Variation in the 12-Month Treatment Trajectories of Children and Adolescents After a Diagnosis of Depression

Nina R. Joyce, PhD; Megan S. Schuler, PhD; Scott E. Hadland, MD, MPH, MS; Laura A. Hatfield, PhD

IMPORTANCE Depression during childhood and adolescence is heterogeneous. Treatment patterns are often examined in aggregate, yet there is substantial variability across individual treatment trajectories. Understanding this variability can help identify treatment gaps among youths with depression.

OBJECTIVE To characterize heterogeneity in 12-month trajectories of psychotherapy and antidepressant treatment in youths with depression.

DESIGN, SETTING, AND PARTICIPANTS This is a longitudinal-cohort study of youths 18 years or younger with a new diagnosis of depression and at least 12 months of follow-up following diagnosis, as determined from commercial insurance claims filed from 2007 to 2014. Latent class models were fit to summary measures of psychotherapy and antidepressant use in the 12 months following the index diagnosis. We examined variation in baseline health, health care utilization, and health outcomes across classes with similar patterns of psychotherapy and antidepressant use. Data analysis took place between June 2016 and March 2017.

MAIN OUTCOMES AND MEASURES Psychotherapy and antidepressant use.

RESULTS The cohort included 84,909 individuals with a mean (SD) age at index diagnosis of 15.0 (2.6) years, of whom 49,995 (59%) were female. Attention-deficit/hyperactivity disorder (n = 14,625; 17%) and anxiety (n = 12,358; 15%) were the most common comorbid diagnoses. During the assessment period, 59,023 individuals (70%) received psychotherapy at any point, and 33,997 individuals (40%) were dispensed antidepressants at any point. Eight classes with distinct treatment trajectories were identified, which we classified into 4 broad groups: 3 classes that received dual therapy (n = 18,710; 22%), 2 classes that received antidepressant monotherapy (n = 15,287; 18%), 2 classes that received psychotherapy monotherapy (n = 40,313; 48%) and 1 class that received no treatment (n = 10,599; 13%). The most common class received psychotherapy monotherapy (n = 35,243; 42%) and had the lowest incidence of attempted suicide (0.8 per 100 person-years [PY]) and inpatient hospitalization (3.5 per 100 PY) during the assessment period and postassessment period (0.5 per 100 PY and 1.3 per 100 PY, respectively). The group receiving dual therapy had the highest incidence of attempted suicide during the assessment period (4.7-7.1 per 100 PY, depending on the class) and postassessment period (1.5-1.7 per 100 PY).

CONCLUSIONS AND RELEVANCE In our sample, 13% of youths received no treatment, and 18% received antidepressants without concomitant psychotherapy. Summary measures of treatment can mask informative patterns of psychotherapy and antidepressant use. Latent class analysis can be used to identify subgroups of individuals with similar treatment trajectories and help identify treatment gaps under current practice patterns.
Depression is a common and costly mental health condition during childhood and adolescence, comprising 44% of all mental health hospitalizations and $1.33 billion in health care spending. Approximately 11% of all youths aged 12 to 17 years have experienced a major depressive episode (MDE) in the past 12 months, of whom 73% also experienced severe impairment in at least 1 domain. Suicide is the third leading cause of death during adolescence, and among youths with depression, 29% experience suicidal thoughts and 11% attempt suicide.

Recommended treatment for youths with depression includes pharmacotherapy and psychotherapy, with individual treatment plans tailored by depression severity, patient characteristics, and patient, family, and clinician preferences. The American Academy of Child and Adolescent Psychiatry recommends psychotherapy as first-line treatment for mild depression; for youths with moderate or severe depression, the AACAP recommend psychotherapy or pharmacotherapy monotherapy or a combination of the 2. A 2014 national survey found that, among youths aged 12 to 17 years with an MDE within the past year, 39% reported seeking counseling or therapy for depression, and 20% reported ever using antidepressants.

