Age and Cohort Patterns of Medical and Nonmedical Use of Controlled Medication Among Adolescents

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Abstract

Objectives—We identified peak annual incidence rates for medical and nonmedical use of prescription opioid analgesics, stimulants, sedatives and anxiolytics (controlled medication), and explored cohort effects on age of initiation.

Methods—Data were gathered retrospectively between 2009–2012 from Detroit area students (n=5185). Modal age at last assessment was 17 years. A meta-analytic approach produced age-, year-, and cohort-specific risk estimates of first-time use of controlled medication. Cox regression models examined cohort patterns in age of initiation for medical and nonmedical use with any of four classes of controlled medication (opioid analgesics, stimulants, sedatives or anxiolytics).

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Results—Peak annual incidence rates were observed at age 16, when 11.3% started medical use, and 3.4% started using another person's prescription for a controlled medication (i.e., engaged in nonmedical use). In the more recent birth cohort group (1996–2000), 82% of medical users and 76% of nonmedical users reported initiating such use by age 12. In contrast, in the less recent birth cohort group (1991–1995), 42% of medical users and 35% of nonmedical users initiated such use by age 12. Time to initiation was 2.6 times less in the more recent birth cohort group (medical use: adjusted hazard ratio [aHR]=2.57 [95% confidence interval (CI)= 2.32, 2.85]; nonmedical use: aHR=2.57 [95% CI=2.17, 3.03]).

Conclusions—Peak annual incidence rates were observed at age 16 for medical and nonmedical use. More recent cohorts reported initiating both types of use at younger ages. Earlier interventions may be needed to prevent adolescent nonmedical use of controlled medication.

Across a variety of substances with abuse potential, prospective, retrospective and longitudinal studies have found associations between younger ages of initiation and heightened risk of use, abuse and dependence later in life (Yamaguchi & Kandel, 1984; Trinkoff et al., 1990; McCabe et al., 2007a; Chen et al., 2009; Substance Abuse and Mental Health Services Administration [SAMHSA], 2013). Few studies have examined this association in relation to opioid analgesics, stimulants, anxiolytics or sedatives - four classes of Schedule II–IV medication controlled by the United States (US) Food and Drug Administration based on their potential for nonmedical use. This is surprising given public health concerns about the prevalence of nonmedical use among adolescents (Boyd et al., 2006; McCabe et al., 2011, 2013a,b) and the young age of first-time nonmedical use (Meier et al., 2012). These concerns are compounded by unease about increasing rates of prescribing controlled medication to children and adolescents in the US (Staller et al., 2005; Thomas et al., 2006; Zuvekas et al., 2006, 2012; Castle et al., 2007; Comer et al., 2010; Fortuna et al., 2010; Garfield et al., 2012; Visser et al., 2014). For instance, between 2007 and 2011, there was a 7% average annual increase in the percentage of US children 4 to 17 years of age who were prescribed ADHD medication (Garfield et al., 2012). Across a 12-year period (1996–2007),Comer et al. (2010) observed a 42% increase in prescribing of anxiolytics and sedatives to children 6 to 17 years of age. Comer et al. (2010) also found that multiclass psychotropic treatment increased from 14.3% of child office visits (1996–1999) to 20.2% (2004–2007).

As the proportion of children and adolescents being prescribed controlled medication for the first time grows, this study provides a timely investigation of whether first age of medical use is decreasing over time across four classes of controlled medication, and whether there may be a corollary decrease over time in first age of nonmedical use of these compounds. The present study is the first to produce estimates for first age of medical use and for starting to use another person's prescription (hereafter referred to as 'nonmedical use') across four classes of controlled medication. This study is also the first study to examine the temporal relationship between first age of *medical* use and first age of *nonmedical* use with opioid analgesics, stimulants, anxiolytics and sedatives.

METHODS

Data Source and Sample

The data analyzed here were collected as part of the *Secondary Student Life Survey* (SSLS), a web-based longitudinal survey of middle and high school students attending two public school districts in the Detroit metropolitan area. The University of Michigan Institutional Review Board approved the study, and a Certificate of Confidentiality was obtained from the National Institutes of Health. All parents in the school districts were sent letters requesting permission for their children to participate in the SSLS, explaining that participation was voluntary, describing the relevance of the study, and assuring that all responses would be kept confidential. Active child assent was also obtained. The SSLS took approximately 40 minutes to complete.

