Legal Performance-Enhancing Substances and Substance Use Problems Among Young Adults

Kyle T. Ganson, PhD, MSW,^a Deborah Mitchison, MClinPsych, MSc, PhD,^{b,c} Stuart B. Murray, DClinPsych, PhD,^d Jason M. Nagata, MD, MSc^e

BACKGROUND: Legal performance-enhancing substance(s) (PES) (eg, creatine) are widely used among adolescent boys and young men; however, little is known about their temporal associations with substance use behaviors.

abstract

METHODS: We analyzed prospective cohort data from the National Longitudinal Study of Adolescent to Adult Health, Waves I to IV (1994–2008). Logistic regressions were used to first assess adolescent substance use (Wave I) and use of legal PES (Wave III) and second to assess use of legal PES (Wave III) and subsequent substance use–associated risk behaviors (Wave IV), adjusting for potential confounders.

RESULTS: Among the sample of 12 133 young adults aged 18 to 26 years, 16.1% of young men and 1.2% of young women reported using legal PES in the past year. Adolescent alcohol use was prospectively associated with legal PES use in young men (odds ratio 1.39; 95% confidence interval [CI] 1.13–1.70). Among young men, legal PES use was prospectively associated with higher odds of problematic alcohol use and drinking-related risk behaviors, including binge drinking (adjusted odds ratio [aOR] 1.35; 95% CI 1.07–1.71), injurious and risky behaviors (aOR 1.78; 95% CI 1.43–2.21), legal problems (aOR 1.52; 95% CI 1.08–2.13), cutting down on activities and socialization (aOR 1.91; 95% CI 1.36–2.78), and emotional or physical health problems (aOR 1.44; 95% CI 1.04–1.99). Among young women, legal PES use was prospectively associated with higher odds of emotional or physical health problems (aOR 3.00; 95% CI 1.20–7.44).

CONCLUSIONS: Use of legal PES should be considered a gateway to future problematic alcohol use and drinking-related risk behaviors, particularly among young men.



^aFactor-Inwentash Faculty of Social Work, University of Toronto, Toronto, Ontario, Canada; ^bTranslational Health Research Institute, School of Medicine, Western Sydney University, Sydney, New South Wales, Australia; ^cDepartment of Psychology, Macquarie University, Sydney, New South Wales, Australia; ^dDepartment of Psychiatry and the Behavioral Sciences, University of Southern California, Los Angeles, California; and ^eDivision of Adolescent and Young Adult Medicine, Department of Pediatrics, University of California, San Francisco, San Francisco, California

Dr Ganson collaboratively conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Nagata completed the statistical analysis and collaboratively conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript; Drs Mitchison and Murray critically reviewed the manuscript for important intellectual content and appropriate statistical analysis, as well as provided manuscript edits; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. WHAT'S KNOWN ON THIS SUBJECT: Substance use is common among adolescents, and performance-enhancing substances (PES) are widely used among young men. In contrast to research documenting the adverse consequences of steroid use, investigation of the potential adverse outcomes associated with legal PES has been neglected.

WHAT THIS STUDY ADDS: Alcohol use among adolescent boys is prospectively associated with legal PES use in young adulthood. Among men, legal PES use is prospectively associated with subsequent problematic alcohol use and drinking-related risk behaviors after accounting for adolescent substance use.

To cite: Ganson KT, Mitchison D, Murray SB, et al. Legal Performance-Enhancing Substances and Substance Use Problems Among Young Adults. *Pediatrics.* 2020;146(3): e20200409

Performance-enhancing substances (PES) are often used to improve athletic performance,¹ as well as used for the purpose of altering one's appearance to a more muscular and lean body type.² There is inconsistency of the legal status of PES in federal and state laws in the United States. For the purposes of this article, we refer to protein powders, creatine monohydrate, dehydroepiandrostenedione, and amino acids, as "legal PES" and anabolic-androgenic steroid (AAS) derivatives, when not prescribed for medical purposes, as "illegal PES." Much research has been conducted on the adverse health outcomes associated with AAS, including mood disorders, aggression, and violence,^{3,4} and substance use disorders,⁵ as well as several health issues related to the cardiovascular,⁶⁻⁸ neuroendocrine,⁹ musculoskeletal,¹⁰ renal, liver,⁷ and immune¹¹ systems of the body. However, much less is known about the possible adverse mental, physical, and social health outcomes associated with legal PES use, particularly among young adults.