Given the relapsing and remitting nature of depression, treatment is often a dynamic process that varies over time in response to an individual’s clinical trajectory. The temporal context is important for understanding clinical appropriateness of care. Yet, treatment patterns for depression are often assessed using cross-sectional summary measures, which cannot describe the time-variable nature of treatment. For instance, individuals who abruptly discontinue their medication and individuals who taper medication under medical direction would both be classified as “off pharmacotherapy” in a cross-sectional analysis, yet these individuals would represent 2 distinct clinical scenarios. Thus, several recent studies of depression in adults have sought to characterize heterogeneity in the longitudinal trajectories of both treatment and disease course. Musliner et al identified 4 distinct patterns of treatment over a 10-year period in adults with depression: brief contact, high initial contact, persistent contact, and later reentry. However, to our knowledge, no studies have characterized the longitudinal patterns of treatment in youths with depression.

The present study addresses this gap in the literature by identifying distinct classes of individuals within a cohort of youths with newly diagnosed depression who exhibited similar trajectories of antidepressant use and psychotherapy. Characterizing heterogeneity in treatment for depression is central to understanding the factors driving variation in treatment in youths, and it can assist in identifying targets for interventions designed to close treatment gaps and improve outcomes. We therefore identified baseline characteristics associated with membership in classes, as well as the associations between class membership and inpatient hospitalizations for depression and attempted suicide.

Methods

Data Source and Structure
Data for this study came from the MarketScan Commercial Claims research database for calendar years 2007 through 2014.

Key Points

Question: How do patterns of psychotherapy and antidepressant use vary after newly diagnosed depression in youths 18 years and younger?

Findings: Latent class analysis was used to identify 8 distinct classes of patients who had similar treatment trajectories in the year following diagnosis in a cohort of 84,909 youths. Youths receiving psychotherapy monotherapy had the lowest incidence of inpatient hospitalization for depression and attempted suicide; youths receiving dual therapy had the highest rates.

Meaning: Understanding the heterogeneity of treatment for depressed youths may assist in identifying treatment gaps under current practice patterns.

Figure 1. Study Cohort Timeline

In each patient, the baseline period is a minimum of 12 months preceding any diagnosis of depression; the index diagnosis is the first of 2 outpatient visits or 1 inpatient admission with a primary diagnosis of depression; the assessment period is a period of 30 days following the index diagnosis; and the postassessment period is a period of variable length from the end of assessment through the end of follow-up or through December 31, 2014, whichever came first. During assessment, latent class models were fit based on summary measures of antidepressant and psychotherapy use in each 30-day period.

This database contains all enrollment information and inpatient, outpatient, and pharmacy claims for the employees of a set of employers across the country; the dependents of the employees are also included. The study was considered exempt by the Harvard Medical School institutional review board. Youths 18 years or younger who did not have a baseline diagnosis for bipolar disorder were eligible for inclusion if they were continuously enrolled in an insurance plan that covered both prescription drugs and behavioral health for the 12 months prior to a qualifying new diagnosis for depression and for 12 or more continuous months following the index diagnosis. The index diagnosis of incident depression was defined as a single inpatient admission or 2 outpatient claims (in a 12-month period) in which a person received a primary diagnosis of depression (International Classification of Diseases, Ninth Revision [ICD-9] codes 296.2x, 296.3x, and 311). The total observation time for each individual was divided into 3 periods: the 12 months prior to index diagnosis (baseline period), the 12 months following the index diagnosis, during which treatment trajectories were measured (assessment period); and the period from the end of the assessment period through the end of follow-up (postassessment period, which varied in length between individuals) (Figure 1). Data analysis was completed between June 2016 and March 2017.

Figure 1. Study Cohort Timeline

<table>
<thead>
<tr>
<th>Baseline period</th>
<th>Assessment period</th>
<th>Postassessment period</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 mo</td>
<td>12 mo</td>
<td>Variable, average length, 23 mo</td>
</tr>
<tr>
<td>Index date</td>
<td>First of 2 outpatient visits or first inpatient admission for depression</td>
<td>End of follow-up or End of health insurance coverage December 31, 2014</td>
</tr>
</tbody>
</table>

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Variation in Treatment Trajectories of Youths With Depression

Statistical Analysis

Longitudinal Summary Features

We used 4 parsimonious summary measures of individual longitudinal trajectories during the 12-month assessment period: (1) the number of months with at least 1 psychotherapy visit; (2) the number of months with any antidepressant use; (3) the number of months from diagnosis to the first psychotherapy visit (if applicable); and (4) the number of months from diagnosis to the first dispensing of an antidepressant (if applicable).