Data were collected at four time points between academic years 2009 and 2013. The final retention rate for the SSLS was 89% for Time 1-Time 2; 91% for Time 2-Time 3; 83% for Time 1-Time 2-Time 3; and 75.2% for Time 1-Time 2-Time 3-Time 4. This compares favorably with *The Monitoring the Future* study of substance use among high school seniors in the US (Johnston et al., 2014). Table 1 describes characteristics of the study sample (n = 5,185; 49.6% female; 60.7% white, 33.8% black, 5.5% Hispanic and other). Respondents in the sample were aged 12 to 18 years and had completed at least one of the four time points of the SSLS between 2009 and 2013. Each measure used in the present study was measured at each assessment. At the last assessment completed by each respondent in the sample (n = 5,185) (i.e., not necessarily at Time 4), modal age was 17, and there were 740 individuals, on average, in each year-by-year age group (Standard Deviation: 309.5).

Measures

Medical use was measured at each assessment using the following question: "The following questions are about the use of prescribed medicines. We are not interested in your use of over-the-counter medicines that can be bought in drug or grocery stores without a prescription, such as aspirin, Sominex, Benadryl, Tylenol PM, cough medicine, etc. On how many occasions **in your lifetime** has a doctor, dentist, or nurse prescribed the following types of medicine for you?" Respondents who reported one or more occasions of medical use in their lifetime were asked (separately for each drug class): "About what age did you begin using this medication?"

Nonmedical use was measured at each assessment using the following question: "Sometimes people use prescription medicines that were meant for other people, even when their own Health Professional (e.g., doctor, dentist, nurse) has not prescribed it for them. On how many occasions **in your lifetime** have you used the following types of medicines **not** prescribed to you?" As with the medical use measure, this question was asked separately for each medication class. Respondents who reported one or more occasions of nonmedical use were asked, "About what age did you begin using the following medicines **not prescribed to you**?"

The supplement provides descriptions of compounds. Descriptions of other measures used in this study may be found in previous studies (Boyd et al., 2006, 2007; McCabe et al., 2011).

Analytic Approach

Detailed methods for generating the meta-analytic estimates have been previously published (Meier et al., 2012). Standard errors for all estimates reported in this study fell below .05. The cumulative incidence proportions reported convey the estimated 'risk' of starting medical use or nonmedical use of prescription controlled medication between the ages of 5 (the youngest age respondents were permitted to report initiating medical or nonmedical use) and 17, and between the years of 1996 and 2012 (Meier et al., 2012). If a respondent reported more than one first age for a type of use across medication classes (for instance, age 15 for sedatives, and age 16 for stimulants), the minimum first age of use was retained for cross-medication-class analyses (15 years in this example for first age of controlled medication use). For analyses by individual medication classes, the minimum first age of use within an individual medication class was used. Statistical analyses and the estimation approach were performed on commercially available software (STATA, version 13; and SPSS, version 21). The meta-analysis summary estimates reported were calculated using a random effects meta-analysis software program ('meta', STATA, version 13) that weights each year by the inverse of its variance.

We fit separate multivariate Cox regression models to determine risk factors for younger initiation with opioid analgesics, stimulants, anxiolytics, and sedatives, as well as for all four of these medication classes combined. Data were right-censored to control for respondents completing their last assessment at different ages (modal age 17), and left-censored at age 5 to control for the fact that respondents were not permitted to report a first age of use less than age 5 years. We inspected Kaplan-Meier survivor probabilities and statistical tests of proportionality to confirm that the proportional hazards assumption was satisfied.

Sex, race/ethnicity, and highest degree of education completed by either guardian (described in Table 1) were tested in each initial survival analysis model and retained in subsequent models if significant. Respondents were born over a ten-year period, between 1991 and 2000. We divided birth cohort groups into two equal five-year groups, with the first ranging from 1991 to 1996, and the second ranging from 1997 to 2000, to ensure that the proportional hazards assumption was satisfied when comparing birth cohorts. Additional control measures used in the survival models are described in Table 1.

RESULTS

Medical Use

In our sample of 5,185 adolescents, 20.1% (n=1,044) were first prescribed at least one of the four controlled medication classes prior to age 12, and 37.8% of the sample was first prescribed by the last assessment (modal age 17). Figure 1 illustrates estimates of age-, year-, and cohort-specific cumulative incidence rates per 100 individuals for starting to medically use controlled medication for the first time. Peak ages of onset for medical use within each class of medication are reported in Figure 1. The peak age of onset for medical use across the four classes of controlled medication was age 16.

