

High Prevalence and Early Onsets: Legal and Illegal Substance Use in an Urban Cohort of Young Adults in Switzerland

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Keywords

Adolescent drug use · Adolescents · Age at onset ·
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Abstract

Introduction: Debates about the legalization of illegal substances (e.g., cannabis) continue around the globe. A key consideration in these debates is the adequate protection of young people, which could be informed by current prevalence and age-of-onset patterns. For Switzerland, such information is limited, which is particularly true for women, despite advanced political efforts to legalize cannabis. The objective of the current study was to investigate substance use prevalence rates and ages of onset in a community-representative sample of female and male young adults in Switzerland. **Methods:** Data came from the Zurich Project on the Social Development from Childhood to Adulthood (z-proso). In 2018, participants ($N = 1,180$, 50.8% females) were ~20 years old. Lifetime and past-year use of alcohol, tobacco, cannabinoids, stimulants, hallucinogens, opioids, and benzodiazepines were assessed with an extensive sub-

stance use questionnaire. Additionally, ages of onsets of the respective substances were estimated by averaging participants' self-reported ages of onsets from ages 13 to 20 (max. 4 assessments). **Results:** 57% of 20-year-olds had used cannabinoids, 16% stimulants, 15% opioids (mostly codeine), and 8% hallucinogens in the past year. Males had higher prevalence than females for most drugs; nevertheless, females' prevalence rates were notably high. Legal substance use was typically initiated 1.3–2.7 years before legal selling age. Thus, almost half of the sample had consumed alcohol and tobacco by age 14. More than 40% of the total sample had smoked cannabis by age 16. Males initiated use of legal substances and cannabis earlier than females. **Discussion:** Our recent community-representative data suggested unexpectedly high levels and early onsets of substance use compared to a previous Swiss surveys and also the European average. Drug policy debates should consider urban substance use patterns when considering legalization efforts.

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Introduction

Young people's brains develop and reorganize fundamentally until their early to mid-20 s. Such plasticity provides both, windows of opportunity and vulnerability in brain development [1–3]. Research on animals and humans shows that exposure to substances during adolescence and into young adulthood potentially results in long-term negative consequences, including heightened risk for substance use disorders, decreases in cognitive, motivational, and psychosocial functioning, and additional psychiatric impairments [1, 4–10]. For example, frequent cannabis use during adolescence has been linked with later substance use disorders [1, 11, 12], psychosis [1, 13–15], and worse functional outcomes, including delinquency, financial, and social problems [16–25], reduced intellectual ability [26], and educational attainment [18–20].

Several countries have eased their cannabis use policies during the last decade [27]. In Switzerland, cannabis is illegal, but legalization debates have drawn out for decades, and drug policy based on prohibition are being critiqued [28]. Accordingly, Switzerland is currently implementing the first cannabis legalization trials [29, 30]. Although youth protection has been identified as a central aspect of cannabis regulation [31], it has recently been suggested in the Swiss legalization debate that cannabis use should be legal already beginning at age 16, given that the prevalence rates are typically highest in late adolescence [32]. Thus, public policy discussions must be critically informed by young people's current use and age-of-onset patterns in order to implement suitable, feasible, and reliable protection and prevention strategies. However, for Switzerland, such numbers are incomplete yet.

Globally, substance use is highest between the ages of 18–25 – the transition from adolescence to adulthood [33]. According to the latest European Drug Report of the European Monitoring Center for Drugs and Drug Addiction, an estimated 18.5% of the European adolescents and young adults aged 15 to 24 have used illegal substances in the past year, with rates was almost twice as high in males (23.3%) compared to females (13.6%) [34]. Cannabis showed the highest last-year prevalence in this age-group (mean 17.1%, range across countries 2.4–27.6%) followed by 3–4% “Ecstasy,” mean 2.2%, range 0.2–8.6%), cocaine (mean 2.2%, range 0.1–6.2%), and amphetamine (mean 1.3%, range 0–3.8%) [34]. Switzerland does not belong to the European Union; therefore, it does not contribute data to such annual reports of the European Monitoring Center for Drugs and Drug Addiction yet. However, sev-

eral population-representative Swiss studies offer substance use prevalence data, including, for example (1) the Swiss part of the WHO's Health Behavior in School-aged Children study (HBSC) [35], (2) the Swiss Addiction Monitoring survey (Suchtmonitoring Schweiz, www.suchtmonitoring.ch) [36], and (3) the Swiss conscript-based Study on Substance Use Risk Factors (C-SURF; [37]). Results from these studies suggest that the prevalence of illegal substance use among adolescents and adults in Switzerland is lower or similar to the European Union average, with the exception of cannabis, for which prevalence seem to be higher ([38], for review see [39]). The former conclusions were, however, recently challenged by results of waste water analyses [40] revealing that concentrations of MDMA and the cocaine metabolite benzoylecgonine were considerably higher in several Swiss cities than many other European cities [39].

Indeed, although the previous surveys were representative of broad segments of young people in Switzerland, they came with limitations that could lead to underestimating substance use. First, the HBSC study focused on youth aged 11–15 only, missing critical older ages of adolescence and young adulthood during which illegal substances are typically first taken and their consumption increases dramatically [41]. Second, the Swiss Addiction Monitoring relied on telephone interviews only, which typically result in considerable underreporting of substance use [42–46] also issues with representativeness given that “hidden” populations, such as young people and frequent substance users, are not always reached [47]. Third, the recruitment of the C-SURF cohort took place at 3 of 6 army recruitment centers in Switzerland, during the compulsory medical examination that all Swiss young men must undergo when registering for military (or civil) service. Although the research assessment was subsequently primarily done via online questionnaires and the independence of the study from the Swiss army was emphasized, it is possible that participants did not fully disclose their substance use due to the army context. Finally, C-SURF assessed males only, generating no knowledge about female substance use or sex differences in substance use. Taken together, most population-representative surveys of young people's substance use in Switzerland likely suffer from systematic underreporting, provide insufficient data on females and sex differences, and also feature limited information on ages of onset of illegal drugs. It is exactly these types of data, however, that could be crucial for informing drug-related policy-making.

