Published in final edited form as:

Addict Behav. 2016 January ; 52: 8–12. doi:10.1016/j.addbeh.2015.08.002.

Prevalence and Correlates of Co-Ingestion of Prescription Tranquilizers and Other Psychoactive Substances by US High School Seniors: Results from a National Survey

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Abstract

Introduction—Nonmedical tranquilizer use (NMTU) is a concerning and understudied phenomenon in adolescents, despite being the second most prevalent form of nonmedical use in this population. Thus, this work aimed to examine the sociodemographic and substance use correlates of past-year co-ingestion of a prescription tranquilizer and another substance among adolescents.

Methods—Data were from the Monitoring the Future study, a nationally representative survey of US high school students. Data from 11,444 seniors (12th graders) completing form 1 of the survey were used. The participants represented a population that was 52.7% female, 61.8% White, and had a modal age of 18. Weighted frequencies and Rao-Scott chi-square analyses were computed to describe the target population and examine associations of interest.

Results—An estimated 5.3% of the population engaged in past-year NMTU during this time period, with an estimated 72.6% of those users engaged in past-year co-ingestion of a tranquilizer and another substance. Marijuana and alcohol were the most commonly co-ingested substances. Those engaged in co-ingestion were more likely than past-year nonmedical users without co-ingestion to be engaged in other substance or nonmedical use (including past year nonmedical Xanax® (alprazolam) use), have an earlier onset of NMTU, and endorse recreational motives.

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Conclusions—Adolescent nonmedical tranquilizer users engaged in co-ingestion may be a particularly vulnerable population, with higher rates of other substance use, other nonmedical use and problematic NMTU characteristics than nonmedical users without co-ingestion. Identification of and intervention with adolescent co-ingestion users is an important avenue for future research and clinical practice.

Keywords

Co-ingestion; simultaneous use; prescription tranquilizers; adolescents; nonmedical use; polydrug use

1. Introduction

Nonmedical prescription tranquilizer use (NMTU) is the second most prevalent type of nonmedical use in adolescents and across the U.S. population (SAMHSA, 2012). Given the potential for adverse outcomes, NMTU represents an ongoing public health concern (CDC, 2012). Work by McCabe and colleagues (2012) highlighted adolescent opioid co-ingestion users as a vulnerable population, suggesting the need to elucidate tranquilizer co-ingestion processes.

Investigations of co-ingestion of prescription medication and another psychoactive substance have focused on college or young adult populations and co-ingestion involving opioids or stimulants. Co-ingestion appears to be common in young adult nonmedical users at nightlife venues (Kelly, Wells, Pawson, Leclair, & Parsons, 2013), and co-ingestion is common at both the most recent and first ever nonmedical use episode (Barrett, Darredeau, & Pihl, 2006; Olthuis, Darredeau, & Barrett, 2013). Co-ingestion users had elevated levels of substance use and other risk indicators relative to nonmedical users without co-ingestion (Garnier, et al., 2009; McCabe, Cranford, Morales, & Young, 2006).

In the only published study on adolescent co-ingestion, approximately 5.6% of adolescents co-ingested a prescription opioid and another drug; co-ingestion users were more likely to engage in problematic drug use and have recreational (versus self-treatment) motives than nonmedical users without co-ingestion (McCabe, West, Teter, & Boyd, 2012). Nattala and colleagues (2012) conducted the only study of adult nonmedical sedative use (including benzodiazepines) with co-ingestion; there, 61% of nonmedical users co-ingested a sedative and alcohol, and co-ingestion users were younger, more likely to have used marijuana, and more likely to have recreational motives (Nattala, et al., 2012).