To construct these measures, we created binary measures of any psychotherapy and any antidepressant use in each 30-day period during the assessment period. Psychotherapy visits were defined as claims with a Current Procedural Terminology (CPT) code for psychotherapy and a primary diagnosis for depression. To construct monthly indicators of antidepressant use, we first calculated the proportion of days covered (PDC) in each month using a recently published algorithm for estimating the PDC over short periods using claims data. This method is more sensitive to changes in medication use and can better distinguish irregular patterns of use from continuous low-level use of a drug. Our monthly indicator of antidepressant use was defined as a PDC greater than 0. (eTables 1 and 2 in the Supplement provide psychotherapy CPT codes and antidepressant medications included in the analysis; although only fluoxetine and escitalopram have been approved for treatment of major depressive disorder in youths, we included all antidepressants approved by the US Food and Drug Administration for use in adults, to account for the high prevalence of off-label prescribing).

Latent Class Analysis

Latent class models were used to identify subgroups of individuals with similar longitudinal patterns of psychotherapy and antidepressant use based on the 4 summary measures described in the last subsection. Latent class analysis is a form of finite mixture modeling in which data are assumed to be composed of a set of mutually exclusive subgroups (classes) that cannot be measured directly but can be indirectly measured through a set of observed variables. Thus, latent class analysis can be a useful tool for identifying homogenous clusters within a heterogeneous population.

We fit latent class models with 1 to 10 classes, using the Polytomous Variable Latent Class Analysis (polLCA) package in R (R Development Core Team). The 4 summary measures were included as categorical variables. Indicators for months of use ranged from 0 to 12, and indicators for month of initiation ranged from 0 to 12, where 0 indicated that use was never initiated, 1 indicated that use was initiated immediately on diagnosis, and 12 indicated that use was initiated 12 months after diagnosis. Model selection was based on a combination of minimizing fit statistics (Bayesian Information Criteria, Akaike Information Criteria, log-likelihood, and entropy measures) and model interpretability. Eight classes were deemed to provide optimal fit to our data (see eTable 3 and eTable 4, eMethods, and eFigures 1, 2, and 3 in the Supplement for model selection criteria and results of a split-sample validation analysis).

Correlates of Class Membership

Covariates Measured at Baseline

We quantified the univariate association between class membership and youths’ characteristics measured over the baseline period. The baseline characteristics of interest were age, sex, attempted suicide, and comorbid mental health diagnoses (attention-deficit/hyperactivity disorder, conduct disorder, psychosis, substance use disorder, and anxiety disorder; ICD-9 codes for all diagnoses are listed in eTable 5 in the Supplement). Additional measures included health care utilization during the baseline period, including the number of inpatient admissions, outpatient visits, and number of distinct prescription drugs dispensed. We used χ² tests of associations to compare categorical variables across classes and 1-way analysis of variance comparison of means to compare continuous measures.

Inpatient Hospitalization and Attempted Suicide

We examined the univariate association between class membership and incidence of attempted suicide in the baseline period, and incidence of both attempted suicide and inpatient hospitalization for depression in the assessment and postassessment periods. Inpatient hospitalizations were defined as an inpatient claim with a primary diagnosis for depression. To measure attempted suicide in youths, we used a validated algorithm to identify patients through a combination of ICD-9 codes in claims data for attempted suicide, external cause of injury codes (E codes), and hospital length of stay. Because individuals had varying durations of follow-up time in the postassessment period, we calculated the incidence rate in that period as the number of individuals with an attempted suicide or hospitalization divided by the total observed person-years (PY). Likewise, we report the incidence of attempted suicide during the baseline period and both attempted suicide and inpatient hospitalization during assessment periods per 100 PY for comparability.