The current study addresses these gaps in research by drawing on a community-representative sample of $N =$

1,180 males and females from an urban area of Switzerland in order to assess the age 20 prevalence of the most common substances in 2018. Participants first began reporting ages of onset for common substances at age 13 (in 2011). Indeed, the age-of-onset of substance use was estimated by average ages 13, 15, 17, and 20 self-reports. At age 20, an extensive substance use questionnaire was assessed including alcohol, tobacco, cannabis and cannabinoids, stimulants, hallucinogens, opioids, benzodiazepines, and some NPS with multiple subcategories for each substance group.

We expected to find higher prevalence rates of substance use for the most common substances (e.g., cannabis, cocaine, Ecstasy, and amphetamines) in this urban community-representative sample, compared to the other Swiss studies and the European average as described above [34, 37]. In addition, we generally expected higher rates of substance use in males than females, as previously described for Switzerland and Europe [34, 36].

Methods

Recruitment and Participants

Data came from the prospective-longitudinal Zurich Project on the Social Development from Childhood to Adulthood (z-proso). Participants were selected using a cluster-stratified randomized sampling approach. The initial target sample included 1,675 children from 56 primary schools randomly selected from the 90 public schools in Zurich, the largest city of Switzerland. Stratification took into account school size and socioeconomic background [48–50]. $N = 1,360$ participants were first assessed in 2004, when the sample was largely representative of first-graders attending public schools in Zurich. Seven additional assessments were completed since. Data for the current article primarily came from the most recent assessment in 2018, at age 20, when $N = 1,180$ participants (males $n = 581$; females $n = 599$) completed a detailed interview of their substance use. In addition, age-of-onset data from ages 13, 15, 17, and 20 were used. Information on sample attrition and nonresponse in the analytic sample can be found in online supplement 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000520178).

Consistent with Switzerland's immigration policies and the city's diverse population, parents of participants had been born in over 80 different countries; the majority of participating 20-year-olds were, however, born in Switzerland (90.3%). Parental educational background was diverse; 30.1% of participants had at least 1 parent with a university degree. The mean household International Socioeconomic Index of Occupational Status [51] was $M = 47.1$ ($SD = 19.7$). The International Socioeconomic Index of Occupational Status is an internationally comparable index of socioeconomic status based on occupation-specific income and the required educational level, with scores ranging from 16 (e.g., unskilled worker) to 90 (e.g., judge).

Data were collected with paper/pencil questionnaires up to age 17 in random groups of $n = 3–25$ (not classes) in classrooms, and

with computer-administered surveys at age 20 in a university laboratory environment. Adolescents received a cash incentive for their participation, increasing from ~USD 30 at age 13 to ~USD 75 at age 20.

Assessment of Substance Use Prevalence

At age 20, an extensive substance use questionnaire was administered. Participants were asked whether they had used the following substances in the past year or ever in their life at least once. Examples of relevant drugs, currently on the Swiss market, were provided: (1) tobacco (e.g., cigarettes and shisha/hookah); (2) beer/wine/alcopops; (3) liquor (e.g., vodka, whisky, and gin); (4) cannabinoids, including cannabis (e.g., hashish, grass/weed/marihuana, and cannabis); CBD (e.g., CBD-enriched hemp, cigarettes with CBD-enriched hemp, and CBD tinctures), cannabis substitutes (e.g., synthetic cannabinoids, herbal incense, "herbal smoking blends," such as "Dutch Orange", "Spice", "K2", and "Ganja Style"); (5) stimulants, including "Ecstasy" (MDMA), cocaine, and amphetamine/methamphetamine (e.g., "Speed," "Pepp," "Ice," "Crystal Meth"); (6) hallucinogens, including LSD/psilocybin (e.g., magic mushrooms/truffles), 2C substances (e.g., Bromo," Erox," "Nexus," "Venus"), and ketamine ("Special K," "Vitamin K"); (7) opioids, including nonmedical use of codeine-based cough medicine (e.g., Resyl plus™, Makatussin™, Pectocal-mine N™, and Codein Knoll™), and nonmedical use of opioid painkillers (e.g., Tramal™, Sevredol™, Sevre-Long™, Temgesic™, Oxycontin™, Palladon™, and Durogesic™); and (8) benzodiazepines (e.g., Valium™, Rohypnol™, and Xanax™).

Assessment of Onset Ages

At the age 13, 15, 17, and 20 assessments, participants were also asked at what age they had first used the substances assessed at that age (i.e., tobacco, alcohol, and cannabis at age 13; tobacco, alcohol, cannabis, Ecstasy, cocaine, [meth-]amphetamine, LSD, and psilocybin at ages 15 and 17; all substances listed in the previous section at age 20). All available onset ages were averaged. The repeated age-of-onset measures showed moderate to good reliability, with the exception of LSD/psilocybin (see intraclass coefficients in online suppl. Table 1).

Analytic Strategy

Analyses were conducted in SPSS 25 (IBM Corp., Germany) and R (<http://www.R-project.org>). All respondents at age 20 have been included in the analysis. Prevalence estimates of substance use were computed for the overall sample and for males and females separately. We report lifetime prevalence and 12-month prevalence – for groups of substances and also for individual substances. Sex differences in prevalence rates were tested using χ^2 statistics. Sex differences in ages of onset distributions were tested using Wilcoxon rank sum. There were no oversampling or other stratification procedures during recruitment that would have required the use of sampling/survey weights in our statistical analyses.