Table 2 presents the estimated hazard ratios from unadjusted and adjusted Cox regression models for the variable "being prescribed a controlled medication for the first time". In the

more recent birth cohorts (1996–2000), time until first prescription was 2.6 times less (aHR: 2.57 [95% CI: 2.32–3.85]) (Table 2), with 82% of the medical users in these cohorts receiving their first prescription by age 12, compared with 41.9% of medical users in the earlier cohorts (1991–1995). When each class of controlled medication was analyzed individually, birth cohort remained a significant factor predicting less time until first prescription across all four classes of medication. Compared to males, females had less time until first prescription for stimulants (aHR: 1.27 [95% CI: 1.01–1.59]), and marginally less time (*P*=.052) with anxiolytics and sedatives (combined) (aHR: 1.21 [95% CI: .99–1.46]) (Table 2).

Nonmedical Use

Approximately fourteen percent (n=740) of respondents first nonmedically used a controlled medication by their last assessment (modal age 17). About six percent (n=307) of respondents started nonmedical use prior to age 12. Figure 1 illustrates estimates of age-, year-, and cohort-specific cumulative incidence rates per 100 individuals. The peak age of onset for nonmedical use across all four classes of controlled medication was age 16. Peak ages of onset for nonmedical use with each class of medication are reported in Figure 1.

Table 2 presents estimated hazard ratios from unadjusted and adjusted Cox regression models for first nonmedical use with a controlled medication by age and birth cohort. In the more recent birth cohorts (1996–2000), time until first nonmedical use was 2.6 times less than in the earlier cohorts (1991–1995) (aHR: 2.57 [95% CI: 2.17–3.03]). 75.7% of nonmedical users in the more recent cohorts starting by age 12, compared with only 34.8% starting by age 12 in the earlier cohorts. Results from Cox regression analyses by medication class showed similar associations between recent birth cohort membership and shorter time until initiation of nonmedical use.

Black respondents had less time until initiation of nonmedical use (aHR: 1.21 [95% CI: 1.03–1.43]) and had 2.3 times fewer years until first nonmedical use of stimulant medication (aHR: 2.31 [95% CI: 1.22–4.38]), when compared with other race/ethnicity groups.

As illustrated in Figure 2, within each birth cohort group, cumulative hazard rates by age for first medical use closely paralleled those of first nonmedical use. Of the 740 respondents who reported nonmedical use, 34.3% (n=254) had never been prescribed a controlled medication; 36.2% (n=268) had been prescribed, but not prior to first nonmedical use; and 29.5% (n=218) reported receiving their first prescription for a controlled medication prior to first nonmedical use. We ran further analyses on a subgroup of respondents who (a) nonmedically used for the first time at least one year in age after receiving their first prescription, and (b) who nonmedically used the same class of controlled medication they had previously been prescribed. We ran an additional set of Cox regression models (with the same controls reported in Table 2) with this subgroup comparing those who received their first prescription for a controlled medication prior to age 12 with those who had not. We found that adolescents who had received their first prescription prior to age 12 initiated nonmedical use more than 2 times earlier across all four classes of medication (aHR: 2.16 [95% CI: 1.56 – 2.98]); with opioid analgesics (aHR: 2.02 [95% CI: 1.08 – 3.75]); and with anxiolytics and sedatives (combined) (aHR: 3.16 [95% CI: 1.42 – 7.05]). In contrast, first

being prescribed stimulants prior to age 12 was not associated with shorter time until subsequent initiation of nonmedical use of stimulants, even while controlling for self-reported ADHD.

DISCUSSION

In our sample of secondary school students, more than one in three reported having been prescribed a controlled medication and more than one in ten reported illegally using another person's controlled medication. Adolescents belonging to the more recent birth cohorts (1996–2000) initiated both medical use and nonmedical use 2.6 times earlier than adolescents in the less recent birth cohorts (1991–1995). These findings may reflect corollary changes in prescribing practices for medication classes known to have high potential for nonmedical use. Our results indicate that receiving a first prescription for a controlled medication prior to age 12 may be associated with less time until initiation of nonmedical use with the same class of medication during subsequent years. This association was observed across the four medication classes, analyzed in combination, as well as individually for opioid analgesics, anxiolytics, and sedatives - but not with stimulants. There is some evidence that stimulant medication therapy for ADHD in early childhood does not increase subsequent risk for nonmedical use of prescription stimulants or other substance use behaviors (Biederman et al., 1999; Barkley et al., 2003; McCabe et al., 2006; Kaloyanides et al., 2007; Katusic et al., 2007; Mannuzza et al., 2008; Volkow & Swanson, 2008). To better understand potential risks associated with prescribing opioid analgesics, anxiolytics, and sedatives in early childhood, prospective studies are needed that control for medication class, dose amounts, medical adherence, exact age at first exposure, duration of exposure, and the clinical indications these medication are prescribed to treat (Volkow & Swanson, 2008).