Results

Study Cohort

Among our study cohort of 84,909 individuals, the mean age at diagnosis was 15.0 years, with 50% of youths between the ages of 14 and 18 years at time of diagnosis; 59% of the cohort was female, and the most common comorbid mental health diagnoses at baseline were attention-deficit/hyperactivity disorder (n = 14,625; 17%) and anxiety (n = 12,358; 15%). Overall, most youths (n = 59,023; 70%) received any psychotherapy during the initial 12-month assessment period, while fewer than half (n = 33,997; 40%) received any antidepressant medication. Across the entire study period, the overall incidence of attempted suicide was 2.7 attempts per 100 PY. The incidence of attempted suicide was 0.8 attempts per 100 PY during the baseline period and 3.1 attempts per 100 PY during the assessment period. Individuals were observed for an average of 23 months after the assessment period ended, during which the incidence of attempted suicide was 0.8 per 100 PY. During the assessment period, the incidence of inpatient hospitalization was 15.8 admissions per 100 PY, while in the postassessment period the incidence was 1.6 admissions per 100 PY (Table 1).
we instead differentiated by the duration of antidepressant use in the first month after diagnosis. youths in these classes were instead differentiated by the duration of antidepressant use: those in drug 1 used antidepressants for an average of 5.5 months compared with 10.2 months for those in drug 2.

The final 3 classes were characterized by dual therapy (drug 1 through drug 3). For individuals in dual 1 (n = 40313, 47.5%), antidepressant use preceded psychotherapy use; drug 2 (n = 3531, 6.3%) and drug 3 (n = 3654, 4.3%) first initiated psychotherapy and subsequently added antidepressants. Individuals in dual 1 immediately initiated antidepressant use and continued for an average of 10.4 months, added psychotherapy in month 2.6, and received combination therapy for an average of 4.7 months. youths in class dual 2 and dual 3 had similar timing of treatment initiation (beginning psychotherapy in months 2.3 and 2.2 and antidepressant use in months 2.9 and 4.0, respectively), but were differentiated by duration of both psychotherapy and antidepressant use. youths in drug 2 received antidepressants for 4.0 months and psychotherapy for 4.2 months, while youths in dual 3 received antidepressants for 7.0 months and psychotherapy for 5.9 months.

Table 1. Cohort Characteristics at Baseline and Rates of Hospitalization and Attempted Suicide in Baseline, Assessment, and Postassessment Periods

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Individuals, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient characteristics at baselinea</td>
<td>84 909 (100)</td>
</tr>
<tr>
<td>Age at index diagnosis, y, mean (SD)</td>
<td>15.0 (2.6)</td>
</tr>
<tr>
<td>Female</td>
<td>49 995 (59)</td>
</tr>
<tr>
<td>Mental health comorbidities</td>
<td></td>
</tr>
<tr>
<td>Substance use disorder</td>
<td>957 (1)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>12 358 (15)</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>3170 (4)</td>
</tr>
<tr>
<td>Psychosis</td>
<td>1746 (2)</td>
</tr>
<tr>
<td>ADHD</td>
<td>14 625 (17)</td>
</tr>
<tr>
<td>Any of the above</td>
<td>27 145 (32)</td>
</tr>
<tr>
<td>Health care utilization, No. of visits, mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>0.1 (0.4)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>9.9 (11.6)</td>
</tr>
<tr>
<td>Unique medications prescribed, No., mean (SD)</td>
<td>3.1 (3.3)</td>
</tr>
<tr>
<td>Attempted suicide, No. (No. per 100 PY)b</td>
<td>695 (0.8)</td>
</tr>
<tr>
<td>Assessment period, No. (No. per 100 PY)b</td>
<td></td>
</tr>
<tr>
<td>Attempted suicide</td>
<td>2633 (3.1)</td>
</tr>
<tr>
<td>Inpatient hospitalization for depression</td>
<td>13 395 (15.8)</td>
</tr>
<tr>
<td>Postassessment period, No. (No. per 100 PY)c</td>
<td></td>
</tr>
<tr>
<td>Attempted suicide</td>
<td>27 145 (0.8)</td>
</tr>
<tr>
<td>Inpatient hospitalization for depression</td>
<td>2216 (1.6)</td>
</tr>
</tbody>
</table>

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; PY, person-years.

a Defined as the 12 months prior to index diagnosis.

b Defined as the 12 months following index diagnosis.

c Defined as the time after the assessment period; length varied by individual.

Table 2 presents summary measures used to identify classes.

We identified 8 distinct trajectories of antidepressant use and psychotherapy that can be grouped into 4 broad patterns of treatment: psychotherapy monotherapy (n = 40 313, 47.5%; psych 1 and psych 2 trajectories), dual therapy (n = 18 710, 22.0%; dual 1 through dual 3 trajectories), antidepressant monotherapy (n = 15 287, 18.0%; drug 1 and drug 2 trajectories), and no treatment (n = 10 599, 12.5%; none trajectory).