Results

Overall Lifetime Prevalence

The vast majority of young people had used alcohol and tobacco by age 20 (Fig. 1a). Over 69% had used can-

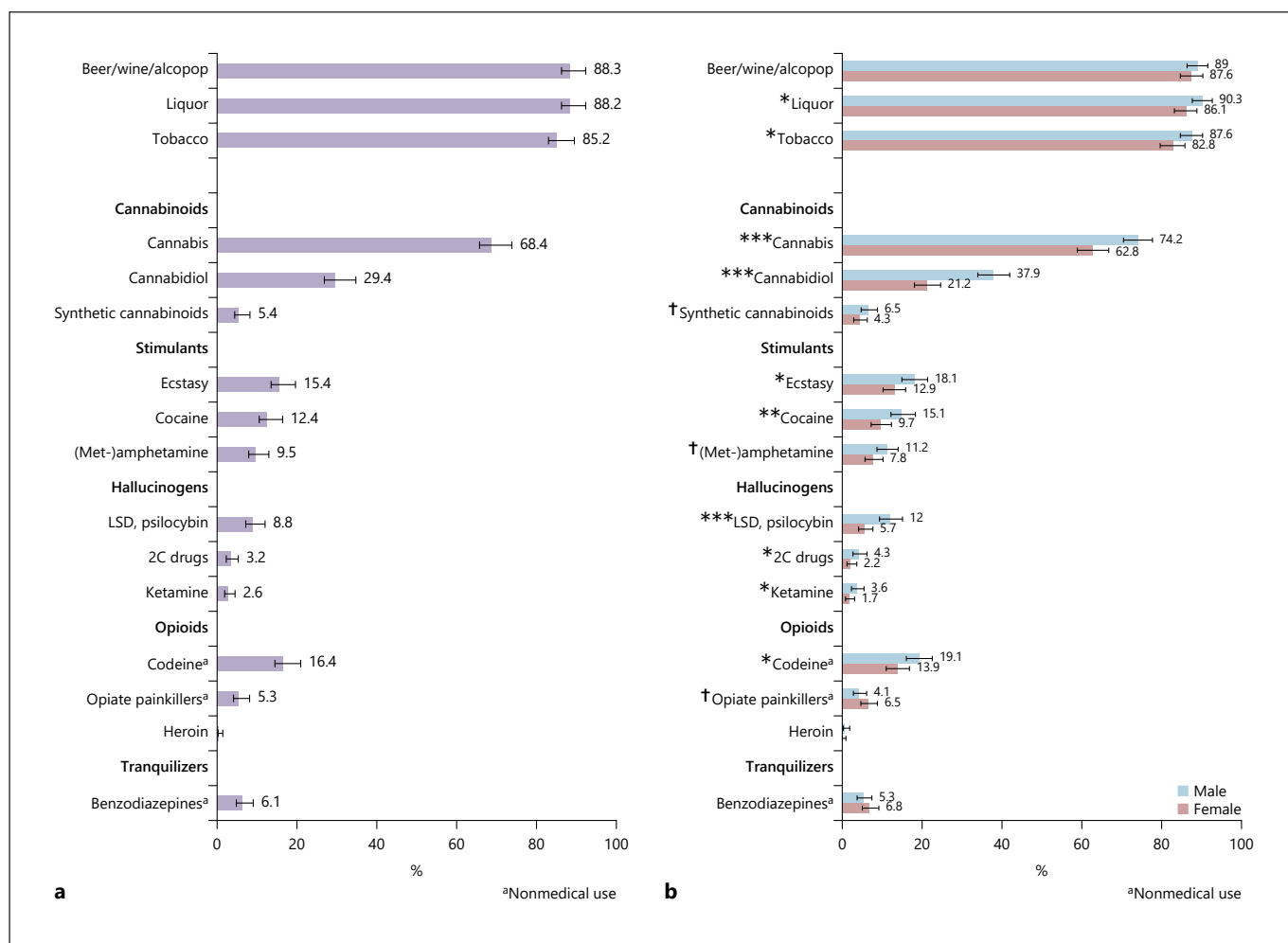


Fig. 1. a Lifetime prevalence of substance use at age 20 in overall sample. **b** Sex-specific lifetime prevalence of substances use at age 20. † $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ for sex difference.

nabinoids, 19 stimulants, 19 opioids, and 10% hallucinogens, respectively. Among cannabinoids, cannabis was most prevalent, with over 3 in 4 20 year olds having used it. Surprisingly, one-third of the sample had used CBD; >5% reported use of synthetic cannabinoids. With respect to stimulants, Ecstasy was most prevalent, followed by cocaine and amphetamines. For opioids, one in 6 20-year-olds reported lifetime nonmedical use of codeine; >5% had used opioid painkillers nonmedically. Notably, almost 9% of participants reported lifetime use of LSD/psilocybin and >6% nonmedical use of benzodiazepines. 2C drugs, ketamine, and heroin were the least used substances (<5% of sample).

Sex-Specific Lifetime Prevalence

Liquor and tobacco were more commonly used by males than females, but prevalence in females was nevertheless high (>80%) (Fig. 1b). Furthermore, almost all groups of illegal substances were more commonly used by males than females, including cannabinoids, stimulants, and hallucinogens, but not opioids (Table 1). One in 3 males (vs. 1 in 5 females) had used CBD. One in 5 males (vs. 1 in 7 females) reported nonmedical use of codeine. One in 6 males (vs. 1 in 8 females) had used Ecstasy. One in 7 males (vs. 1 in 10 females) had used cocaine. For example, more than two-thirds of females had used cannabinoids by age 20. After Bonferroni corrections, significant sex differences remained for cannabis, CBD, and LSD/psilocybin ($p_{\text{corr}} < 0.05$).