Adolescence and young adulthood may be particularly salient developmental periods for experimentation with legal PES.¹ However, research relating to legal PES use among adolescents and young adults has typically been focused on establishing prevalence rates and predictors rather than explicating the risk inherent to these behaviors, both legal and otherwise.¹² Notwithstanding, evidence from a sample of adolescents in Minnesota indicates that 35% of boys and 21% of girls use protein powders and/or shakes and 10.5% of boys and 5.5% of girls use other PES (eg, creatine monohydrate, amino acids, hydroxy methylbutyrate, dehydroepiandrosterone, or growth hormone) to increase their muscle mass or tone.¹³ In addition, among college athletes and nonathletes, prevalence rates of past-year use of

PES are relatively high. For example, 46% of male nonathletes and 56% of male athletes, as well as 25% of female nonathletes and 30% of female athletes, are using these substances.14 Predictors of legal PES use include sports participation, inaccurate body weight perception, and weight gain behaviors.¹⁵ Importantly, there appears to be a subsequent progression and predictive relationship from legal PES use (eg, protein and creatine monohydrate) to illegal PES use (eg, AAS).¹⁶ Substance use, including alcohol use,¹⁵ binge drinking, and drug use,¹⁷ is also associated with muscularity concerns and muscularity-oriented behaviors, including PES use. Of the preliminary work used to assess the consequences of legal muscleenhancing, weight loss, or energy supplements use among children, adolescents, and young adults, research has revealed there is a significant increase in the risk of a severe medical event. This may include emergency department visits, disability, or premature death.¹⁸

In concert with the elevated risk for experimentation with legal PES, young adulthood is also associated with peak risk for the onset and intensification of legal and illegal substance use behaviors.^{19,20} Data from major adolescent substance use tracking surveys, including the Centers for Disease Control and Prevention, continue to reveal that alcohol use, drinking to intoxication, binge drinking (\geq 5 alcoholic drinks in a row in men or ≥ 4 in women), cigarette use, and marijuana use are common substance use behaviors among young people.^{21,22} In addition, empirical research continues to reveal the high prevalence rates of alcohol, tobacco, and marijuana use among adolescents and young adults.²⁰ Although these behaviors occur among both young adult men and young adult women, they are overall more common among young

adult men.19,22 Alongside wellestablished adverse health outcomes,^{23,24} social problems (eg, legal problems, violence, work problems, impulsivity), 2^{2-27} and the significant economic impact,²⁸ it has recently been shown that substance use, and polysubstance use in particular, is associated with muscularity concerns,^{17,24} steroid and diet pill use, fasting, and purging²⁹ among adolescent boys and young adult men. Furthermore, muscle dysmorphia, the pathologic pursuit of muscularity, which is common among young adult men,^{30,31} is characterized by PES use as a means to alter their body.^{31–33} Muscle dysmorphia is also associated with additional substance use disorders.³³ This suggests a particularly potent link between muscularity-oriented pursuits, including legal and illegal PES use, and substance use.

This relationship may be explained theoretically by using the gateway hypothesis. This theory posits that substance use among adolescents follows a sequential process in which the initial use of 1 licit substance can lead to the use of additional, illicit substances later in life.^{34,35} Within this framework, experimentation with substances during adolescence may lead to legal PES use given that legal PES are easily accessible, unregulated,¹² and socially sanctioned among adolescents given their high rates of use.¹³ It can then be conceived that alcohol use can act as a gateway to legal PES use, which can then lead to further problematic alcohol use, drinking-related risk behaviors, cigarette smoking, and marijuana use, as well as polysubstance use among adolescents and young adults.

Guided by the this expanded gateway hypothesis that includes legal PES as a gateway substance, we had 2 specific aims. First, we aimed to investigate whether alcohol use, cigarette use, and marijuana use were prospectively associated with legal PES use in young adulthood. Second, in ascertaining the directionality of this prospective association, we aimed to investigate whether use of legal PES in young adulthood, controlling for baseline alcohol use, cigarette use, and marijuana use, was prospectively associated with problematic alcohol use, drinkingrelated risk behaviors, cigarette smoking, and marijuana use at a 7year follow-up. First, we hypothesized that there would be significant associations between adolescent alcohol use, cigarette use, and marijuana use with legal PES use in young adulthood. Second, we hypothesized that legal PES use in young adulthood would be prospectively associated with problematic alcohol use and drinkingrelated risk behaviors, cigarette smoking, and marijuana use at a 7vear follow-up given the association between legal PES use and substance use behaviors.¹⁷

METHODS

Study Population

In this study, we use cross-sectional data from the National Longitudinal Study of Adolescent to Adult Health (Add Health). Add Health is a longitudinal cohort study of a nationally representative sample of adolescents in the United States who are followed into adulthood.^{36,37} The baseline sample was collected in 1994 to 1995 when subjects were adolescents (11-18 years) and used systematic sampling methods and implicit stratification to ensure that the high schools (N = 80) and paired middle schools selected were representative of US schools with respect to region of the country, urbanicity, size, type, and ethnicity. For this particular study, we used the nationally representative, restricteduse samples from Wave III (18-26 years; 2001-2002) and Wave IV (24-32 years; 2008). The University

of North Carolina Institutional Review Board approved all Add Health study procedures. Further details about the study design can be found elsewhere.³⁷

Measures

The primary measures of this study include baseline alcohol use, cigarette use, and marijuana use, legal PES use in the past year, binge drinking in the past 12 months, drinking-related risk and problematic behaviors, cigarette smoking in the past 30 days, and marijuana use in the past 30 days. Covariates include age, sex, race and/ or ethnicity, household income, BMI, and baseline substance use (alcohol, cigarette, and marijuana) (see Supplemental Table 4 for full description of the measures).