In our sample, peak risk of using someone else's prescription for the first time was observed at age 16 across four classes of controlled medication (stimulants, opioid analgesics, anxiolytics, and sedatives). Our findings on peak ages of first medical use closely preceding or coinciding with peak ages of first nonmedical use do not constitute a causal connection, but point toward the possibility that more recent birth cohorts may be using someone else's prescription for controlled medication at earlier ages due to greater availability of these medicines among their prescribed peers and family members. Past research has demonstrated that the primary sources of diversion for controlled medication among adolescents are friends and family members, not drug dealers or the web (McCabe & Boyd, 2005; Boyd et al., 2007; McCabe et al., 2007b, 2011, 2013a,b; Ford & Lacerenza, 2011; Burghardt et al., 2013; Cottler et al., 2013; Jones et al., 2014). Regardless of how these adolescents are illegally obtaining access to prescriptions belonging to other people, these findings are concerning because nonmedical use at earlier ages is associated with greater risk of developing substance use disorders (McCabe et al., 2007a).

Strengths and Limitations

This is the first study to produce age-, year-, and cohort-specific incidence rates for both medical and nonmedical use of four classes of controlled medication among adolescents. It

is also the first study to examine the temporal association between first medical use and first nonmedical use with controlled medication in an adolescent sample. As such, it has several strengths. The study includes a large, ethnically diverse sample of adolescents. The fact that retrospective data were collected during the adolescent years when these incidents and behaviors were most likely to occur may reduce the chance of recall bias (Fendrich & Rosenbaum, 2003). These retrospective data also allowed us to produce incidence rates, and explore temporal relationships, dating back to early childhood and extending through late adolescence. Further, the response and attrition rates are consistent with national studies (Johnston et al., 2014). Nonetheless, there are limitations in the study design that reduce the ability to make causal inferences and to generalize to other populations.

Many national studies fail to distinguish between *nonmedical use* (using another person's prescription) and *medical misuse* (using too much of one's own prescription to get high or for other reasons not intended by the prescribing physician) even though they are quite different. It is important to note that both types of use are associated with heightened risk of substance use disorders (McCabe et al., 2005, 2007a,b, 2011, 2013a,b). There are a few reasons we chose to focus on nonmedical use even though the choice might limit the ability to compare our findings with those from other studies. First, nonmedical use is up to three times more prevalent than medical misuse (e.g., for opioid analgesics) (McCabe et al., 2013a,b). Second, whether stolen, bought, traded, or freely given, diversion of one's own prescription for a controlled medication is a felony offense, as is use of someone else's prescription for a controlled medication. Despite this, there is evidence that diversion of prescription medication is a relatively frequent occurrence among adolescents (Boyd et al., 2007; McCabe et al., 2005, 2006, 2007b, 2011, 2013a,b; Ford & Lacerenza, 2011; Cottler et al., 2013).

The sample was from one region and included only adolescents attending secondary schools, which may limit the generalizability of our findings. Additionally, in retrospective studies, there is great reliance on self-report of substance use history. In longitudinal studies with young adults, respondents frequently tend to either under-report substance use, 'recant' previous admissions of substance use (Fendrich & Rosenbaum, 2003), or engage in 'forward telescoping' – the inflating of age at first use over time (Golub et al., 2000). Furthermore, adolescents may have trouble accurately recalling which drug they were prescribed, or even if a drug was prescribed to them (versus to a parent), when they were between the ages of 5 and 12. Accurately recalling which type of medication a peer offered them or that they took at a party many years before may be even more of a challenge.