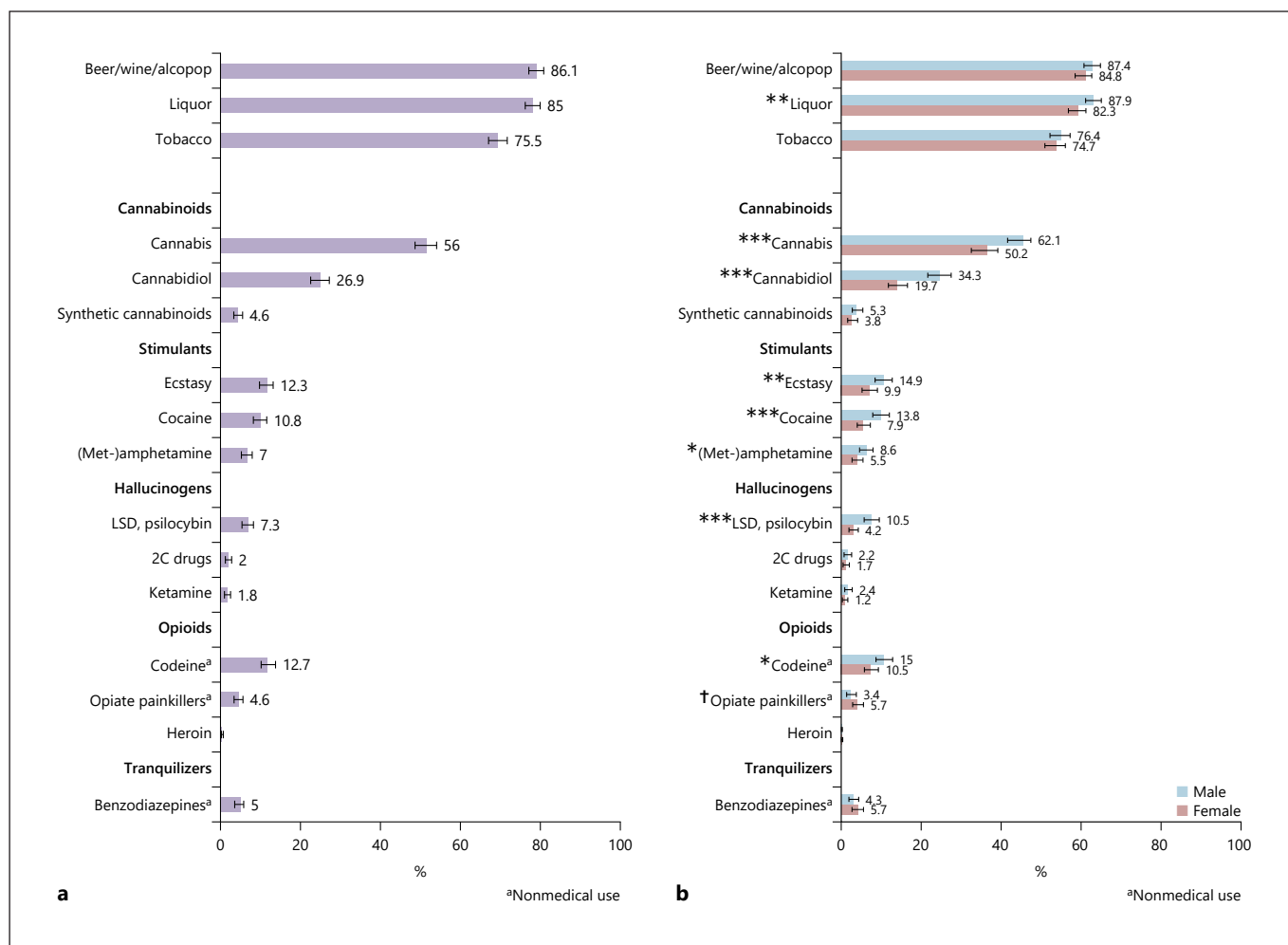


Fig. 2. a Past-year prevalence of substance use at age 20 in overall sample. **b** Sex differences in past-year substance use at age 20. †*p* < 0.10, **p* < 0.05, ***p* < 0.01, ****p* < 0.001 for sex difference.

Table 1. Lifetime and 12-month prevalence rates of groups of substances and associated 95% CIs

	Overall % (95% CI)	Male % (95% CI)	Female % (95% CI)	<i>p</i> for sex difference
Lifetime prevalence				
Cannabinoids	69.1 (66.3–71.7)	75.2 (71.5–78.7)	63.1 (59.1–67.0)	<0.001
Stimulants	18.6 (16.4–20.9)	22.2 (18.9–25.8)	15.1 (12.3–18.2)	0.002
Opioids	18.6 (16.5–21.0)	20.5 (17.3–24.0)	16.9 (13.9–20.1)	0.110
Hallucinogens	10.3 (8.6–12.1)	13.6 (10.9–16.7)	7.0 (5.1–9.4)	<0.001
Twelve-month prevalence				
Cannabinoids	57.1 (54.2–60.0)	63.7 (59.6–67.6)	50.8 (46.7–54.8)	<0.001
Stimulants	16.2 (14.1–18.4)	19.9 (16.7–23.3)	12.6 (10.0–15.5)	<0.001
Opioids	14.9 (13.0–17.1)	16.4 (13.5–19.7)	13.5 (10.9–16.5)	0.165
Hallucinogens	8.3 (6.8–10.0)	11.6 (9.1–14.5)	5.2 (3.5–7.3)	<0.001

CI, confidence interval.

Fig. 3. Age-of-onset distributions for alcohol, tobacco, and cannabis. Note: reported onset ages below age 10 were recorded to 10. Red dashed lines represent the legal selling age for tobacco, beer and wine (age 16), and alcopops and liquor (age 18) in Switzerland.

