 Uniform Crime Report.[51] Criminality inputs were sourced from a study among individuals aged 6–64 years, which reported weighted treatment initiation and non-initiation incidence rates (per 1000 person-years) and the initiation versus non-initiation incidence rate ratio. Rates were converted to 1-year probabilities and re-expressed as the relative effect of non-initiation versus initiation by the inversion incidence rate ratio of non-initiation.[33] In the model, non-initiation was designated as the suboptimal response group. The total annual estimated number of offenses attributable to the ADHD cohort was then obtained by multiplying the total annual offense counts by the proportion of offenses in the ADHD population. Finally, these events were monetized by multiplying the estimated ADHD offense counts by per-offense unit costs for violent and non-violent offenses separately, thereby deriving the total annual crime-related economic burden among individuals with ADHD. Unit costs for violent and non-violent offenses were sourced from a study that employed a comprehensive methodology for estimating costs across different crime categories, utilizing data from the literature and various data sources.[34] In their analyses, tangible costs were comprised of the costs to the crime victim, the criminal justice system, and the crime career (opportunity costs related to the criminal's choice to engage in illegal rather than legal and productive activities).

Disability

An annual excess disability cost was applied to adults who exhibited a suboptimal treatment response. This cost represents the additional household income required to support an adult with a disability.[47,48] This expense was attributed solely to the suboptimal response, under the assumption that effective symptom control mitigates disability-related financial burdens.

Indirect Costs

Indirect economic impacts were captured through excess productivity-related costs associated with ADHD for individuals exhibiting suboptimal symptom control. Cost categories were stratified by age to reflect educational and labor-market roles. Costs were derived from the published literature.[4,24–26]

Among children, the costs of grade retention (repeating a school year) and informal caregiving (the value of unpaid family caregiver time, such as income loss due to job loss, changed responsibilities, or missed work, parental mental health services, and additional childcare) were included. Among adolescents, the grade retention and caregiving categories were retained, with the addition of three labor-market components: productivity loss, comprising costs related to absenteeism (missed days) and presenteeism (reduced on-the-job performance), unemployment, and premature mortality (the present value of future earnings lost through early death). For working-age adults (18–64 years), costs related to productivity loss, unemployment, premature mortality, and informal caregiving (eg, assistance with transportation to and from medical appointments, reminders to take medication) were considered. For older adults (≥65 years), only informal caregiving costs were considered. Children <12 years and adults ≥65 years were excluded from labor-market costs, given minimal workforce participation.

Schein et al (2022) estimated excess indirect costs associated with ADHD, including productivity loss, unemployment, premature mortality, and caregiving, using a human capital approach in which costs were derived based on paid work compensation rates (ie, an individual's productivity valued at their expected market earnings).[4,25] Productivity loss among adults was sourced from a survey study that utilized the Work Productivity and Activity Impairment–General Health questionnaire.[26]

Grade retention data were sourced from Robb et al (2011), which considered educational placement (ie, regular, specific learning disability, serious emotional disturbance, and approved private placement) during the year in which the student was held back.[24]

All excess costs were applied exclusively to the suboptimal response, reflecting the assumption that adequate symptom control mitigates the majority of these productivity impairments.

Model Outcomes

In this analysis, the mean total cost per person for each cost category was summarized. The primary outcome was the incremental cost difference per person on Dyanavel XR versus other ER stimulants with IR supplementation, calculated to quantify the additional or reduced expenditures attributable to Dyanavel XR. To estimate the national impact, the average per-person excess costs were scaled by the number of individuals with ADHD treated with stimulants, using national prevalence rates and census data. The benefit-cost ratio was defined as the ratio of total monetized cost offsets (avoided downstream costs with Dyanavel XR compared to other ER stimulants) to the treatment cost of Dyanavel XR. A benefit-cost ratio > 1 indicates that societal savings exceed the cost of Dyanavel XR.

Analyses

Base-Case Analysis

The primary (base-case) analysis was conducted from a societal perspective over a 1-year time horizon, encompassing all age groups combined. This approach captured stimulant medication, direct medical, direct non-healthcare, and indirect costs attributable to ADHD treatment, providing a comprehensive assessment of the economic impact of Dyanavel XR versus other ER stimulants within one year. The 1-year horizon reflects short- to medium-term decision needs and the stability of available inputs, while minimizing compounded uncertainty. Discounted projections up to 5 years are presented to illustrate the durability of estimates. Future costs and benefits in analyses extending beyond one year were discounted at an annual rate of 3.5% to reflect time preference and the opportunity cost of capital.