In our sample, respondents who reported lifetime use were asked a follow-up question about what age they began using and on average – across the four classes of medication – 2% to 4% did not answer the follow-up question (1.73% for first medical use, 3.95% for first nonmedical use). On the other hand, some respondents in our sample answered the follow-up question at more than one assessment. On average – across the four classes of medication – less than 1% of respondents (0.14% for first nonmedical use, and 0.63% for first medical use) reported a first age of use below age 12 at one assessment, and above age 12 at another assessment. These findings indicate that a small proportion of respondents reporting first medical use or first nonmedical use may have over- or under-reported their age of first use,

or may have had difficulty recalling their exact first age of use if it occurred many years before the age of their first assessment (Fendrich & Rosenbaum, 2003). Although approximate estimates may be obtained from cross-sectional or longitudinal data using retrospective first age of use reports, as used in the present study, these limitations highlight the need for thoughtfully designed prospective studies to closely track and monitor cohort effects and annual incidence rates for substance use initiation.

Conclusions

Despite these limitations, findings from this study indicate that both first-time medical and nonmedical use of controlled medication may be occurring at earlier ages than anticipated – especially among more recent birth cohorts. Furthermore, findings indicate that receiving a first prescription for an opioid analgesic, anxiolytic or sedative prior to adolescence (prior to age 12) may heighten subsequent risk of initiating use of another person's prescription for these classes of medication. When prescribing controlled medication to children and adolescents, health care providers might consider discussing the health and legal risks associated with nonmedical use, medical misuse and diversion of these classes of medication (e.g., potential for nonmedical use, accidental overdose, potentially fatal interactions with other medication). Both health care providers and childhood educators are also in an excellent position to engage parents in preventing their children from using another person's prescription by discouraging the "sharing" of medication among family members and by emphasizing the importance of supervising the appropriate use, storage, and disposal of both their own and their children's medication (Boyd et al., 2011; Ross-Durow et al., 2013). School policies also play an important role in ensuring that controlled medicines are securely stored and administered under a nurse's supervision during the school day. These findings underscore the importance of providing continuing education for health care providers about the risks of nonmedical use and diversion of controlled medication among adolescents, and about alternatives to controlled medication that may be more appropriate for certain child and adolescent patients – such as those with a family history of alcohol or drug use disorder.

Acknowledgements

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Age-Specific Incidence Rate Estimates[a] for First Age of Medical Use (FAMU) and First Age of Nonmedical Use (FANMU) of Controlled Medication, by Drug Class.
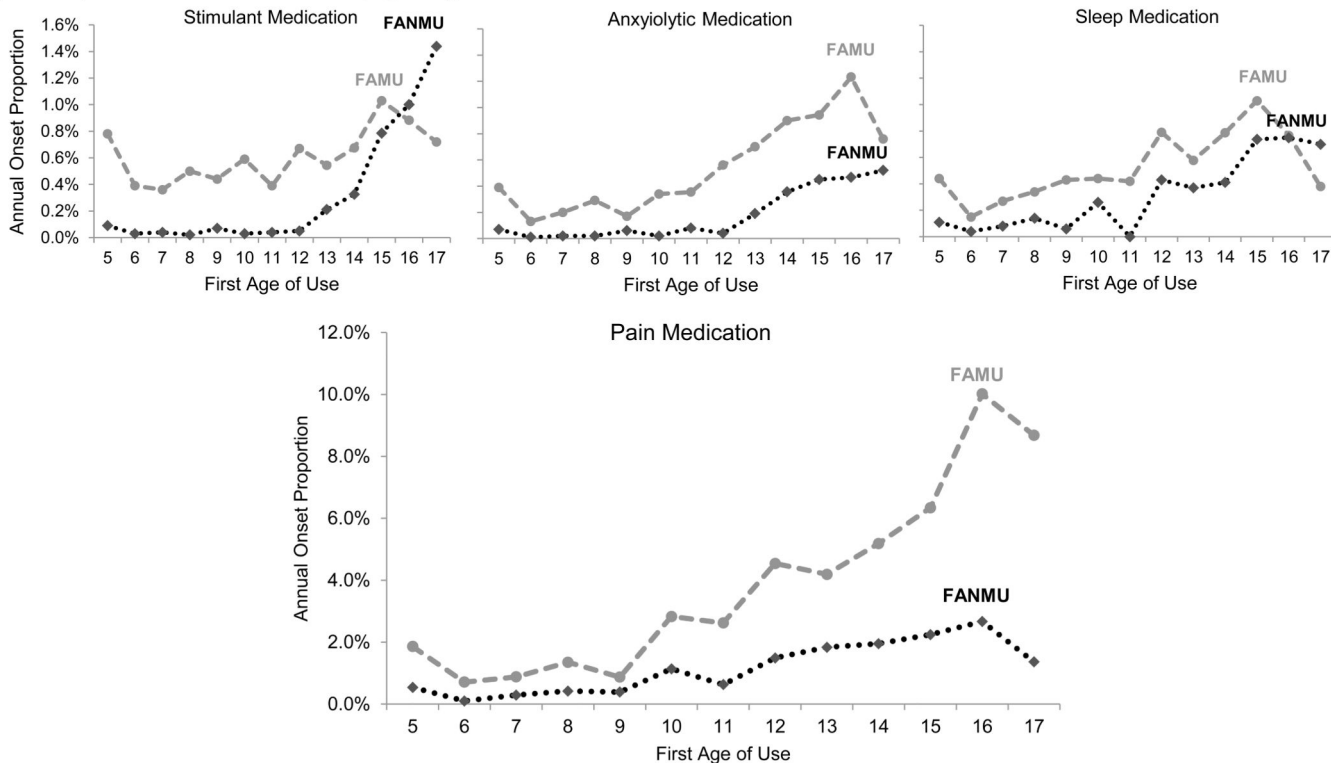