Among individuals using psychotherapy monotherapy (47.5%), classes psych 1 and psych 2 differed by the timing of psychotherapy. Most youths belonged to class psych 1 (n = 35 243, 41.5%), which was characterized by the immediate initiation of psychotherapy and declining visits over time. By contrast, individuals in psych 2 (n = 5070, 6.0%) initiated psychotherapy 3.8 months after diagnosis on average, and by the end of the assessment period had reached the same frequency of use as youths in psych 1.

Among individuals using antidepressant monotherapy, there was less variation in the month of initiation: 75% in class drug 1 (n = 9445, 11.1% of the full study cohort) and 98% of youths in drug 2 (n = 5842, 6.9%) were dispensed antidepressants in the first month after diagnosis. youths in these classes were instead differentiated by the duration of antidepressant use: those in drug 1 used antidepressants for an average of 5.5 months compared with 10.2 months for those in drug 2.

The final 3 classes were characterized by dual therapy (drug 1 through drug 3). For individuals in dual 1 (n = 40313, 47.5%), antidepressant use preceded psychotherapy use; drug 2 (n = 3531, 6.3%) and drug 3 (n = 3654, 4.3%) first initiated psychotherapy and subsequently added antidepressants. Individuals in dual 1 immediately initiated antidepressant use and continued for an average of 10.4 months, added psychotherapy in month 2.6, and received combination therapy for an average of 4.7 months. Youths in class dual 2 and dual 3 had similar timing of treatment initiation (beginning psychotherapy in months 2.3 and 2.2 and antidepressant use in months 2.9 and 4.0, respectively), but were differentiated by duration of both psychotherapy and antidepressant use. Youths in drug 2 received antidepressants for 4.0 months and psychotherapy for 4.2 months, while youths in dual 3 received antidepressants for 7.0 months and psychotherapy for 5.9 months.

Correlates of Class Membership

We report the characteristics of individuals in each class in Table 3. youths using dual therapy and antidepressant monotherapy were older at their index diagnosis and more likely to be female than youths in classes with psychotherapy monotherapy or no treatment at all. Noticeably, the prevalence of concomitant comorbidities differed across the classes within each broad treatment group. Specifically, both the lowest and highest prevalences of concomitant anxiety were observed among the dual therapy group: 396 (11%) in dual 3 and 632 (12%) in dual 2 vs 1816 (19%) in dual 1. Likewise, the prevalence of anxiety differed significantly across classes in the antidepressant monotherapy group: 1361 (14%) in drug 1 vs 1359 (23%) in drug 2. The same was not true for measures of health care utilization at baseline, where patterns within broad treatment categories tended to be more homogeneous.

Inpatient Hospitalization and Attempted Suicide Rates

Overall, incidence of attempted suicide and inpatient hospitalization declined from the assessment period to the postassessment period. The incidence of attempted suicide in the postassessment period generally returned to baseline rates, with the exceptions of 3 classes. Among the youths in dual 1 and dual 3, the postassessment incidence was notably higher than the baseline incidence (in dual 1, 1.7 attempts per 100 PY in the postassessment period vs 1.2 attempts per 100 PY in the baseline period; in dual 3, 1.5 attempts per 100 PY in postassessment vs 0.7 in the baseline period). In the class receiving no treatment, postassessment incidence of attempted suicide (0.7 per 100 PY) was notably lower than at baseline (1.2 per 100 PY).

People in classes characterized by psychotherapy monotherapy (psych 1 and psych 2) had the lowest rates of inpatient hospitalization in assessment period (in psych 1, 3.5 admissions per 100 PY; in psych 2, 8.0 admissions per 100 PY) and postassessment period (in psych 1, 1.3 admissions per 100 PY; in psych 2, 1.4 admissions per 100 PY). (Hospitalization was an eligibility criterion for the study and was therefore not present in the baseline period by definition.) The individuals in the psychotherapy monotherapy classes also had the low-
The incidence of attempted suicide across the baseline period (0.5 attempts per 100 PY and 0.7 attempts per 100 PY in psych 1 and psych 2, respectively), assessment period (0.8 and 1.9 attempts per 100 PY in psych 1 and psych 2, respectively), and postassessment period (0.5 and 0.7 attempts per 100 PY in psych 1 and psych 2, respectively).