Deterministic Sensitivity Analysis

To assess the impact of key model parameters on study outcomes, a deterministic (one-way) sensitivity analysis was conducted by varying each input parameter individually by ±20% around its base-case value. This range reflects plausible uncertainty and is consistent with conventional practices in health economics. The results of the sensitivity analysis were summarized in a tornado diagram, highlighting the parameters with the most notable influence on the incremental cost and

benefit-cost ratio of Dyanavel XR versus other ER stimulants. The parameters tested included adherence rates, symptom-control probabilities, and cost estimates. This sensitivity analysis was designed to reflect the uncertainty inherent in secondary data and to demonstrate that the main findings are not driven by any single literature-based estimate.

Results

Base-Case Costs and Outcomes

Based on IQVIA data, the IR supplementation probability for Dyanavel XR was 9.3% lower than that of other ER stimulants, pooled across all age groups. Cost outcomes presented account for the probability of IR supplementation for both groups: Dyanavel XR (6.1%) and other ER stimulants (15.4%).

Per-Person Costs

Based on a one-year societal analysis, Dyanavel XR was associated with lower total costs per person compared to other ER stimulants. Over the course of one year, total per-person costs were $43,219 for Dyanavel XR versus $51,071 for other ER stimulants, resulting in a cost savings of $7,852 per person (Table 2). While adherence-weighted stimulant medication spending (including IR supplementation) was higher with Dyanavel XR than with other ER stimulants ($650 vs $317), total per-person costs were lower with Dyanavel XR due to downstream offsets across medical, non-medical, and indirect cost categories.

Per-person cost savings with Dyanavel XR versus other ER stimulants, pooled across all age groups, amounted to $15,273 over 2 years, $22,280 over 3 years, $28,888 over 4 years, and $35,114 over 5 years.

Net cost differences favored Dyanavel XR in every age group. Over one year, cost savings with Dyanavel XR increased sharply from a modest $219 per person in the 6–12-year cohort to a peak of $9,580 among 18–24-year-olds,

Table 2 Costs per Person Among Individuals with ADHD, Societal Perspective Over 1 year, Pooled Across All Ages

Cost Type	Dyanavel XR + IR Supplementation	Other ER + IR Supplementation	Net Benefit (Dyanavel XR vs Other ER)
Treatment costs			
Stimulant medication	$650	$317	$332
Direct healthcare costs			
ADHD-related medical care	$1,598	$2,000	-$401
Substance use disorder	$605	$862	-$257
Injury-related medical care	$867	$1,237	-$370
Stimulant abuse, misuse, and diversion	$56	$122	-$66
Direct non-healthcare costs			
Training and special education	$85	$105	-$20
Motor vehicle accidents	$28,323	$30,675	-$2,352
Crime and offenses	$77	$110	-$33
Disability	$4,965	$7,090	-$2,125
Indirect costs			
Productivity loss	$5,992	$8,553	-$2,561
Total costs	**$43,219**	**$51,071**	**-$7,852**

Notes: 1. All costs were adjusted to 2025 United States dollars. 2. Medication costs are adherence-weighted and include IR supplementation where applicable. 3. Cost outcomes presented account for IR supplementation for both groups, Dyanavel XR (6.1%) and other ER stimulants (15.4%). 4. Net benefit is calculated as the cost of Dyanavel XR minus the cost of other ER stimulants; a negative value indicates cost savings with Dyanavel XR (and a positive value indicates higher costs).
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ER, extended-release; IR, immediate-release.