FIGURE 1.

Meta-Analysis Summary Estimates: Age-Specific Risk of Starting Medical or Nonmedical Use of Controlled Medication

[a] Age-specific summary estimates based on meta-analysis of estimates; each birth cohort provides an independent sample. Data are from the *Secondary Student Life Survey* 2009–2012 (n=5,185).

Cumulative Hazard of First Medical Use or First Nonmedical Use, by Age and Birth Cohort
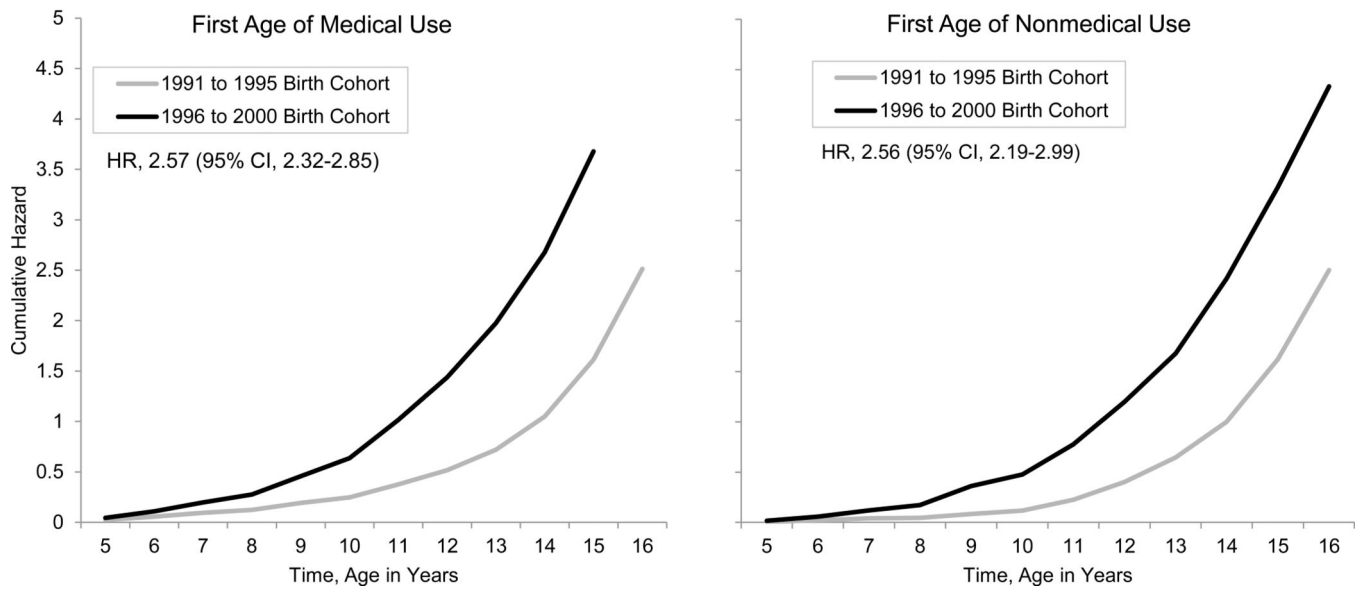