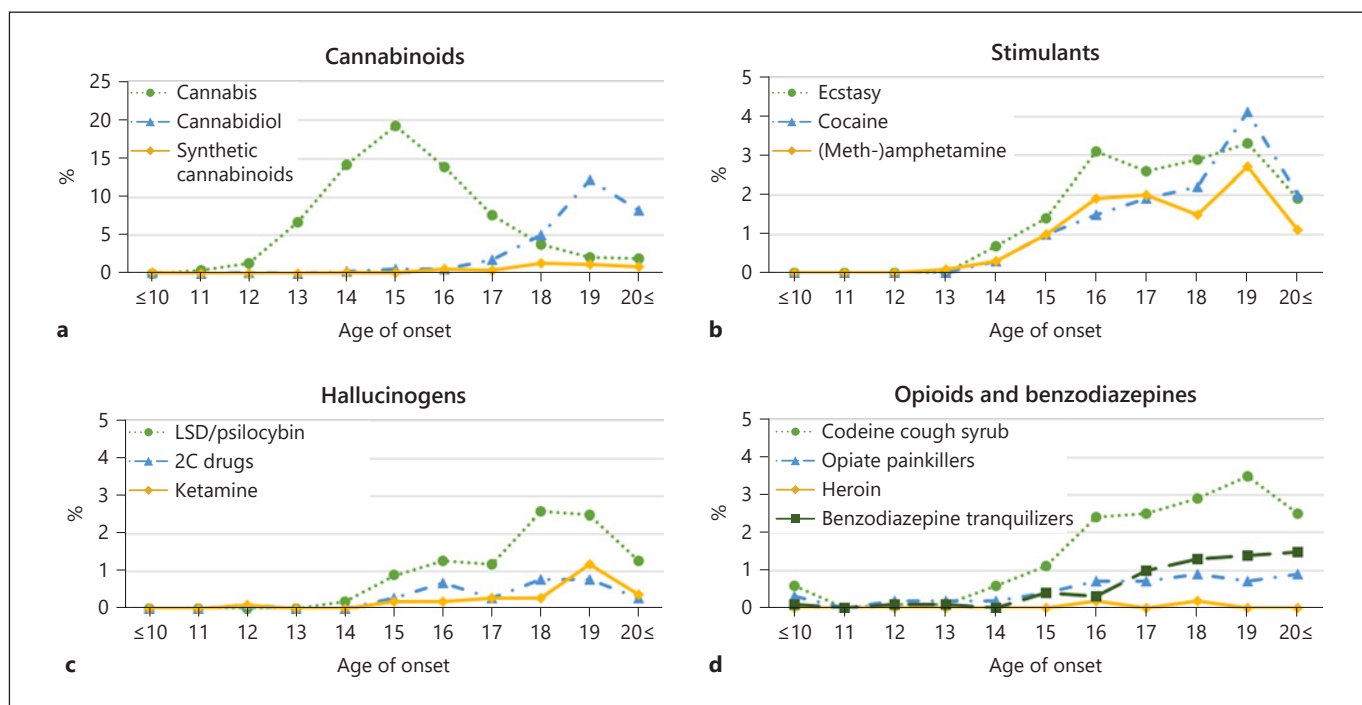
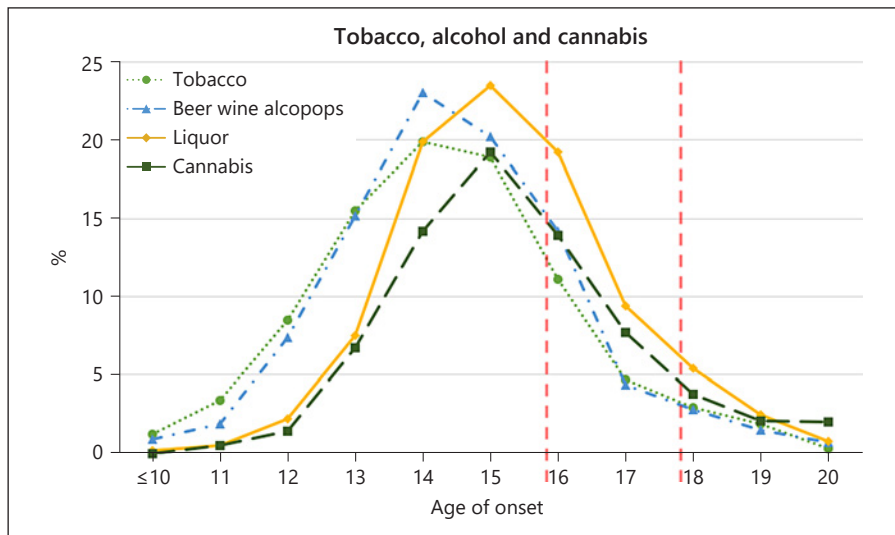


Fig. 4. Age-of-onset distributions for (a) cannabinoids, (b) stimulants, (c) hallucinogens, and (d) opioids and benzodiazepines. Note: responses below age 10 were recorded to 10. Given the low prevalence of stimulants, hallucinogens, and opioid and benzodiazepines, they were depicted on a different scale than cannabinoids.