No studies have examined co-ingestion of prescription tranquilizers and psychoactive substances in U.S. adolescents. This work will examine this phenomenon in a nationally representative sample of U.S. high school seniors, examining correlates (e.g., motives for NMTU) based on past research (see Measures). This work had three aims. First, we evaluated the prevalence of co-ingestion both overall and by the substance co-ingested with tranquilizer medication. Second, we investigated the prevalence of selected substance use and mental health outcomes as a function of NMTU status and (among nonmedical users) co-ingestion status. Finally, we evaluated whether selected nonmedical (e.g., age of NMTU

onset) and mental health variables differed among nonmedical users based on the number of substances co-ingested with tranquilizer medication.

2. Methods

The Monitoring the Future (MTF) study is a nationally representative, cross-sectional annual survey of 8th, 10th and 12th grade students in the U.S. The MTF uses multi-stage sampling, with selection of primary sampling units (PSU), followed by identification of schools within the PSU for administration. One-sixth of participants were randomly assigned form 1 (of six), which included assessment of co-ingestion of prescription tranquilizers and other drugs from 2002 to 2006. Response rates were either 82 or 83%. For more information, see Johnston and coauthors (2007). This work was granted a waiver from the Texas State University IRB.

2.1 Participants

From 2002 to 2006, 12,441 12th grade students completed form 1, with 11,444 (92.0%) providing sufficient data for analyses. The weighted population was 52.7% female, 61.8% Caucasian, 10.1% African-American, and 28.1% endorsing some other or not specifying a race/ethnicity. The modal age was 18 years.

2.2 Measures

Nonmedical tranquilizer use (NMTU) was assessed by asking about the frequency (if ever) of prescription tranquilizer use “on your own – that is, without a doctor telling you to take [it]...” Participants are dichotomized into those who did or did not engage in past year NMTU. The substance use assessment of the MTF study, including of nonmedical use, is recognized as reliable and valid (Johnston, et al., 2007).

Past year mental health treatment was assessed by asking the frequency with which a participant saw a “doctor or other professional...for some emotional or psychological symptom”. Participants were dichotomized into those endorsing treatment and those denying, as past year mental health treatment is a NMTU correlate (Schepis & Krishnan-Sarin, 2008).

2.2.1 Measures in those endorsing NMTU—Co-Ingestion of tranquilizers and another substance was assessed by asking how often participants engaged in NMTU and use of another substance such that “their effects overlapped.” Co-ingestion substances included: alcohol; marijuana; LSD; non-LSD hallucinogens; barbiturates; and amphetamines. Responses ranged from 1 (never) to 5 (every time).

Motives for NMTU were investigated through a single question with multiple, non-exclusive responses. Participants were asked “What have been the most important reasons for your taking tranquilizers without a doctor's orders?” Selected motives were based on previous work (McCabe, Boyd, & Teter, 2009; McCabe, et al., 2012).

Typical intoxication during NMTU were assessed by asking “how high do you usually get” when using a prescription tranquilizer. Participants were dichotomized into those endorsing

getting “moderately or very high” and those endorsing “a little high”, “not high” or “I do not take them to get high”. This categorization was based on the work of McCabe et al. (2012).

Age of NMTU onset assessed when the participant first engaged in NMTU. Participants were dichotomized into a group initiating NMTU before 10th grade and those who initiated during 10th grade or later, based on evidence that adolescents initiating NMTU prior to age 16 (roughly 10th grade) had significantly elevated DSM-IV tranquilizer dependence rates (McCabe, West, Morales, Cranford, & Boyd, 2007).

Likelihood of NMTU in 5 years was assessed by asking whether the participant “will be using tranquilizers without a doctor’s orders five years from now?” Answers were dichotomized as: definitely/probably will not and definitely/probably will.