FIGURE 2.
Cumulative Hazard of Starting Medical or Nonmedical Use of Controlled Medication, by Age and Birth Cohort

TABLE 1

Characteristics of Study Participants Stratified by Two Birth Cohort Groups

Characteristic	1991 and 1995 Birth Cohort (*n* = 2453)	1996 and 2000 Birth Cohort (*n* = 2732)	Total (*N* = 5185)
Gender			
Female	1244 (50.7)	1330 (48.7)	2574 (49.6)
Male	1209 (49.3)	1402 (51.3)	2611 (50.4)
Race/ethnicity			
White	1447 (59.0)	1700 (62.2)	3147 (60.7)
Black	889 (36.2)	861 (31.5)	1750 (33.8)
Hispanic and Other[a]	117 (4.8)	171 (6.3)	288 (5.6)
Highest Degree Completed by Guardian			
Less than High School to Some College	674 (27.5)	450 (16.5)	1124 (21.7)
College or Graduate Degree	1696 (69.1)	2078 (76.1)	3774 (72.8)
Baseline Characteristics:			
ADHD Diagnosis (Lifetime)	311 (12.7)	322 (11.8)	633 (12.2)
Trouble Sleeping (at First Assessment) (Scale of 1 to 7), Mean ± SD	2.93 ± 2.05	2.40 ± 1.86	2.65 ± 1.97
Anxiety-Depression (at First Assessment) (Scale of 0 to 26), Mean ± SD	4.66 ± 4.66	3.90 ± 4.07	4.26 ± 4.38
Controlled Medication Exposure:			
First medical use < age 12	268 (10.9)	517 (18.9)	785 (15.1)
First medical use age 12	746 (30.4)	429 (15.7)	1175 (22.7)
First nonmedical use < age 12	49 (1.9)	162 (5.9)	211 (4.1)
First nonmedical use age 12	324 (13.2)	205 (7.5)	529 (10.2)
First nonmedical use > First medical use and First medical use < age 12[b]	49 (2.0)	83 (3.0)	132 (2.5)
First nonmedical use > First medical use and First medical use age 12	55 (2.2)	31 (1.1)	86 (1.7)

Percentage within guardian education group does not add to 100% due to missing data.

[a]Total sample for Hispanic: 97 (1.9%); Other: 191 (3.7%).

[b]This subgroup consists of respondents who: (a) nonmedically used for the first time at least one year in age after receiving their first prescription, and (b) who nonmedically used the same class of controlled medication they had previously been prescribed (at or before the age specified).

TABLE 2

Estimated Hazard of Starting Medical or Nonmedical Use with Controlled Medication, by Age and Birth Cohort

Medication and Birth Cohort Group *(1991–1995 Cohort is Reference)*	First Age of Use of Controlled Medication			
	Medical Use		Nonmedical Use	
	HR (95% CI)	aHR (95% CI)	HR (95% CI)	aHR (95% CI)
I. Controlled Medication, 1996–2000 Cohort	2.57 (2.32–2.85)	2.57 (2.32–2.85)	2.56 (2.19–2.99)	2.57 (2.17–3.03)
II. Pain Medication, 1996–2000 Cohort	2.91 (2.60–3.25)	2.91 (2.60–3.25)	2.46 (2.07–2.92)	2.60 (1.88–3.60)
III. Stimulant Medication, 1996–2000 Cohort	1.67 (1.32–2.11)	1.68 (1.33–2.12)	1.95 (1.27–2.98)	2.03 (1.31–3.13)
IV. Anxiolytic & Sleeping Medication, 1996–2000 Cohort	2.46 (2.01–2.99)	2.45 (2.01–2.98)	2.97 (2.23–3.95)	3.68 (2.39–5.66)

Note. P < .05 for all results reported in this table from fitted Cox regression models. CI = confidence interval. HR = unadjusted Hazard Ratio. aHR = Adjusted Hazard Ratio. Self-reported gender, race/ethnicity, guardians' highest degree of education completed were tested and retained in the final model if statistically significant. Nonmedical use models I and IV adjusted for trouble sleeping and anxiety and depression symptoms at first assessment, and nonmedical use models I and III controlled for lifetime ADHD diagnosis. Among the variables adjusted for, only gender and race/ethnicity were significant: gender was significant in medical use models II and III, and race/ethnicity was significant in nonmedical use models I and II (results reported in text).