Overall 12-Month Prevalence

The large majority of 20-year olds reported beer/wine/alcopops, liquor, and also tobacco use in the past year (Fig. 2a); >50% of the sample had used cannabinoids (57%). Past-year use of stimulants, opioids, and halluci-

nogens was at 16, 15, and 8%, respectively. Cannabis use was the most commonly used substance in the cannabinoids category, at 56%; nevertheless, more than 1 in 4 participants had used CBD and almost 5% had used synthetic cannabinoids. More than 1 in 10 participants had

Table 2. Mean and median self-reported onset ages of the total sample, males, and females who participated in age 20 assessments

Substance	Total sample				Males				Females				Sex diff	
	N	mean	median	stand. dev	N	mean	median	stand. dev	N	mean	median	stand. dev	W	p
Beer/wine/alcopops ²	1,087	14.8	14.7	1.7	540	14.6	14.5	1.6	547	15.0	15.0	1.7	126,890	<0.001
Liquor ²	1,074	15.5	15.3	1.5	538	15.4	15.3	1.6	536	15.6	15.3	1.5	131,060	0.010
Tobacco ²	1,042	14.6	14.7	1.8	528	14.4	14.3	1.8	514	14.8	15.0	1.7	117,286	<0.001
Cannabis ²	843	15.6	15.5	1.7	449	15.3	15.0	1.6	394	15.8	15.7	1.7	71,868	<0.001
Cannabidiol ¹	344	18.7	19	1.4	218	18.7	19.0	1.4	126	18.7	19.0	1.3	14,110	0.656
Synthetic cannabinoids ¹	62	17.9	18	2.1	36	17.9	18.0	1.6	26	17.9	18.0	1.6	510	0.545
Ecstasy ³	188	17.5	18	1.6	108	17.7	18.0	1.7	80	17.4	17.5	1.5	4,813	0.177
Cocaine ³	154	18.0	18.0	1.6	93	18.1	18.0	1.5	61	17.8	18.0	1.7	3,043	0.437
(Meth-)Amphetamine ³	125	17.5	17.5	1.7	73	17.8	18.0	1.6	52	17.2	17.0	1.8	22,255	0.097
LSD, psilocybin ³	117	17.8	18.0	1.5	78	18.0	18.0	1.5	39	17.4	18.0	1.6	1,816	0.083
2C drugs ¹	36	17.5	18	1.8	23	17.2	17.0	1.8	13	18.0	18.0	1.7	109.5	0.184
Ketamine ¹	31	18.2	19	1.8	21	17.9	19.0	2.1	10	18.7	19.0	1.1	84.5	0.373
Codeine ¹	190	17.3	18	2.5	108	17.7	18.0	2.2	82	17.0	17.0	2.3	5,317	0.016
Opioid painkillers ¹	59	16.9	17	2.8	22	16.7	17.0	3.0	37	17.1	18.0	2.5	385	0.734
Heroin ¹	<5	17.0	17	1.2	<5	-	-	-	<5	-	-	-	-	-
Benzodiazepines ¹	71	17.9	18	2.2	30	17.9	18.5	2.5	41	18.0	18.0	1.6	661	0.589

¹ Assessed at age 20 only. ² Mean based on up to 4 assessments (ages 13–20). ³ Mean based on up to 3 assessments (ages 15–20).

used codeine, Ecstasy, and cocaine, respectively. Within the group of hallucinogens >7% reported LSD or psilocybin use. Nonmedical use of opioid painkillers and benzodiazepines was unexpectedly high, at almost 1 in 20. Heroin was the least commonly used drug. For associations between the uses of different substances, see online supplement 2. Briefly, significant bivariate associations emerged for most substance combinations.

Sex Differences in 12-Month Prevalence

Sex differences were not identified for beer/wine/alcopops or tobacco (Fig. 2b). Males were more likely than females to report use of liquor. Males were also more likely to report use of any cannabinoids, any stimulants, and any hallucinogens (Table 1). Past-year opioids use did not differ by sex. With respect to specific substances, cannabis, CBD, all stimulants, LSD, and codeine use were more commonly used by males than females, but prevalence in several of these categories was still high among females. After Bonferroni corrections, significant sex differences remained for cannabis, CBD, cocaine, and LSD/psilocybin ($p_{\text{corr}} < 0.05$).

Onset Ages: Overall Sample

Age-of-onset distributions (Fig. 3; Table 2) revealed that tobacco, alcohol, and cannabis had the earliest onset ages (median age-of-onset ~15 years). In fact, more than one half of adolescents had used alcohol or tobacco before the legal selling age of 16 in Switzerland: 67.4% for tobacco and 68.9% for beer/wine/alcopops. Of the participants, 53.8% had consumed liquor before age 16, and 87.2% before age 18 (i.e., the legal selling age for liquor in Switzerland). Forty-two percent of participants had smoked cannabis before age 16, and 63.6% before age 18. Onset ages of cannabinoids other than cannabis were older (Fig. 4a; Table 2): 3.8% of participants had consumed CBD before age 18 and 1.7% synthetic cannabinoids.

The age-of-onset distribution of stimulants shows 2 peaks (1 at age 16, another at age 19, Fig. 4b). Roughly half of the youth whoever consumed Ecstasy or other amphetamines did so before age 18, with 7.8% of the total sample having consumed Ecstasy before age 18 and 5.3% having consumed amphetamines before age 18. Cocaine use had a slightly later onset: 4.7% of participants had consumed cocaine before age 18. Age-of-onset curves for hallucinogens did not have distinct peaks (Fig. 4c; Table 2), but LSD/psilocybin most commonly had their onsets around ages 18 and 19; 3.6% of participants had consumed LSD/psilocybin before age 18 and 1.4% of participants had used 2C substances before age 18, and 0.8% ketamine.

Opioids and benzodiazepines showed relatively flat age-of-onset distributions (Fig. 4d; Table 2), increasing with age only slightly; 7.4% of participants had used codeine cough syrup nonmedically before age 18, 2.7% had used opioid painkillers nonmedically before age 18, and 0.2% of participants had used heroin before age 18; 2% benzodiazepine.

In sum, a large percentage of adolescents who used an illegal substance by age 20 did so before age 18. Onset ages for legal substances peaked between 1.3 (tobacco and beer/wine/alcopops) and 2.7 years (liquor) before legal selling age, and more than 2 in 5 adolescents had used cannabis by age 16. For correlations between onset ages, see online supplement 3. Online supplement 4 documents what percentage of individuals whoever took a substance by age 20, initiated use of that substance by age 16 or 18. Results illustrate that in the cases of several illegal substances such as Ecstasy, amphetamines, or 2C drugs, almost half of those whoever used this substance by age 20 had initiated used at age 18 or younger.