Statistical Analysis

Data analysis was performed by using Add Health's preconstructed sample weights to provide a nationally representative sample.38,39 Comparisons between legal PES users versus nonusers of legal PES in descriptive characteristics were calculated by using Pearson's χ^2 tests for categorical variables and independent samples t tests for continuous variables, stratified by sex. Multiple logistic regressions were used to identify baseline (Wave I) adolescent substance use (alcohol, cigarette, marijuana) prospectively associated with legal PES use in young adulthood (Wave III), adjusting for age, race and/or ethnicity, and household income. Multiple logistic regressions were used to assess legal PES use (Wave III) and subsequent substance use outcomes (alcohol, cigarette, marijuana) at Wave IV, adjusting for substance use at baseline (Wave I alcohol, cigarette, and marijuana) and Wave III whenever possible (binge drinking, cigarette, and marijuana use). All models included the covariates age, race and/or ethnicity, household income, and BMI.³⁹⁻⁴¹ Analyses were stratified by sex given the different

rates of legal PES use in young men and young women.¹ The significance level for all analyses was set at α = .05. Analyses were conducted by using Stata 15.0 (Stata Corp, College Station, TX).⁴²

RESULTS

Demographic characteristics of the sample ($N = 12\,133$) by use of legal PES at age 18 to 26 years are reported in Table 1. Overall, 16.1% of young men and 1.2% of young women reported using legal PES in the past year. The sample was racially and ethnically diverse. A higher proportion of male legal PES users were white and had a higher mean household income than that of nonusers. Female legal PES users had a lower BMI on average than that of nonlegal PES users.

At baseline, both male and female legal PES users had a greater likelihood of ever using alcohol and smoking cigarettes. Male legal PES users had a greater likelihood of ever using marijuana, whereas female nonlegal PES users had a greater likelihood of ever using marijuana. The unadjusted substance use outcomes at the 7-year follow-up (ages 24-32 years) are also listed in Table 1. The likelihood of reporting all of the alcohol-related behaviors was higher in young men who had reported use of legal PES 7 years earlier compared with male nonusers. Among young women, those who had reported earlier use of legal PES had higher rates of hurting themselves or engaging in risky behaviors while under the influence of alcohol compared with nonusers at the 7year follow-up, but there were not significant differences in other alcohol-related behaviors. Cigarette smoking and marijuana use at the 7year follow-up were not associated with earlier endorsement of legal PES use among young men or young women.

TABLE 1	Demographic	and Health	Characteristics	of	12 133	Young	Adult	Participants	in	Add	Health
e e	Stratified by L	.egal PES l	lse								

	Young Adult Men			Young Adult Women			
	Legal PES Use	No Legal PES	Р	Legal PES Use	No Legal PES	Р	
	<i>n</i> = 878	<i>n</i> = 4640		<i>n</i> = 89	<i>n</i> = 6526		
Demographic characteristics (Wave III, 18–26 y)							
Age, y, mean ± SE	21.8 ± 0.1	21.9 ± 0.1	.149	21.4 ± 0.3	21.7 ± 0.1	.364	
Race and/or ethnicity, %			.002*			.222	
White (non-Hispanic)	77.9	67.1	_	74.3	68.6		
Black or African American (non- Hispanic)	8.9	15.2	_	6.4	16.0	—	
Hispanic	9.1	12.6	_	14.3	11.3		
Asian American or Pacific Islander (non-Hispanic)	2.5	3.7	—	3.4	3.1	—	
American Indian	0.5	0.6	_	1.6	0.5		
Other	1.1	0.9	_	0.0	0.6		
Household income, US \$ (Wave I), mean \pm SE	52 435 ± 2110	44 184 ± 1518	<.001*	$\frac{58547}{8696} \pm$	46 645 ± 1523	.171	
BMI, mean \pm SE	26.4 ± 0.2	$26.4~\pm~0.2$.948	$23.8 \pm$	$26.4~\pm~0.2$.003*	
				0.8			
Baseline substance use (ever use,							
Wave I, 11-18 y), %							
Alcohol	65.00	55.00	<.001*	64.10	55.30	.233	
Cigarette	64.5	57.0	<.001*	60.9	57.7	.636	
Marijuana	31.9	27.0	.058	22.3	24.4	.640	
Substance use outcomes (Wave IV, 24–32 y)							
Alcohol, %							
Binge drinking in past 12 mo	70.8	55.3	<.001*	55.6	43.2	.087	
Hurt or risky behaviors while under the influence of alcohol	44.5	28.5	<.001*	39.2	23.2	.027*	
Legal problems while under influence of alcohol	40.3	30.8	.017*	16.7	13.6	.678	
Cut down on activities and socialization that interfere with alcohol use	11.9	6.0	<.001*	9.4	3.4	.264	
Continued to use alcohol despite emotional or physical health problems	12.6	8.2	.006*	16.0	5.6	.097	
Cigarette smoking in past 30 d, %	39.7	43.1	.186	27.6	34.2	.302	
Marijuana use in past 30 d, %	24.2	21.7	.225	19.9	12.6	.252	

All means and percentages are calculated with weighted data to reflect the representative proportion in the target US population. —, not applicable.