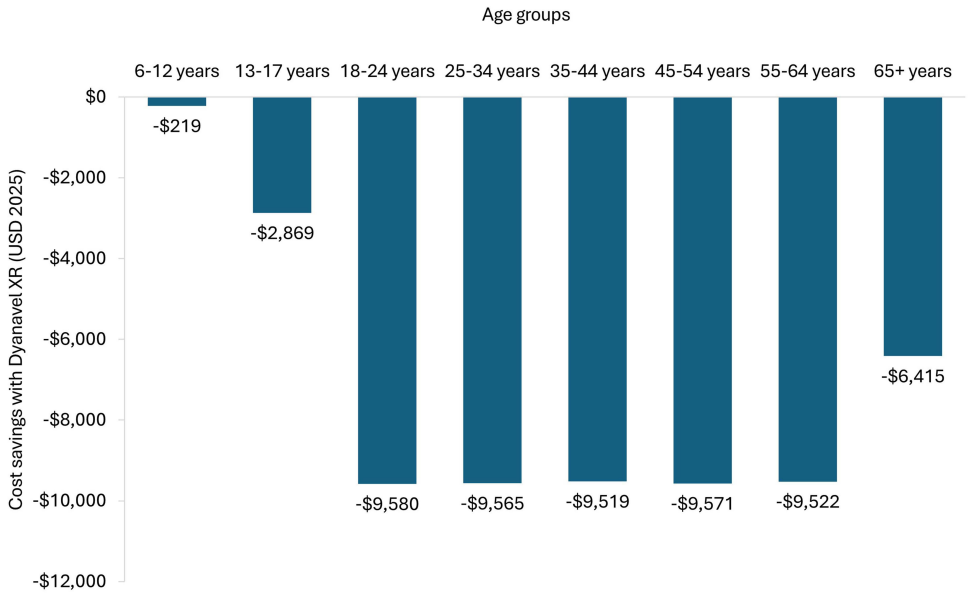

Figure 2 Cost savings per person among individuals with ADHD (Dyanavel XR + IR supplementation vs other ER stimulants + IR supplementation), societal perspective over 1 year, stratified by age.
Notes: Cost difference is calculated as the cost of Dyanavel XR minus the cost of other ER stimulants; a negative value indicates cost savings with Dyanavel XR (and a positive value indicates higher costs). Cost outcomes presented account for IR supplementation for both groups, Dyanavel XR (6.1%) and other ER stimulants (15.4%).
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ER, extended-release; IR, immediate-release; USD, United States dollar.

reflecting greater absolute reductions in healthcare and non-medical costs during young adulthood. Per-person savings remained strong through middle age, at $9,565 for 25–34-year-olds and ~$9,538 for those 35–64, before tapering off for individuals 65 and older (Figure 2).

Population-Level Costs

When extrapolated to the US ADHD population receiving treatment with stimulants, total societal costs with Dyanavel XR amounted to $245.3 billion versus $289.9 billion with other ER stimulants, yielding aggregate cost savings of $44.6 billion over a 1-year time horizon. These savings were consistently observed across all non-treatment categories, most notably productivity loss, substance abuse, driving-related incidents, crime and offenses, healthcare services, medication misuse, disability, and injury, underscoring the broad economic benefits of Dyanavel XR at the population level (Table 3).

Table 3 Total Costs for All Individuals with ADHD Using Prescription Stimulant Medication, Societal Perspective Over 1 year, Pooled Across All Ages

Cost Type	Dyanavel XR + IR Supplementation	Other ER + IR Supplementation	Net Benefit (Dyanavel XR vs Other ER)
Treatment costs			
Stimulant medication	$3.7B	$1.8B	$1.9B
Direct healthcare costs			
ADHD-related medical care	$9.1B	$11.3B	–$2.3B
Substance use disorder	$3.4B	$4.9B	–$1.5B
Injury-related medical care	$4.9B	$7.0B	–$2.1B
Stimulant abuse, misuse, and diversion	$0.3B	$0.7B	–$0.4B

(*Continued*)

Table 3 (Continued).

Cost Type	Dyanavel XR + IR Supplementation	Other ER + IR Supplementation	Net Benefit (Dyanavel XR vs Other ER)
Direct non-healthcare costs			
Training and special education	$0.5B	$0.6B	–$0.1B
Motor vehicle accidents	$160.8B	$174.1B	–$13.3B
Crime and offenses	$0.4B	$0.6B	–$0.2B
Disability	$28.2B	$40.2B	–$12.1B
Indirect costs			
Productivity loss	$34.0B	$48.5B	–$14.5B
Total costs	**$245.3B**	**$289.9B**	**–$44.6B**

Notes: 1. All costs were adjusted to 2025 United States dollars. 2. Cost outcomes presented account for IR supplementation for both groups, Dyanavel XR (6.1%) and other ER stimulants (15.4%). 3. Net benefit is calculated as the cost of Dyanavel XR minus the cost of other ER stimulants; a negative value indicates cost savings with Dyanavel XR (and a positive value indicates higher costs).
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; B, billion; ER, extended-release; IR, immediate-release.