Onset Ages: Sex Differences

Wilcoxon rank sum tests were applied to test sex differences in Age-of-onset distributions. These tests accounted for the nonparametric distributions of onset ages (Table 2). Results revealed that males had a younger onset age for beer/wine/alcopops, liquor, tobacco, and cannabis than females. In turn, females initiated nonmedical use of codeine earlier than males and, marginally, also amphetamines and LSD/psilocybin use. For the age-of-onset distributions for males and females, see online supplement 5.

Relationship between Age-of-Onset and Substance Use Prevalence at Age 20

In general, earlier age-of-onset of alcohol, tobacco, and cannabis use correlated with higher probability of use of several substances at age 20 (see online supplement 6). The strongest associations ($r > 0.25$) were found for early onset of alcohol use and later cannabis and CBD use; early onset of cannabis use and later CBD, MDMA, cocaine, and amphetamine use; early use of hallucinogens and later LSD use; early use of opioids and later tobacco and codeine use; as well as early and later benzodiazepine use.

Discussion

In the face of debates about the legalization of illegal substances around the globe [28], including in Switzerland [52], our pre-legalization data revealed high levels

and early onsets of substance use in a community-representative urban sample of young adults. Almost half of participants had used tobacco or alcohol by age 14; >40% had used cannabis by age 16. Use of illegal substances other than cannabis was initiated before age 18 by a substantial number of participants. By age 20, almost 70% of participants had used cannabis, 1 in 10 had used hallucinogens, and 1 in 5 had used stimulants and/or opioids – both substance classes with strong harm and addictive potential [53].

These high percentages of substance use among urban adolescents are remarkable specifically as youth protection is a stated goal of the current cannabis legalization efforts in Switzerland [31]. Given that legalization efforts tend to increase youths' perceptions that substances under discussion are safe, which has led to increased and earlier use [54], Swiss legalization debates could possibly exacerbate the early use patterns observed here. However, early onset of a substance may hamper young people's attainment of physical, psychosocial, educational, and professional milestones [1] because of its negative neurodevelopmental impact on circuits linked to psychosocial functioning, cognition, and motivation [4, 9, 10, 55, 56].

Prevalence at Age 20

Among the illegal substances, specifically lifetime and 12-months prevalence of cannabis use in our study was considerably higher than previous representative Swiss surveys [36, 37] and to the European average [38]. When comparing the male prevalence rates at the same age between our and the C-SURF study directly, much higher rates were detected in the z-proso sample for all compared substances. χ^2 -tests, comparing prevalence rates of the overlapping substances between only male z-proso participants with the male C-SURF conscripts, confirmed significantly higher rates in the z-proso sample (Bonferroni-corrected p values < 0.0001). Of note, C-SURF was conducted 7–8 years before z-proso. However, it is less likely that the very large differences in prevalence rates are explained only by temporal changes in substance use in Switzerland. According to Swiss Addiction Monitoring, lifetime prevalence and past-year prevalence has increased between 2011 and 2016 by 6.1 and 2.3%, respectively [36], while, in contrast, our study comparison showed a difference of 22.6% for lifetime and 31.4% for past-year prevalence. The case of the other investigated substances is similar. One may argue that C-SURF measured more participants from rural than from urban areas (41% vs. 59%, respectively) and that substance use is over-represented in urban regions as assessed in z-proso. How-

ever, in C-SURF the differences between rural and urban areas in substance use prevalence were surprisingly small [57]. Moreover, although waste water analyses reflect the entire age spectrum and not only substance use of young people, the high cocaine and MDMA prevalence rates in our sample are in line with recent waste water testing revealing that benzoylecgonine (the main metabolite of cocaine) and MDMA concentrations in selected Swiss cities, including Zurich, ranked among the highest in European city comparisons [40].

Our cohort's in-person interviews with participants took place beginning at age 7. The trust and rapport built with participants over time and beginning at a young age could have been more conducive to disclosing potentially illegal and socially undesirable behaviors than anonymous telephone surveys (Swiss Addiction Monitoring) or interviews conducted in the context of military recruitment (C-SURF). Thus, we believe that our results are more valid than existing previous surveys, although they are only locally and not nationally representative.

Several findings with respect to specific substances are noteworthy. First, lifetime prevalence of cannabis use by age 20 was high at 68%. Cannabis use is illegal in Switzerland, but it is often tolerated by law enforcement [58]. Indeed, there is some cultural normalization around cannabis [59], especially in the Canton of Zurich [52]. Other prospective-longitudinal studies (e.g., USA.-based) had reported similarly high lifetime rates [41], but at older ages (i.e., age 30). Nevertheless, in the US cannabis has become the first psychoactive substance that adolescents start using [60]. In contrast, the alcohol use in youth is steadily declining in the USA but also in other countries [61, 62].

Prevalence of CBD – which is freely available for purchase in Switzerland – but also synthetic cannabinoids was also unexpectedly high. However, onsets for both CBD and synthetic cannabinoids were at later ages than for cannabis, perhaps due several reasons, including that CBD products spread on the legal market only since 2016 [63] and also that cannabis law enforcement is less strict in Switzerland compared to other countries. Thus, cannabis is easy to access already at earlier ages making synthetic cannabinoids less attractive in this age-group [29, 58].