* P <.05

The prospective associations between baseline substance use and legal PES use in young adulthood are reported in Table 2. Among young men, adolescent alcohol use was prospectively associated with legal PES use (odds ratio [OR] 1.39; 95% confidence interval [CI] 1.13–1.70). Cigarette smoking and marijuana use were not associated with legal PES use among young men. Any adolescent substance use was not prospectively associated with legal PES use among young women. Reported in Table 3 are the prospective associations between use of legal PES in young adults 24 to 32 years of age and incident substance use at the 7-year follow-up, when adjusted for age, race and/or ethnicity, household income, BMI, Wave III behaviors when available (binge drinking, cigarette smoking, and marijuana use), and baseline (Wave I) substance use behaviors. Among young men, legal PES use was prospectively associated with higher odds of all 5 problematic alcohol use and drinking-related risk behaviors, including binge drinking (adjusted odds ratio [aOR] 1.35; 95% CI 1.07–1.71), injurious and risky behaviors (aOR 1.78; 95% CI 1.43-2.21), legal problems (aOR 1.52; 95% CI 1.08-2.13), cutting down on activities and socialization (aOR 1.91; 95% CI 1.36-2.78), and emotional or physical health problems (aOR 1.44; 95% CI 1.04-1.99). Among young women, legal PES was prospectively associated with higher odds of only emotional or physical health problems (aOR 3.00; 95% CI 1.20-7.44). Legal PES use was not associated with cigarette smoking or marijuana use in young men or young women, except that it was marginally associated with lower odds (aOR 0.75; 95% CI 0.58-0.88) of cigarette smoking in young men.

DISCUSSION

Our overall aim of this study was to investigate the associations between legal PES use and substance use behaviors across adolescence and young adulthood. Our first specific aim was to investigate whether adolescent alcohol use, cigarette use, and marijuana use were prospectively associated with legal PES use in young adulthood. Our second specific aim was to investigate whether use of legal PES in young adulthood, controlling for baseline alcohol use, cigarette use, and marijuana use, was prospectively associated with problematic alcohol use, drinking-related risk behaviors, cigarette smoking, and marijuana use at the 7-year follow-up.

Results from our first aim reveal that alcohol use in adolescence is prospectively associated with legal PES use in young adulthood among boys. There were no significant associations between substance use behaviors and prospective legal PES use among girls. Results from our second aim reveal that, similarly, young adult men who used legal PES

TABLE 2 Associations Between Adolescent Baseline Predictors and Young Adult Legal PES Use

Baseline Predictors (Wave I, Ages 11-18)	Boys		Girls		
	OR (95% CI)	Р	OR (95% CI)	Р	
Demographic					
Age	0.93 (0.88-0.98)*	.005*	0.90 (0.74-1.10)	.317	
Race and/or ethnicity					
White (referent)					
Black or African American	0.54 (0.39-0.74)*	<.001*	0.41 (0.16-1.07)	.069	
Hispanic	0.73 (0.53-0.99)*	.047*	1.26 (0.46-3.44)	.645	
Asian American or Pacific Islander	0.68 (0.43-1.06)	.092	1.04 (0.30-3.57)	.950	
American Indian	0.99 (0.45-2.19)	.982	4.12 (0.63-27.08)	.139	
Other race and/or ethnicity	1.20 (0.42-3.39)	.731			
Household income	1.00 (1.00-1.00)	.027	1.00 (1.00-1.00)*	.031*	
Substance use					
Alcohol	1.39 (1.13-1.70)*	.002*	1.76 (0.91-3.40)	.093	
Cigarette	1.18 (0.94–1.48)	.158	1.02 (0.51-2.01)	.956	
Marijuana	1.13 (0.88–1.45)	.315	0.73 (0.39–1.36)	.321	

—, not applicable.

* P < .05.

had significantly greater likelihood of engaging in all 5 problematic alcohol use and drinking-related risk behaviors after 7 years. For young adult women, those who used legal PES had significantly greater likelihood of engaging in 1 of the 5 problematic alcohol use and drinkingrelated risk behaviors. Legal PES use among young men and young women was not significantly associated with later increased use of marijuana, and legal PES use was associated with later lowered odds of cigarette smoking among young adult men. Guided by the gateway theory, which posits that substance use follows a pattern among adolescents into young adulthood,^{34,35} the results provide partial support for the hypotheses of this study. Alcohol use among adolescent boys appears to increase the likelihood of using legal PES, whereas subsequent legal PES use among young adult men appears to increase the likelihood of adopting problematic alcohol use and drinkingrelated risk behaviors among men in later years. Although evidence to date has demonstrated that early

 TABLE 3 Prospective Association Between Legal PES in Young Adults 24 to 32 Years of Age and Incident Substance Use at 7-Year Follow-up, Adjusted for Covariates