Nationally, aggregate cost savings with Dyanavel XR versus other ER stimulants, pooled across all age groups, totaled $86.7 billion over 2 years, $126.5 billion over 3 years, $164.0 billion over 4 years, and $199.3 billion over 5 years.

Benefit-Cost Metrics

Pooled across all age groups, the benefit-cost ratio for Dyanavel XR was 12.59, indicating that for every $1 of treatment cost, society gains $12.59 in benefits. In other words, the benefits of Dyanavel XR are ~12.6 times greater than the treatment expenditure with Dyanavel XR required to manage ADHD compared to ER alternatives.

The benefit-cost ratio for Dyanavel XR improved over time, increasing from 12.67 at 2 years to 12.76 at 3 years, 12.84 at 4 years, and 12.92 at 5 years.

Age-stratified benefit-cost ratios varied by life stage. In children 6–12 years old, the benefit-cost ratio was 0.89, suggesting that cost outweighed the benefit in this age group. Over one year, benefit-cost ratios with Dyanavel XR increased markedly from 0.89 in the 6–12-year cohort to a peak of 16.89 among 18–24-year-olds, indicating that each dollar spent yields about $17 in societal benefits among young adults. Ratios remained strong through midlife, before gradually declining in individuals 65 years and older. This pattern highlighted the most pronounced economic value of Dyanavel XR in young adults (Figure 3).

One-Way Deterministic Sensitivity Analysis

In one-way deterministic sensitivity analysis, net per-person savings with Dyanavel XR versus other ER stimulants ranged from approximately $5,808 to $10,099 over one year. The most considerable swings in cost savings were driven by the odds ratio for end-of-dose crash with Dyanavel XR, followed by the probability of IR supplementation with other ER stimulants, driving-related costs among suboptimal responders, the probability of IR supplementation with Dyanavel XR, and driving-related costs among optimal responders. Other notable drivers included the productivity loss costs, disability costs, probability of symptom control with stimulants, the treatment cost of Dyanavel XR, and adherence to Dyanavel XR. Across every parameter bound, Dyanavel XR remained cost-saving, underscoring the robustness of the economic benefit and the critical role of real-world IR supplementation, symptom control, and event-cost inputs (Figure 4).