In contrast, dual therapy classes had high rates of attempted suicide and inpatient hospitalization across all periods. Attempted suicide among the 3 dual therapy subgroups ranged from 0.7 attempts per 100 PY to 1.4 attempts per 100 PY in the baseline period, from 4.7 attempts per 100 PY to 7.1 per 100 PY in the assessment period, and from 1.4 attempts per 100 PY to 1.7 per 100 PY in the postassessment period. Across the 3 dual groups, inpatient hospitalization ranged from 22.0 admissions per 100 PY to 36.3 per 100 PY during the assessment period and from 3.1 admissions per 100 PY to 3.3 per 100 PY during the postassessment period. However, the pattern within the broad treatment groups was more complicated. For example, youths in dual 3 had a lower incidence of attempted suicide during the baseline period (0.7 attempts per 100 PY) and the assessment period (4.7 attempts per 100 PY) and a lower incidence of inpatient hospitalization during the baseline period (22.0 admissions per 100 PY) than the youths in dual 1 (who attempted suicide at a rate of 1.2 attempts per 100 PY in the baseline period and 7.1 per 100 PY in the assessment period, and were hospitalized at a rate of 36.3 admissions per 100 PY in the assessment period). The youths in dual 1 also showed elevated rates of suicide attempts and hospitalizations relative to dual 2 (who attempted suicide at a rate of 1.4 attempts per 100 PY in the baseline period and 6.0 per 100 PY in the assessment period, and who were hospitalized at a rate of 31.6 admissions per 100 PY in the assessment period). Youths in dual 1 and dual 3 also had the highest incidence across all classes of inpatient hospitalization (mean, 3.3 per 100 PY) in the postassessment period (compared with 3.1 hospitalizations per 100 PY in dual 2) (Table 3).
Table 2. Longitudinal Characteristics of Classes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group and Class</th>
<th>Antidepressant Monotherapy</th>
<th>Psychotherapy Monotherapy</th>
<th>Dual Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Cohort</td>
<td>No Treatment^a</td>
<td>Drug 1^b</td>
<td>Drug 2^b</td>
</tr>
<tr>
<td>No. (%)</td>
<td>84 909 (100)</td>
<td>10 599 (12.5)</td>
<td>9445 (11.1)</td>
<td>5842 (6.9)</td>
</tr>
<tr>
<td>Months after index diagnosis of first antidepressant use^a</td>
<td>1.9</td>
<td>NA</td>
<td>1.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Months after index diagnosis of first psychotherapy^a</td>
<td>1.7</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Total months of antidepressant use</td>
<td>3.0</td>
<td>NA</td>
<td>5.5</td>
<td>10.2</td>
</tr>
<tr>
<td>Total months of psychotherapy attendance</td>
<td>3.0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Total months of dual therapy^a</td>
<td>0.8</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.
^a Unless otherwise indicated, all data are reported as mean values.
^b For definitions of all classes, please see the Latent Class Analysis subsection in the Methods section.
^c Among individuals with any psychotherapy use in the first 12 months after the index diagnosis.
^d Among individuals with any antidepressant use in the first 12 months after the index diagnosis.
^e Variable not included in latent class models.

Discussion

In this study of 84 909 youths with an index diagnosis of depression, we identified 8 distinct trajectories of treatment using latent class analysis. Trajectories were characterized by 4 broad treatment patterns: no treatment, antidepressant monotherapy, psychotherapy monotherapy, and dual therapy (comprising both antidepressant use and psychotherapy). As in prior research,24,18 we found that most youths do not receive antidepressants. Instead, early initiation of psychotherapy monotherapy is the most common treatment pattern (class psych 1).