Self-Reported Health Outcomes	Men		Women		
	a0R ^a (95% CI)	Р	a0R ^a (95% CI)	Р	
Alcohol					
Binge drinking in past 12 mo	1.35 .012		1.04 .882		
	(1.07-1.71)*		(0.59–1.86)		
Hurt or risky behaviors while under the influence of	1.78	<.001*	1.78	.055	
alcohol ^b	(1.43–2.21)*		(0.99–3.23)		
Legal problems while under influence of alcohol ^b	1.52	.016*	1.04	.947	
	(1.08-2.13)*		(0.33–3.29)		
Cut down on activities and socialization that	1.91	<.001*	2.44	.146	
interfere with alcohol use ^b	(1.36-2.78)*		(0.73-8.16)		
Continued to use alcohol despite emotional or	1.44	.029*	3.00	.018*	
physical health problems ^b	(1.04–1.99)*		(1.20-7.44)*		
Cigarette smoking in past 30 d	0.75	.038*	0.86	.747	
	(0.58-0.98)*		(0.34–2.17)		
Marijuana in past 30 d	0.88	.445	1.13	.816	
	(0.63–1.22)		(0.40-3.15)		

^a Adjusted for age, race and/or ethnicity, household income, BMI, baseline alcohol, baseline cigarette, baseline marijuana, and risk behavior at Wave III.

^b Question asked only at Wave IV.

* P < .05.

engagement in substance use results in a greater array of subsequent substance use,^{34,35,43-45} it is suggested in our findings that legal PES must be integrated into the gateway hypotheses of substance use. To date, legal PES have not been largely considered as part of the spectrum of substances used among adolescents, have not been subject to the same regulatory scrutiny as other substances known to be linked to subsequent substance use, and are freely available over the counter to adolescents. Clearly, the robust reciprocal temporal relationship between substance use and legal PES suggests that each may serve as

a gateway for the other.

In existing evidence, it is suggested that extreme body image ideals and disorders (eg, eating disorders, body dysmorphic disorder, and muscle dysmorphia) among boys and men may drive PES use in pursuit of a muscular and lean ideal.⁴⁶ Boys and men who are seeking this body image ideal may subscribe to more traditional norms of masculinity, such as risk-taking and emotional control,47,48 which may include problematic alcohol use and drinkingrelated risk behaviors. Additionally, research has revealed a significant positive association between substance use behaviors, including alcohol use and PES use, among men who experience eating disorders⁴⁹ and muscle dysmorphia.31-33,50 This further supports the notion that polysubstance use may be common among young adult men. Importantly, biological mechanistic explanations of the association between these substances are difficult to elucidate because of the known error and inconsistency in PES labeling and content.^{51,52} Therefore, it is posited that the association between these substances are likely due to psychological, behavioral, and/or sociocultural influences.

Overall, legal PES use was more prevalent among young adult men

compared with that of young adult women. This aligns with previous research^{13,14} and may provide additional support for the notion that men seek a body ideal that is focused on greater muscle mass⁵³ and overall improved athletic performance.¹ Similarly, use of alcohol, including binge drinking and drinking to intoxication, is more prevalent among young men compared with young women.¹⁹ In this study, we found that both young men who used legal PES and those who had not used legal PES had greater prevalence of all alcohol use and drinking-related risk and problematic behaviors compared with young women, with 1 exception (female legal PES users had greater prevalence of continuing to drink despite emotional or physical health problems compared with male legal PES users). Alcohol use is socialized to be a part of the male gender role, and there are social sanctions placed on women that discourage drinking behaviors.⁵⁴ Furthermore, the use of legal PES among women may be less socially acceptable because of the female body ideal being one primarily focused on thinness.⁵⁵ Thus, social expectations and gender norms may provide additional explanation for the association between these forms of substance use.

With the results from this study, we provide further confirmation that men often experience greater physical and behavioral problems associated with alcohol use,⁵⁶ particularly young men who have previously used legal PES. This is especially concerning because men have higher rates of death and incur a greater rate of total burden measured by disabilityadjusted life years associated with alcohol compared with women.⁵⁷ Alcohol use also has a significant burden on US gross domestic product, health care costs, and law enforcement costs.²⁸ With these results, we provide further support for legislation that would provide greater oversight of, and restrict

access to, legal PES among particularly vulnerable populations (eg, adolescents).¹² These prevention methods may ultimately reduce problematic alcohol use and drinking-related risk behaviors among adults who have previously used legal PES.

A surprising finding from this study is that legal PES use acted as a protective factor for cigarette smoking among men. This may not be surprising given that cigarette smoking is less prevalent among men who participate in regular athletic activities.⁵⁸ Cigarette smoking may also be used as a weight loss behavior⁵⁹ and thus may not have beneficial weight-related side effects for young men aiming to achieve a larger, more muscular body.