2.3 Data Analysis

MTF participant responses are weighted to create nationally representative estimates, and all analyses herein employed the MTF weight variable to ensure unbiased estimation. Estimates of past year NMTU rates and co-ingestion prevalence (Aim 1) were computed using weighted cross-tabulations. Analyses to complete Aims 2 and 3 used Rao-Scott chi-square tests of homogeneity (Rao & Scott, 1984) to compare those engaged in past year NMTU with co-ingestion to those without co-ingestion, and compare those two groups to those with no past year NMTU. Analyses for Aim 2 compared all three groups in terms of various outcomes, while analyses for Aim 3 compared past year nonmedical tranquilizer users by number of substances co-ingested with the tranquilizer in the past year: 0, 1, 2, or 3 or more. An average MTF design effect factor was used to multiply all linearized estimates of variance based on the MTF weights (Johnston, et al., 2007) to correct for the complex cluster sampling effects of the MTF (West & McCabe, 2012). Similarly, all weighted chi-square statistics were divided by this average design effect factor (Rao & Scott, 1984). Analyses were conducted in Stata, version 13.1 (StataCorp, College Station, TX, 2013), using the survey data analysis commands.

3. Results

3.1 Prevalence of NMTU and Co-ingested Substance Frequency

An estimated 72.6% of past year nonmedical tranquilizer users engaged in co-ingestion. Marijuana and alcohol were the most commonly co-ingested substances (59.0% and 57.6%, respectively). Amphetamine (14.4%), barbiturate (11.9%), non-LSD hallucinogen (10.9%) and LSD (7.5%) co-ingestion were less common. Marijuana and alcohol were also the most frequently co-ingested substances, with 27.8% and 21.3% (respectively) endorsing co-ingestion “most” or “every” time.

3.2 Outcomes based on NMTU and Co-ingestion Status

All substance use outcomes evidenced significant differences (all $ps < .001$) between participants grouped by both NMTU and co-ingestion status. Prevalence of the substance use characteristic appeared to increase in a stepwise fashion from those with no past year NMTU to those endorsing co-ingestion. These outcomes are summarized in Figure 1. Past

year mental health treatment also evidenced significant prevalence differences by NMTU status, though no difference was found within nonmedical users (no co-ingestion: 19.0%; co-ingestion: 19.2%).

3.3 NMTU Characteristics and Motives among Nonmedical Users based on Co-Ingestion Status

Those who endorsed co-ingestion were more likely to get moderately or very high from use (co-ingestion: 68.1%; no co-ingestion: 41.2%), to have nonmedically used Xanax® in the past year (co-ingestion: 63.5%; no co-ingestion: 38.7%), to predict that they will probably or definitely be engaged in NMTU in five years (co-ingestion: 25.2%; no co-ingestion: 13.2%), and initiate NMTU prior to 10th grade (co-ingestion: 38.3%; no-co-ingestion: 21.5%). Co-ingestion users were also more likely to endorse to experiment or to feel good/get high (experiment: 55.8%; feel good/get high: 60.8%) as an NMTU motive than those without co-ingestion (experiment: 32.0%; feel good /get high: 26.9%). All differences were significant with $p < 0.01$. No differences were found in relaxation or sleep promotion motives.

3.4 Outcomes based on Number of Substances Co-Ingested

There were significant differences in NMTU characteristics, past year mental health treatment and most examined motives based on the number of substances co-ingested (all $p < .05$). These outcomes are summarized in Table 1.

4. Discussion

This was the first national investigation of co-ingestion of tranquilizer medication with other psychoactive substances among U.S. adolescents. Here, 5.3% of high school seniors engaged in past year NMTU and 72.6% of nonmedical users engaged in co-ingestion. Marijuana and alcohol were the most common substances co-ingested, perhaps due to the frequency of adolescent marijuana and alcohol use (SAMHSA, 2012). Furthermore, adolescent perceptions of marijuana's harmfulness have declined (Johnston, O'Malley, Bachman, & Schulenberg, 2013), possibly signaling similar perceptions of reduced harm from co-ingestion with marijuana. Also, cannabinoids, benzodiazepines and ethanol have anxiolytic and hypnotic properties, with synergistic anxiolysis when co-ingested (Naderi, et al., 2008; van Steveninck, et al., 1993). Endorsement of NMTU to relax did not differ by co-ingestion status, though, so euphoric enhancement may matter more. This is speculative, and future longitudinal work should examine these associations.