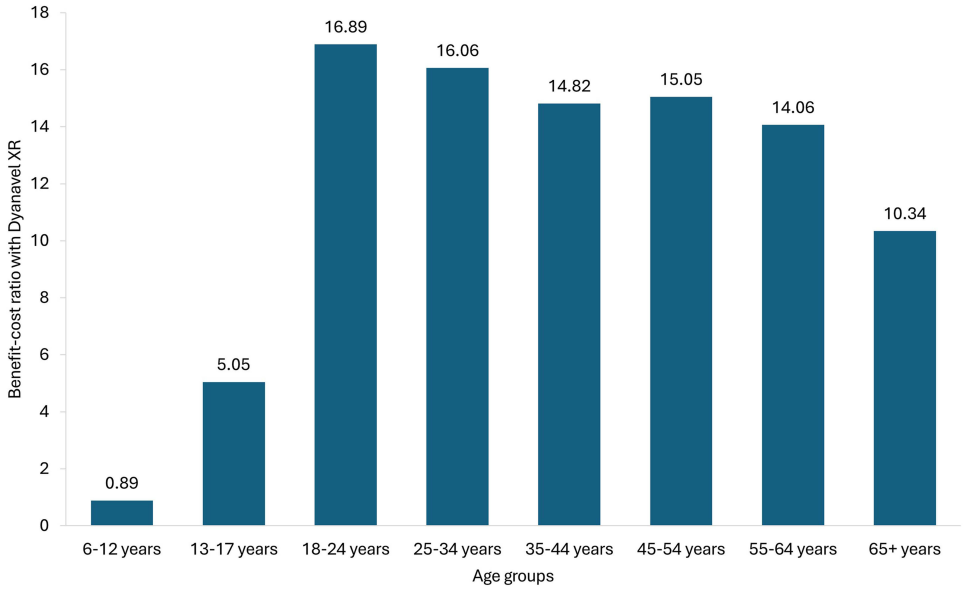

Figure 3 Benefit-cost of Dyanavel XR + IR supplementation among individuals with ADHD, societal perspective over 1 year, stratified by age.
Notes: Benefit-cost ratio was defined as the ratio of total economic benefits (eg, avoided costs due to reduced healthcare resource use, productivity loss, etc.) to the treatment cost of Dyanavel XR. Benefit-cost ratio > 1, benefits outweigh the costs of treatment. Cost outcomes presented account for IR supplementation for both groups, Dyanavel XR (6.1%) and other ER stimulants (15.4%).
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ER, extended-release; IR, immediate-release.