Despite the important findings of this study, there are limitations to be noted. First, the legal PES use variable conflates multiple substances (eg, "creatine monohydrate or androstenedione").^{60,61} This limits the ability to identify the outcomes of each specific substance. Future research should aim to investigate the nuances between these substances. Second, several of the problematic alcohol use and drinking-related risk behaviors were not asked of participants in Wave III of data collection. This did not allow for them to be controlled for during analyses; thus, we could not examine the relative increase in rates of these behaviors from Wave III to Wave IV. On the other hand, analyses did adjust for Wave III rates of binge drinking, cigarette smoking, and marijuana use, as well as baseline substance use, and thus bolsters our confidence that legal PES acts as a risk factor for increased use of these behaviors and is not merely a correlate. Third, it is important to investigate prospective illegal and/or other substance use (eg, cocaine, heroin, and nonmedical use of prescription drugs) behaviors associated with legal PES use. The

wording of the measures investigating these substances in the Add Health survey did not allow for clear prospective analysis. Fourth, although the Add Health legal PES measure directly names "creatine monohydrate or andro" as legal substances, there are limitations and nuances to labeling these substances as legal versus illegal. Finally, responses from participants are based on self-report; therefore, responses may be impacted by social desirability bias.

CONCLUSIONS

With this study, we found that alcohol use during adolescence was prospectively associated with legal PES use in young adulthood. Additionally, legal PES use was prospectively associated with increased likelihood of problematic alcohol use and drinking-related risk behaviors at a 7-year follow-up. These associations were particularly strong for adolescent boys and young adult men. These results provide further evidence in support of the gateway theory and prospective health risk behaviors associated with legal PES and substance use. This can inform policy on further regulation of legal PES, particularly among minors. It is important for medical providers and clinicians to assess problematic alcohol use and drinking-related risk behaviors among young adult men who have previously used legal PES.

ABBREVIATIONS

AAS: anabolic-androgenic steroid Add Health: National Longitudinal Study of Adolescent to Adult Health aOR: adjusted odds ratio CI: confidence interval OR: odds ratio PES: performance-enhancing substance(s) This research uses data from Add Health, a program project directed by Kathleen Mullan Harris and designed by J. Richard Udry, Peter S. Bearman, and Kathleen Mullan Harris at the University of North Carolina at Chapel Hill, and funded by grant P01-HD31921 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 23 other federal agencies and foundations. Information on how to obtain the Add Health data files is available on the Add Health website (https://addhealth.cpc.unc.edu). No direct support was received from grant P01-HD31921 for this analysis.

DOI: https://doi.org/10.1542/peds.2020-0409

Accepted for publication May 28, 2020

Address correspondence to Jason M. Nagata, MD, MSc, Division of Adolescent and Young Adult Medicine, Department of Pediatrics, University of California, San Francisco, 550 16th St, 4th Floor, Box 0110, San Francisco, CA 94158. E-mail: jasonmnagata@gmail.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2020 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Dr Nagata was a participant in the Pediatric Scientist Development Program (K12HD00085033), funded by the American Academy of Pediatrics and the American Pediatric Society, and a recipient of the American Heart Association Career Development Award (CDA34760281). Dr Murray was supported by the National Institutes of Health (K23 MH115184). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

- LaBotz M, Griesemer BA; Council on Sports Medicine and Fitness. Use of performance-enhancing substances. *Pediatrics*. 2016;138(1):e20161300
- Pope HG Jr., Wood RI, Rogol A, Nyberg F, Bowers L, Bhasin S. Adverse health consequences of performanceenhancing drugs: an Endocrine Society scientific statement. *Endocr Rev.* 2014; 35(3):341–375
- Perry PJ, Kutscher EC, Lund BC, Yates WR, Holman TL, Demers L. Measures of aggression and mood changes in male weightlifters with and without androgenic anabolic steroid use. *J Forensic Sci.* 2003;48(3):646–651
- Pope HG Jr., Kouri EM, Hudson JI. Effects of supraphysiologic doses of testosterone on mood and aggression in normal men: a randomized controlled trial. Arch Gen Psychiatry. 2000;57(2):133–156
- Lundholm L, Käll K, Wallin S, Thiblin I. Use of anabolic androgenic steroids in substance abusers arrested for crime. *Drug Alcohol Depend*. 2010;111(3): 222–226
- Ahlgrim C, Guglin M. Anabolics and cardiomyopathy in a bodybuilder: case report and literature review. *J Card Fail.* 2009;15(6):496–500
- Bispo M, Valente A, Maldonado R, et al. Anabolic steroid-induced cardiomyopathy underlying acute liver

failure in a young bodybuilder. *World J Gastroenterol.* 2009;15(23):2920–2922

- Vanberg P, Atar D. Androgenic anabolic steroid abuse and the cardiovascular system. *Handb Exp Pharmacol.* 2010; (195):411–457
- Daly RC, Su TP, Schmidt PJ, Pagliaro M, Pickar D, Rubinow DR. Neuroendocrine and behavioral effects of high-dose anabolic steroid administration in male normal volunteers. *Psychoneuroendocrinology.* 2003;28(3): 317–331
- Nikolopoulos DD, Spiliopoulou C, Theocharis SE. Doping and musculoskeletal system: short-term and long-lasting effects of doping agents. *Fundam Clin Pharmacol.* 2011; 25(5):535–563
- Brenu EW, McNaughton L, Marshall-Gradisnik SM. Is there a potential immune dysfunction with anabolic androgenic steroid use? A review. *Mini Rev Med Chem.* 2011;11(5):438–445
- 12. Ganson KT, Murray SB, Nagata JM. A call for public policy and research to reduce use of appearance and performance enhancing drugs and substances among adolescents. *Lancet Child Adolesc Health*. 2019;4(1):13–14
- Eisenberg ME, Wall M, Neumark-Sztainer D. Muscle-enhancing behaviors among adolescent girls and boys. *Pediatrics*. 2012;130(6):1019–1026