The prevalence of examined substance use outcomes (including other nonmedical use) all increased in a stepwise manner from those not engaged in NMTU to nonmedical users with past year co-ingestion, while mental health treatment prevalence only differed by NMTU status. There was also evidence of increases in outcome prevalence with increasing number of co-ingested substances (see Table 1). The significantly higher rates of nonmedical Xanax® (alprazolam) use among co-ingestion users was noteworthy, given its association with risky decision-making (Lane, Tcheremissine, Lieving, Nouvion, & Cherek, 2005), increased toxicity in overdose (Isbister, O'Regan, Sibbritt, & Whyte, 2004) and clinical concerns about its use (Goodnough, 2011). When these results are combined with those of

McCabe and colleagues (2012), we see similar patterns of polydrug use in nonmedical users of prescription opioids and tranquilizers. As such, development of pharmaceutical combination products to block or dampen drug-specific effects of commonly co-ingested drugs with tranquilizers could be warranted. An analogous pharmacotherapeutic approach is the use of medications with distinct mechanisms in one formulation (e.g., low-dose naltrexone and bupropion for weight loss). In addition, implementation of prevention programs with effectiveness in limiting adolescent nonmedical use (Crowley, Jones, Coffman, & Greenberg, 2014) and efforts to educate potential adolescents engaged in NMTU and those who might supply medication (e.g., peers, parents) are warranted. Such education needs to particularly emphasize the risks of co-ingestion, in addition to the risks of NMTU without co-ingestion.

4.1 Limitations

First, this examined only high school seniors, so conclusions cannot be extrapolated to other populations. Second, participants may have misrepresented behavior on sensitive measures (e.g., co-ingestion), as the MTF is a school-based, self-report survey. The MTF attempts to minimize misrepresentation by informing potential respondents that participation was voluntary and that data remain confidential (Johnston et al., 2007). Third, the cross-sectional data do not allow for causal inferences, and the choice of correlates was limited by the MTF variables. Future work should examine peer, family, school-related, and control variables to give a fuller picture of adolescent NMTU with co-ingestion. Finally, data from 2002 to 2006 were used because these were the only years in which co-ingestion was assessed; this may limit generalizability to current adolescents.

4.2 Conclusions

The majority (72.6%) of high school seniors reporting past year NMTU engaged in co-ingestion of a tranquilizer and another psychoactive substance. Those engaged in co-ingestion had a greater likelihood of other substance use than nonmedical users without co-ingestion or those not engaged in NMTU. Co-ingestion of a greater number of substances with prescription tranquilizers further increased risky behavior. High school seniors engaged in co-ingestion are a vulnerable group in need of identification and intervention to reduce NMTU and, particularly, co-ingestion.

Acknowledgements

The development of this manuscript was supported by research grants R01DA024678 and R01DA031160 from the National Institute on Drug Abuse, National Institutes of Health. The Monitoring the Future data were collected by a research grant R01DA01411 from the National Institute on Drug Abuse, National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Drug Abuse or the National Institutes of Health. The authors would like to thank the Substance Abuse and Mental Health Data Archive for providing access to these data.

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Highlights

- Past year, 3.8% of US 12th graders co-ingested a prescription tranquilizer and other drug.
- 72.6% of nonmedical tranquilizer users co-ingested, often with marijuana or alcohol.
- Co-ingestion users were more likely to use other substances than other groups.
- Recreational motives and earlier nonmedical use onset were linked to co-ingestion.
- An increasing number of co-ingested substances appeared to increase risk.

Figure 1.
Substance Use and Mental Health Outcomes based on Nonmedical Use and Co-Ingestion Status; all comparisons were significant at $p < 0.001$; PY = past year.