Patients who receive antidepressants (classes drug 1, drug 2, dual 1, dual 2, and dual 3) have greater behavioral health severity and complexity at baseline (as measured by comorbid mental health diagnoses and health care utilization prior to the index depression diagnosis), as well as higher rates of hospitalization and attempted suicide after diagnosis. This is generally consistent with the recommendations to treat more severe depression with pharmaceutical therapy and is in line with findings regarding treatment patterns from prior observational studies.6,10,20

Our findings add to the discussion about antidepressants and suicide risk in children and adolescents. Several studies have suggested that antidepressants may increase the risk of suicide in youths,21,22 but the results are inconclusive, primarily owing to the difficulty of accounting for selection effects.17,23,24 In our study, individuals who used antidepressants (classes drug 1, drug 2, and dual 1 through dual 3) had the highest rates of attempted suicide in the assessment and postassessment periods. However, our results do not imply a causal relationship between antidepressant use and suicide risk, because youths in these classes already had higher rates of attempted suicide at baseline. Instead, our findings highlight the need for studies to disentangle the effect of baseline severity from the potential effects of antidepressants.

Given the Academy of Child and Adolescent Psychiatry’s recommendations, it is particularly noteworthy that 1 in 8 youths in our cohort received no treatment, despite being similar in age to individuals receiving treatment, having behavioral health profiles at baseline comparable to other classes, and having rates of inpatient hospitalization and attempted suicide similar to individuals who received antidepressant monotherapy. Though several studies have documented the high level of unmet need for treatment in youths experiencing depression, most have used survey data and were not limited to individuals with diagnosed depression.25-27 In contrast, our study includes only privately insured youths with both behavioral health and prescription drug coverage who had had a single inpatient visit or 2 outpatient visits with a primary diagnosis for depression. Even in this population, who appear to have fewer barriers to care, a portion are not receiving treatment for depression.

A second notable pattern was the change in the incidence of attempted suicide from the baseline through the postassessment periods. Several studies have documented that patients are at highest risk of attempting suicide immediately before and after starting treatment and that this risk decreases over time.19,23,28 We found the highest incidence of attempted suicide during the assessment period; the incidence in the postassessment period returned to the baseline rates for the youths in all but 3 classes (dual 1 and dual 3, for which the postassessment incidence was higher than the baseline incidence, and the class receiving no treatment, for which it was lower). Again, this pattern is likely reflective of differing baseline severities. However, during the postassessment period, the incidence of attempted suicide and inpatient hospitalization in classes dual 1 and dual 3 is 2 to 3 times the rate of people
receiving psychotherapy monotherapy, highlighting the importance of carefully monitoring these subgroups.

**Limitations**

Several limitations warrant mention. First, our results may not generalize beyond a privately insured population with treatment-seeking behavior. Second, because we can only determine if a patient was dispensed an antidepressant and not if he or she was taking the medication, we may have overestimated the rate of antidepressant use. However, the use of administrative pharmacy claims to estimate the PDC is a standard, well-validated method of measuring adherence.29 Third, our measure of attempted suicides is strictly based on administrative insurance claims and might not include completed suicides or attempted suicides not seen by a medical professional. Thus, our incidence rates may underestimate the true rate of suicide attempts in our sample. Indeed, the 2015 Youth Risk Behavior Surveillance System30 found that while 9% of respondents reported attempting suicide in the past 12 months, only approximately 32% of those were treated by a medical professional; this is consistent with our overall reported suicide attempt rate of 2.7 per 100 PY in the assessment period. Similarly, the psychotherapy use captured in our claims data may be an underestimate if youths received psychotherapy in an alternative setting (eg, school) or if they paid out of pocket for services. Finally, our baselines measures are limited to the year preceding diagnosis and might exclude measures of prior treatment for the percentage of youths for whom the index episode represents recurrent depression. Given that prior treatment is often a strong predictor of future treatment, subsequent research should explore differential treatment patterns between youths with new and recurrent depression diagnoses.

**Conclusions**

Summary measures of treatment often mask substantial variation in the use of psychotherapy and antidepressants among...
youths with depression. Using latent class analysis, we identified 8 distinct classes of youths with similar trajectories of treatment for depression that varied with respect to the timing and duration of psychotherapy and antidepressant use. Additionally, we found that the prevalence of comorbid conditions, as well as the incidence of attempted suicide and inpatient hospitalizations, varied significantly across classes. Characterizing the heterogeneity in treatment trajectories for depression can help researchers and clinicians identify gaps in treatment and develop targeted interventions.

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Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Joyce, Hadland.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: All authors.
Administrative, technical, or material support: Joyce.
Study supervision: Hatfield.

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REFERENCES