- Yusko DA, Buckman JF, White HR, Pandina RJ. Alcohol, tobacco, illicit drugs, and performance enhancers: a comparison of use by college student athletes and nonathletes. J Am Coll Health. 2008;57(3):281–290
- Nagata JM, Murray SB, Bibbins-Domingo K, Garber AK, Mitchison D, Griffiths S. Predictors of muscularityoriented disordered eating behaviors in US young adults: a prospective cohort study. Int J Eat Disord. 2019;52(12): 1380–1388
- 16. Karazsia BT, Crowther JH, Galioto R. Undergraduate men's use of performance- and appearanceenhancing substances: an examination of the gateway hypothesis. *Psychol Men Masc.* 2013;14(2):129–137
- Calzo JP, Horton NJ, Sonneville KR, et al. Male eating disorder symptom patterns and health correlates from 13 to 26 years of age. J Am Acad Child Adolesc Psychiatry. 2016;55(8):693–700
- Or F, Kim Y, Simms J, Austin SB. Taking stock of dietary supplements' harmful effects on children, adolescents, and young adults. *J Adolesc Heal*. 2019; 65(4):455–461
- Schulenberg JE, Johnston LD, O'Malley PM, Bachman JG, Miech RA, Patrick ME. Monitoring the Future national survey results on drug use, 1975–2018, volume II, college students and adults ages 19–60. 2019. Available at: http://

monitoringthefuture.org/pubs. html#monographs. Accessed December 10, 2019

- Wisk LE, Weitzman ER. Substance use patterns through early adulthood: results for youth with and without chronic conditions. *Am J Prev Med.* 2016;51(1):33–45
- Kann L, McManus T, Harris WA, et al. Youth risk behavior surveillance -United States, 2017. *MMWR Surveill Summ*. 2018;67(8):1–114
- Miech RA, Schulenberg JE, Johnston LD, Bachman JG, O'Malley PM, Patrick ME. National adolescent drug trends in 2019: findings released. Available at: http://monitoringthefuture.org/data/ 19data.html#2019data-drugs. Accessed December 5, 2019
- Connor JP, Gullo MJ, White A, Kelly AB. Polysubstance use: diagnostic challenges, patterns of use and health. *Curr Opin Psychiatry.* 2014;27(4): 269–275
- Salom CL, Betts KS, Williams GM, Najman JM, Alati R. Predictors of comorbid polysubstance use and mental health disorders in young adults-a latent class analysis. *Addiction*. 2016;111(1):156–164
- Midanik LT, Tam TW, Weisner C. Concurrent and simultaneous drug and alcohol use: results of the 2000 National Alcohol Survey. *Drug Alcohol Depend*. 2007;90(1):72–80
- Morley KI, Lynskey MT, Moran P, Borschmann R, Winstock AR. Polysubstance use, mental health and high-risk behaviours: results from the 2012 Global Drug Survey. *Drug Alcohol Rev.* 2015;34(4):427–437
- 27. Shin SH, Chung Y, Jeon SM. Impulsivity and substance use in young adulthood. *Am J Addict*. 2013;22(1):39–45
- Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. *Lancet.* 2009;373(9682):2223–2233
- 29. Calzo JP, Turner BC, Marro R, Phillips GL II. Alcohol use and disordered eating in a US sample of heterosexual and sexual minority adolescents. J Am Acad Child Adolesc Psychiatry. 2019;58(2):200–210

- Cafri G, Olivardia R, Thompson JK. Symptom characteristics and psychiatric comorbidity among males with muscle dysmorphia. *Compr Psychiatry*. 2008;49(4):374–379
- Murray SB, Rieger E, Hildebrandt T, et al. A comparison of eating, exercise, shape, and weight related symptomatology in males with muscle dysmorphia and anorexia nervosa. Body Image. 2012;9(2):193–200
- Olivardia R, Pope HG Jr., Hudson Jl. Muscle dysmorphia in male weightlifters: a case-control study. *Am J Psychiatry*. 2000;157(8):1291–1296
- 33. Pope CG, Pope HG, Menard W, Fay C, Olivardia R, Phillips KA. Clinical features of muscle dysmorphia among males with body dysmorphic disorder. *Body Image*. 2005;2(4):395–400
- Kandel D. Stages in adolescent involvement in drug use. *Science*. 1975; 190(4217):912–914
- 35. Kandel DB. Examining the Gateway Hypothesis: Stages and Pathways of Drug Involvement. In: Kandel DB, ed. Stages and Pathways of Drug Involvement: Examining the Gateway Hypothesis. Cambridge, United Kingdom: Cambridge University Press; 2002
- 36. Harris KM, Halpern CT, Whitsel E, et al The National Longitudinal Study of Adolescent to Adult Health: research design. 2017. Available at: https://www. cpc.unc.edu/projects/addhealth/ design/researchdesign_3618_regular. pdf. Accessed November 6, 2019
- Harris KM. The Add Health Study: Design and Accomplishments. Chapel Hill, NC: Carolina Population Center, University of North Carolina at Chapel Hill; 2013
- Chen P. Appropriate Analysis in Add Health: Correcting for Design Effects & Selecting Weights. Chapel Hill, NC: Carolina Population Center, University of North Carolina at Chapel Hill; 2014
- Neumark-Sztainer DR, Wall MM, Haines JI, Story MT, Sherwood NE, van den Berg PA. Shared risk and protective factors for overweight and disordered eating in adolescents. *Am J Prev Med.* 2007;33(5): 359–369
- 40. Haines J, Kleinman KP, Rifas-Shiman SL, Field AE, Austin SB. Examination of