Table 1

Comparing Substance Use and Mental Health Outcomes among Nonmedical Tranquilizer Users Based on Number of Substances Co-Ingested (Source: MTF 2002–06)

	No Co-ingestion	Co-ingestion w/1 substance	Co-ingestion w/2 substances	Co-ingestion w/3+ substances	Rao-Scott chi-square
	% (SE)	% (SE)	% (SE)	% (SE)	
Get moderately/Very high (n = 445)					F(2.99,1329.65) = 11.7, p < 0.001
No	58.8 (6.3)	47.1 (5.6)	33.3 (4.5)	14.7 (3.8)	
Yes	41.2 (6.3)	52.9 (5.6)	66.7 (4.5)	85.3 (3.8)	
PY Xanax use (n = 517)					F(3.00,1547.50) = 7.4, p < 0.001
No	61.3 (5.0)	45.0 (5.4)	35.4 (4.5)	29.1 (5.0)	
Yes	38.7 (5.0)	55.0 (5.4)	64.6 (4.5)	70.9 (5.0)	
Using TRQ in 5 years (n = 529)					F(2.97,1565.97) = 6.1, p < 0.001
Def/Prob Not	86.8 (2.9)	78.4 (4.3)	80.9 (3.3)	62.9 (5.3)	
Def/Prob Will	13.2 (2.9)	21.6 (4.3)	19.1 (3.3)	37.1 (5.3)	
Age of TRQ onset (n = 419)					F(2.98,1244.95) = 7.0, p < 0.001
Grades 10–12	78.5 (4.3)	65.6 (5.5)	71.9 (4.6)	45.7 (6.0)	
Grades 6–9	21.5 (4.3)	34.4 (5.5)	28.1 (4.6)	54.3 (6.0)	
Motive: To experiment (n = 523)					F(3.00,1564.87) = 5.4, p < 0.01
No	68.0 (4.9)	43.7 (5.3)	44.9 (4.5)	44.0 (5.3)	
Yes	32.0 (4.9)	56.3 (5.3)	55.1 (4.5)	56.0 (5.3)	
Motive: To feel good/get high (n = 523)					F(3.00,1565.47) = 16.7, p < 0.001
No	73.1 (4.6)	56.9 (5.2)	32.8 (4.3)	29.2 (4.8)	
Yes	26.9 (4.6)	43.1 (5.2)	67.2 (4.3)	70.8 (4.8)	
Motive: To relax (n = 523)					Non-significant
No	36.0 (4.9)	37.8 (5.0)	32.8 (4.3)	27.5 (4.7)	
Yes	64.0 (4.9)	62.2 (5.0)	67.2 (4.3)	72.5 (4.7)	
Motive: To sleep (n = 523)					F(3.00,1563.50) = 5.9, p < 0.001
No	56.3 (5.0)	69.2 (4.9)	68.9 (4.2)	43.5 (5.4)	
Yes	43.7 (5.0)	30.8 (4.9)	31.1 (4.2)	56.5 (5.4)	
PY Mental Health Tx (n = 430)					F(2.99,1282.69) = 2.9, p < 0.05
No	80.5 (3.9)	88.5 (3.5)	82.4 (4.2)	70.6 (5.2)	

	No Co-ingestion	Co-ingestion w/1 substance	Co-ingestion w/2 substances	Co-ingestion w/3+ substances	Rao-Scott chi- square
	% (SE)	% (SE)	% (SE)	% (SE)	
Yes	19.5 (3.9)	11.5 (3.5)	17.6 (4.2)	29.4 (5.2)	

Notes: MTF = Monitoring the Future; SE = Standard Error of the Percentage; PY = Past Year; TRQ = Tranquilizer; Def = Definitely; Prob = Probably; Tx = Treatment
 Substances assessed for co-ingestion with nonmedical tranquilizer use were alcohol, marijuana, LSD, non-LSD hallucinogens, barbiturates and amphetamines