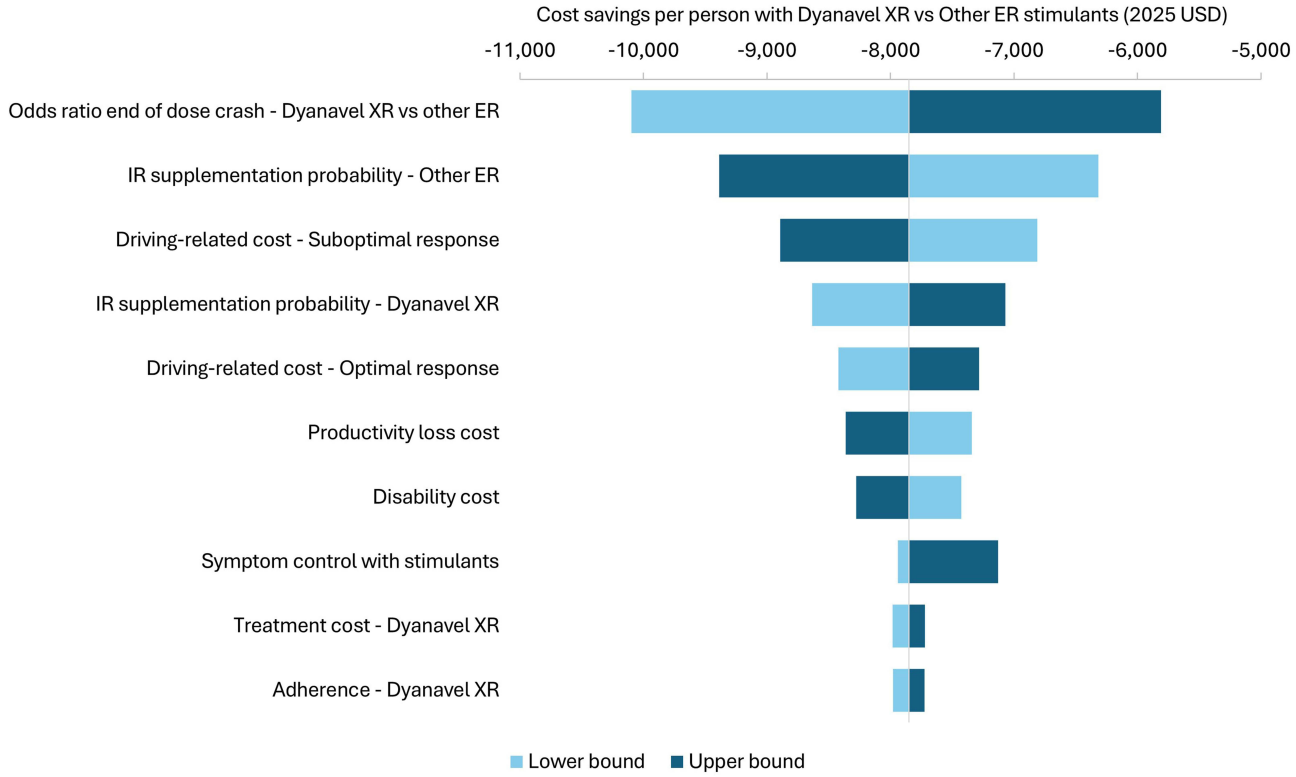

Figure 4 One-way deterministic sensitivity analysis for cost savings per person among individuals with ADHD (Dyanavel XR + IR supplementation vs other ER stimulants + IR supplementation), societal perspective over 1 year.
Notes: Each bar shows how the cost savings change when one parameter is varied between its lowest and highest plausible values, while all other inputs remain at their base-case settings. The "lower bound" represents the model outcome when a specific parameter is set to its minimum value, and the "upper bound" represents the model outcome when a specific parameter is set to its maximum value within the specified range, while holding all other parameters at their base or central values. The vertical line denotes the base-case annual cost savings per person with Dyanavel XR. Parameters are ordered by the magnitude of their impact on cost savings when varied across their plausible low and high bounds. The length of each bar indicates the magnitude of its effect, and its orientation reveals the direction of influence.
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ER, extended-release; IR, immediate-release; USD, United States dollar.

Discussion

In recent years, there has been a substantial push among providers to move away from IR stimulants in ADHD treatment, when possible, particularly among adults. A reliance on IR stimulants is not only problematic for individuals with ADHD, providing variable, short-term symptom control and the burden of multiple doses, but it is also detrimental to the broader public. Lower levels of adherence, combined with a high likeability of IR stimulants, make them more commonly diverted and misused than ER formulations.[10] Moreover, reduced adherence and the fluctuating pharmacokinetic profile of IR stimulants reflect less effective ADHD symptom control. Treating ADHD with medication provides a protective effect on academic outcomes, substance use disorders, criminality, accidents, and injuries.[53] Hence, the implications of inadequately treating ADHD have consequences that impact both the individual and society. This study quantifies the cost of suboptimal ADHD treatment, which includes both adding an IR to an ER stimulant due to a lack of duration or continuing an ER stimulant that does not adequately control symptoms across the entire day. A previous study demonstrated that Dyanavel XR reduces the likelihood of adults with ADHD needing a supplemental IR stimulant dose compared to other extended-release formulations at 90 days,[14] and the present economic analysis shows that reducing IR supplementation use with Dyanavel XR provides a societal cost savings of $7,852 per person over 1 year, yielding an aggregate cost savings of $44.6 billion nationally. Cost savings increased over time, with per-person savings reaching $35,114 over five years, corresponding to $199.3 billion in aggregate national savings. Dyanavel XR was cost-saving compared to other ER stimulants across all age groups. Age-stratified benefit-cost ratios followed the expected pattern, given the mix of monetized offsets by life stage, with the highest values in young adults and lower values in children. The benefit-cost ratio < 1 for children may be driven by a lower potential benefit in this age group, as several cost-saving variables (ie, motor vehicle costs, labor market costs, and more limited justice system costs) do not apply. Thus, a population can be net cost-saving even when its benefit-cost ratio is < 1 if the total offsets exceed the total treatment cost. Projected multi-year findings were directionally consistent with the 1-year base case and remained cost-saving across all parameters tested, reinforcing that conclusions are robust to uncertainty in literature-based inputs and carry-forward assumptions. To our knowledge, this is the first economic evaluation to link an ER stimulant's reduced need for IR supplementation to quantified, multi-sector societal cost offsets at both person and national levels. Together, these quantitative results and their robustness across sensitivity analyses suggest that reduced IR supplementation with Dyanavel XR plausibly translates into meaningful societal savings.

Extended-release stimulants are the gold standard in ADHD treatment; however, these medications can vary in their ability to provide a sufficient duration of action, prompting healthcare providers to add IR formulations to patients' regimens. IR stimulants have a short duration of action with a harsh pharmacokinetic curve defined by a sharp rise in blood levels, which can contribute to feelings of euphoria, increasing abuse potential, and a steep decline resulting in the re-emergence of symptoms and uncomfortable side effects, commonly referred to as a crash. Additionally, multiple doses required by IR stimulants also contribute to reduced adherence, resulting in incomplete ADHD symptom control for patients. Treatment non-adherence has been associated with worse academic outcomes, strained family relationships, and an increase in risky behaviors leading to harm.[54] Furthermore, non-adherence increases the pool of unused IR stimulants.