shared risk and protective factors for overweight and disordered eating among adolescents. *Arch Pediatr Adolesc Med.* 2010;164(4):336–343

- Tabler J, Utz RL. The influence of adolescent eating disorders or disordered eating behaviors on socioeconomic achievement in early adulthood. *Int J Eat Disord*. 2015;48(6): 622–632
- StataCorp. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC; 2019
- Kirby T, Barry AE. Alcohol as a gateway drug: a study of US 12th graders. *J Sch Health*. 2012;82(8):371–379
- 44. Nkansah-Amankra S, Minelli M. "Gateway hypothesis" and early drug use: additional findings from tracking a population-based sample of adolescents to adulthood. *Prev Med Rep.* 2016;4:134–141
- 45. Wagner FA, Anthony JC. Into the world of illegal drug use: exposure opportunity and other mechanisms linking the use of alcohol, tobacco, marijuana, and cocaine. *Am J Epidemiol.* 2002;155(10):918–925
- Murray SB, Nagata JM, Griffiths S, et al. The enigma of male eating disorders: a critical review and synthesis. *Clin Psychol Rev.* 2017;57:1–11
- Gattario KH, Frisén A, Fuller-Tyszkiewicz M, et al. How is men's conformity to masculine norms related to their body image? Masculinity and muscularity across Western Countries. *Psychol Men Masc.* 2015;16(3):337–347
- McCreary DR, Saucier DM, Courtenay WH. The drive for muscularity and masculinity: testing the associations among gender-role traits, behaviors, attitudes, and conflict. *Psychol Men Masc.* 2005;6(2):83–94
- Hudson JI, Hiripi E, Pope HG Jr., Kessler RC. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry.* 2007;61(3):348–358
- Goldman AL, Pope HG, Bhasin S. The health threat posed by the hidden epidemic of anabolic steroid use and body image disorders among young men. J Clin Endocrinol Metab. 2019; 104(4):1069–1074

- Green GA, Catlin DH, Starcevic B. Analysis of over-the-counter dietary supplements. *Clin J Sport Med.* 2001; 11(4):254–259
- 52. Van Wagoner RM, Eichner A, Bhasin S, Deuster PA, Eichner D. Chemical composition and labeling of substances marketed as selective androgen receptor modulators and sold via the internet. JAMA. 2017;318(20):2004–2010
- 53. Cafri G, Thompson JK, Ricciardelli L, McCabe M, Smolak L, Yesalis C. Pursuit of the muscular ideal: physical and psychological consequences and putative risk factors. *Clin Psychol Rev.* 2005;25(2):215–239
- Nolen-Hoeksema S. Gender differences in risk factors and consequences for alcohol use and problems. *Clin Psychol Rev.* 2004;24(8):981–1010
- 55. Stice E. Risk and maintenance factors for eating pathology: a meta-analytic

review. *Psychol Bull*. 2002;128(5): 825-848

- 56. Erol A, Karpyak VM. Sex and genderrelated differences in alcohol use and its consequences: contemporary knowledge and future research considerations. *Drug Alcohol Depend.* 2015;156:1–13
- World Health Organization. Global status report on alcohol and health, 2014. Available at: doi:/entity/ substance_abuse/publications/global_ alcohol_report/en/index.html. Accessed December 5, 2019
- Patterson F, Lerman C, Kaufmann VG, Neuner GA, Audrain-McGovern J. Cigarette smoking practices among American college students: review and future directions. J Am Coll Health. 2004;52(5):203–210
- 59. Neumark-Sztainer D, Wall M, Story M, Sherwood NE. Five-year longitudinal

predictive factors for disordered eating in a population-based sample of overweight adolescents: implications for prevention and treatment. *Int J Eat Disord*. 2009;42(7): 664–672

- 60. Nagata JM, Ganson KT, Griffiths S, et al. Prevalence and correlates of muscleenhancing behaviors among adolescents and young adults in the United States [published online ahead of print June 5, 2020]. Int J Adolesc Med Health. 2020. doi:10.1515/ijamh-2020-0001
- 61. Nagata JM, Ganson KT, Gorrell S, Mitchison D, Murray SB. Association between legal performance-enhancing substances and use of anabolicandrogenic steroids in young adults [published online ahead of print May 18, 2020]. JAMA Pediatr. doi: 10.1001/ jamapediatrics.2020.0883