Second, lifetime prevalence of stimulants, hallucinogens, and nonmedical opioids (cough syrup and painkillers) use was high by age 20. This could, in part, be due to the urban setting in which substances are easily accessible to young people. Indeed, many young people in Zurich come from relatively affluent families, and, thus, have the

means to purchase drugs. In addition, Zurich is the site of many music scenes/festivals, concerts, and parties – including those based on house, techno, and hip hop – each of which come with their own drug culture. The high prevalence of nonmedical use of opioids was nevertheless surprising, especially considering relatively conservative prescription patterns of opioid-based painkillers in Switzerland. However, some opioid-based cough syrups are freely available in Swiss pharmacies, and it is the use of those that is also glamorized by some music scenes (e.g., hip hop) [64, 65].

Third, lifetime prevalence of non-medical benzodiazepine use was at 6%. This trend is important to monitor given unfolding benzodiazepine crises in other countries such as the USA [66]. In recent cohorts in high-income countries, adolescent and young adult females have reported high levels of depressive and anxious symptoms [67]. In the current sample, females also engaged in high rates of behaviors indicative of such emotional distress, including non-suicidal self-injury (for example, [68]). It is possible that the high rates of tranquilizer use in the current sample are indicative of self-medication for emotional and social distress [69].

Age of Onset

The onset ages identified here were young and below average onsets in other countries. This may, in part, be due to earlier legal selling ages of some substances (e.g., alcohol) in Switzerland compared to select other countries (e.g., the USA). The finding that almost half of participants had consumed alcohol or tobacco before or at age 14 suggests that the enforcement of current laws is not sufficiently successful. Importantly, early age-of-onset of several substances such as alcohol, tobacco, and cannabis was associated with a higher probability of illegal substance use at age 20. According to the “gateway” theory, the hindrance of early onsets in legal substance use potentially could prevent progression to more problematic and illegal substance use in later life [70–72]. For example, recent work from the Monitoring the Future study in the USA showed that nicotine use of 12th grade students (approximately 18 years old) decreased to historically low levels from 63% in 2000–24% in 2018. With declining nicotine use, rates of adolescent cannabis use also became much lower than projected [73]. Certainly, the transition from legal substance use during adolescence to substance use disorders in adulthood cannot be solely explained by the gateway theory [74], and the sequences of substance use onsets are “variable and opportunistic rather than uniform and developmentally deterministic” ([75], p. S3).

However, at least for cannabis use, a methodologically sound twin study has shown that early cannabis use in fact predicted later use of substances with stronger harm potential suggesting that genetic and environmental factors might be less strong than expected [76]. Of note, another twin study concluded that the link between early age of alcohol initiation and later alcohol use disorders in adulthood was almost entirely explained by a common genetic risk factor [77].

Sex Differences

Young adult females are traditionally understudied with respect to substance use. Although males in our sample were more likely than females to report use of cannabinoids, stimulants, hallucinogens, and codeine, females' nevertheless had remarkably high prevalence rates and early onsets. For example, more than two-thirds of females had used cannabis by age 20. Interestingly, some sex differences favoring males were significant for lifetime prevalence only, but not for 12-month prevalence (e.g., several hallucinogens and synthetic cannabinoids). Perhaps males experimented with these substances before age 19, but then ceased using them. Indeed, although age-of-onset data in recent cohorts have sometimes suggested that females are beginning to "catch up" with early onsets [78–80], males in the current sample had earlier onsets for beer/wine/alcopops, liquor, tobacco, and cannabis.

The high rate of substance use among young females in Switzerland is of major concern. Females' drug metabolism differs from that of males due, in part, to differences in sex hormones and body composition [81]. Accordingly, the same dose of a substance could have a stronger and longer-lasting effect in females than in males. Furthermore, our results suggest that young females in their reproductive ages consume many substances.

Limitations

Findings may not be generalized to other parts of Switzerland, especially to more rural areas where substances or substance use-relevant party scenes are less accessible compared to Zurich. However, data from the Swiss C-SURF study suggest that rural young males had surprisingly easy access to hard substances [57], indicating that the prevalence differences between rural and urban environments might not be as pronounced as expected. Furthermore, Zurich has a relatively affluent

population, meaning that many youth have the means to buy substances; this could be different in other areas. Substance use assessments took place via self-reports. Although, the long-standing nature of the panel may have contributed to trust and honesty in reporting, objective verification of substance use would be ideal specifically for substances with low-prevalence rates (such as 2C-B, ketamine, heroin, and opioid painkillers) given that specifically self-report of low-prevalence phenomena might be considerably biased by false positive and false negative responses. At age 20, we also collected hair samples from participants. These samples are currently being assayed for substances and substance metabolites. These data are forthcoming and a next step in our program of research will be to test the agreement between self-reported and hair data.

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Statement of Ethics

The study was conducted consistent with national and international ethics standards and was approved by the responsible Ethics Committee (Cantonal Ethics Committee Zurich, BASEC-Nr. 2017–02021). Adolescents provided written informed consent at each assessment; until age 15 parents could opt their child out of the study.

Conflict of Interest Statement

B.B.Q. is an Editorial Board Member of the journal. Beyond that none of the authors declared a potential conflict of interest. The funders of the study did not influence the study design; the collection, analysis, or interpretation of data; or the writing of the manuscript, and they did not impose any restrictions regarding the submission.

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Author Contributions

D.R. and M.E. planned, implemented, and received funding for the z-proso cohort. B.B.Q. and L.S. designed the substance use questionnaire, planned the present analyses, and supervised the study. A.S. and L.B. conducted the statistical analyses. B.B.Q. L.B., and L.S. wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Data Availability Statement

Publicly available datasets were analyzed in this study. Anonymized individual participant data and data dictionaries that underlie the results reported in this article are available to other researchers upon request. Requests including a brief proposal should be sent to D.R. As a research infrastructure supported by the SNSF, the z-proso study is committed to an open data access policy. Anonymized data, protocols, and other metadata from earlier data collections of the study are generally available to the scientific community. Please contact D.R. for this purpose.

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