A large percentage of individuals who abuse prescription stimulants favor short-acting agents due to the rapid "high" and euphoria they can produce.[55] Reducing the number of IR stimulants in the public domain may therefore also reduce the incidence of diversion and misuse at a time when the US Food and Drug Administration and DEA are calling to ensure stimulants are prescribed "thoughtfully and responsibly".[56] At the same time, this pressure from governing bodies may contribute to the undertreatment of ADHD, potentially increasing reluctance to prescribe stimulants in general, which could result in suboptimal treatment for patients who genuinely need them.

The importance of ADHD treatment is highlighted by the significant toll of ADHD, namely, reduced life expectancy,[57] while initiating ADHD medication is associated with lower all-cause mortality.[58] Pharmacologic treatment of ADHD is also associated with reduced risk of suicidal behaviors, substance misuse, criminality, and transport accidents.[33] For example, those driving with under-controlled ADHD could experience more frequent and more severe motor vehicle crashes, resulting in injuries, fatalities, and related economic costs of emergency healthcare, rehabilitation, insurance, and legal services.[32,59,60] Furthermore, undertreated ADHD results in higher educational costs and

productivity losses. In children, educational costs are borne by the public school system for special education or behavioral interventions. In adults, loss of productivity manifests as unemployment, income loss, and decreased work performance. These impacts can be felt personally, damaging self-esteem, straining relationships, and at the societal level, as one's family, employers, and/or government providing support services incur these additional costs.

Immediate-release stimulant use ultimately represents inadequate ADHD symptom control, which is detrimental at both the individual and societal levels. While IR stimulants themselves provide limited symptom control and carry a high risk of diversion and misuse, suboptimal ADHD treatment is associated with numerous outcomes that not only cost the individual but also place an additional burden on society. Dyanavel XR could reduce reliance on IR stimulant supplementation and reduce the downstream individual and societal harms and associated cost of IR stimulant use. These findings align with the study's a priori objectives and link a formulation attribute (reduced reliance on IR supplementation) to downstream clinical and public-health relevant consequences captured in the model.

This analysis should be interpreted in consideration of the following limitations. First, the model's single-cycle decision-tree structure does not reflect the dynamic transitions that occur in real-world ADHD management, such as dose adjustments, switching therapies, or discontinuation. Second, this study relied on published and routinely collected secondary sources, which is appropriate for a societal-perspective economic model spanning multiple domains. Such breadth is not practical to measure within a single primary study, and secondary data enable triangulation across large, representative cohorts while preserving transparency through cited sources and standardized inflation methods. Residual uncertainty was mitigated by harmonizing definitions, applying conservative assumptions, and conducting one-way sensitivity analysis to test all influential parameters. Key clinical inputs, including response rates and end-of-dose crash probabilities derived from a single published source, would benefit from replication to strengthen current findings. Medical and non-medical cost parameters (eg, criminal justice involvement, educational support, and productivity loss) were derived from heterogeneous studies that span different populations, timeframes, and healthcare systems, which limits their direct applicability to this US ADHD cohort. Costs may be under- or over-estimated because some condition-specific cost elements were unavailable, and therefore these cost estimates relied on literature-derived averages. This can introduce overlap between cost categories or result in the omission of certain costs. Third, by relying exclusively on US-centric prevalence, cost, and resource-use data, the findings may not generalize to other geographic or payer settings with different coverage policies, clinical guidelines, or societal cost structures. Fourth, estimates derived from published studies reflect associations observed in real-world practice and heterogeneous cohorts. As such, they are suitable for parameterizing a societal decision model but are not causal effect estimates. Consistent with its decision-modeling purpose, the analysis generates policy-relevant projections rather than causal inferences. Fifth, pooling ER stimulants into a treatment-as-usual comparator may mask product-specific differences in efficacy, tolerability, and dosing due to differing formulations and delivery systems. To address heterogeneity across ER products, market-share-weighted inputs were used where available, and parameter uncertainty was examined through sensitivity analysis. Where segment-specific data become available, future work could present stratified scenarios for treatment baskets to complement the market-basket approach. Sixth, coding "any IR supplementation" as part of a suboptimal response construct may over-classify clinically appropriate add-on dosing from a cost perspective. However, this specification reflects policy-relevant ER-first practice patterns and was tested in sensitivity analyses. Furthermore, IR-supplementation rates from claims can be shaped by formulary coverage or marketing, as well as clinical choice. For a societal-perspective model, these factors appropriately represent real-world utilization and associated costs, but they are not causal effects. This construct is hypothesis-generating and intended to structure societal cost projections. Finally, although deterministic sensitivity analyses were applied to most inputs, structural assumptions such as treatment effect duration, real-world dosing patterns, and quality-of-life utilities were excluded, leaving residual uncertainty around long-term outcomes that warrants validation through future real-world effectiveness and utility studies.

This model combines observed data with assumptions to project outcomes beyond one year. This approach is standard in societal-perspective economic evaluations spanning healthcare and non-health sectors. Projections were constrained by anchoring to observed practice patterns and rates, conservative carry-forward of event rates without compounding treatment effects, and discounting. All influential parameters were tested in sensitivity analyses, and Dyanavel XR remained cost-saving throughout. These features mitigate the concern that results are assumption-driven while preserving

external validity across sectors. Future work could extend and validate these estimates using longitudinal claims or registry data and confirm real-world changes in IR supplementation and downstream events (eg, injuries, driving incidents, and productivity). Such studies would complement the current findings by providing empirical confirmation over time and across settings. If linked, cohort-level datasets become available, future work could explore patient-level microsimulation or multi-state models to examine trajectories and heterogeneity in outcomes while maintaining an economic evaluation focus. Longer horizons could be explored as more stable longitudinal data become available, complementing the present 1- and 5-year policy frames.

Conclusion

The protective effects of optimized ADHD treatment have an impact on patients' lives and related outcomes, which may extend to society. Within a hypothesis-generating decision-analytic framework, this analysis suggests that Dyanavel XR may provide substantial economic advantage over other ER stimulants, over a one-year societal horizon, yielding mean per-person savings of $7,852 and an aggregate national savings of $44.6 billion. The economic value of Dyanavel XR was most pronounced in young adults and was lower in children. The model's benefit-cost ratio suggests that every dollar invested in Dyanavel XR yields $12.59 in broader societal benefits. One-way deterministic sensitivity analysis confirmed the model's robustness across key parameter variations. These results underscore the broad advantages of improving outcomes with adequate symptom control by reducing IR supplementation and end-of-dose crash to mitigate downstream costs and support Dyanavel XR's value as an ADHD treatment option. In interpreting these results, suboptimal response, defined as any IR supplementation or an end-of-dose crash should be viewed as a pragmatic, hypothesis-generating construct rather than a validated clinical endpoint. Future research can empirically assess the construct's predictive validity by testing whether IR supplementation and end-of-dose crash are associated with subsequent clinical outcomes, quality of life, and disability in longitudinal datasets. Further, as a decision-analytic model, these findings should be interpreted alongside noted limitations; prospective real-world studies and longer follow-up would be informative to further confirm durability and magnitude of effects across settings.

Abbreviations

ADHD, Attention-deficit/hyperactivity disorder; AUD, Alcohol use disorder; B, Billion; DEA, Drug Enforcement Administration; DUD, Drug use disorder; ED, Emergency department; ER, Extended-release; FIA, Formulary Impact Analyzer; IR, Immediate-release; PDC, Proportion of days covered; US, United States; United States dollar; XR, Extended-release (used specifically for Dyanavel XR).

Ethics Statement

The study used data from previously published sources or publicly available databases, with no direct involvement of human subjects or access to identifiable private information. All data sources are cited within the manuscript. In accordance with the United States Department of Health and Human Services regulations (45 CFR 46.102(e)(1) and the exemption framework in 45 CFR 46.104) and the United States Food and Drug Administration regulations (21 CFR 56.102), this work does not constitute human subjects research and is not subject to institutional review board oversight. Therefore, review and approval by an institutional review board or ethics committee were not required.

Author Contributions

All authors made a significant contribution to the work reported, including study conception, design, execution, acquisition of data, analysis, and interpretation, and in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

JH, MSK, EPS, and JP are employees of Tris Pharma (manufacturer of Dyanavel® XR), and IC was a paid consultant for this study. The authors report no conflicts of interest in this work.

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