

Onset and progression of drug use in the general population of Catalonia, Spain

Inicio y progresión en el uso de sustancias en la población general de Cataluña, España

ALBERT SÁNCHEZ-NIUBÒ*,**, LUIS SORDO***,****, GREGORIO BARRIO*****,
BLANCA I. INDAVE***,*****, ANTONIA DOMINGO-SALVANY*****.

* Research and Development Unit. Parc Sanitari Sant Joan de Déu, Sant Boi de Llobregat (Barcelona). Spain;
** CIBER de Salud Mental (CIBERSAM). Spain. *** CIBER de Epidemiología y Salud Pública (CIBERESP). Spain.
**** Department of Preventive Medicine and Public Health, Faculty of Medicine. Complutense University, Madrid.
Spain. ***** National School of Public Health. Carlos III Institute of Health, Madrid. Spain. ***** National
Centre for Epidemiology. Carlos III Institute of Health, Madrid. Spain. ***** Drug Abuse Epidemiology
Research Group. Institut Hospital del Mar d'Investigacions Mèdiques de Barcelona (IMIM), Barcelona. Spain.

Abstract

The aim of the present study was to retrospectively study the onset and progression sequence of the most frequent pathways of drug use initiation in a sample of the Spanish general population. Data come from the 2011 household survey on drug use in Catalonia, Spain, on non-institutionalized individuals aged 15-64 in the general population. The final sample was of 2,069 individuals and had the same age distribution as the general population. Progressions of drug initiation were pictured by quantifying transitions from a previous state in terms of the number of individuals and weighted percentages. Survival analyses were employed to assess the most prevalent pathways found in the descriptive analysis using additive regression models. Median ages of onset were decreasing in every cohort from 1965 to 1985-1996: from 17 to 15 in tobacco, 20 to 16 in cannabis and 21 to 18 in cocaine. In people who consumed the three drugs studied, the most frequent pathway was "tobacco-daily tobacco-cannabis-cocaine". These results demand health policies and prevention strategies in order to increase perception of the risks of legal and illegal substances. This, together with well-designed peer interventions could reduce the risk of exposure to illegal drugs such as cannabis and cocaine, thus reducing the likelihood of future problem drug use.

Keywords: Tobacco; Cannabis; Cocaine; Age of onset; Population surveillance.

Resumen

Este estudio tuvo como finalidad realizar un análisis retrospectivo de la secuencia de inicio y progresión de las vías más comunes del inicio del uso de sustancias en una muestra de la población general española. Recopilamos datos de la encuesta nacional de las viviendas del año 2011 sobre el uso de sustancias en Cataluña, España, respecto de personas no-institucionalizadas de la población general con edades entre los 15-64 años. La muestra final estaba compuesta de 2.069 personas con la misma distribución de edad que la población general. Mostramos la progresión en el inicio de uso de sustancias mediante la cuantificación de los cambios de un estado anterior, en términos de número de personas y porcentajes ponderados. Aplicamos análisis de supervivencia para valorar las vías más prevalentes halladas en el análisis descriptivo usando modelos de regresión aditivos. La edad media de inicio de uso fue decreciendo en todas las cohortes desde 1965 hasta 1985-1996: de 17 a 15 para tabaco, de 20 a 16 para cannabis y de 21 a 18 para cocaína. En las personas que usaban las tres sustancias estudiadas, la vía más frecuente fue "tabaco-uso diario de tabaco-cannabis-cocaína". Dichos resultados requieren políticas de salud y estrategias de prevención para aumentar la percepción de los riesgos de las sustancias legales e ilegales. Esto, unido a intervenciones de compañeros bien diseñadas, podría reducir el riesgo de exposición de sustancias ilegales, como cannabis y cocaína, y, por tanto, reducir la probabilidad de un problema de uso de sustancias en un futuro.

Palabras clave: Tabaco; Cannabis; Cocaína; Edad de inicio; Vigilancia poblacional

Received: December 2017; Accepted: June 2018.

Send correspondence to:

Luis Sordo. Department of Preventive Medicine and Public Health, Faculty of Medicine, Complutense University, Madrid, Spain.
913941522. E-mail: lsordo@ucm.es

Early onset of drug use is associated with a variety of long term negative outcomes (Poudel & Gautam, 2017), being one of the factors most strongly associated to a higher prevalence of drug use, as well as to engaging in other risky health behaviors (DuRant, Smith, Kreiter & Krowchuk, 1999). An early initiation of tobacco and/or cannabis could increase the risk of initiating other illicit drugs and later dependence problems (Anthony, 2012; Baggio et al., 2014; Choo, Roh & Robinson, 2008; Fergusson & Boden, 2014; Swift et al., 2012; van Leeuwen et al., 2011), as well as family, social, and legal problems (Hser, Grella, Collins & Teruya, 2003).

The most frequent sequence of drug use involves initiation with legal substances, like tobacco, and followed by use of illicit substances like cannabis and then of cocaine and other stimulants (Mayet, Legleye, Chau & Falissard, 2010; Mayet, Legleye, Chau & Falissard, 2011; Mayet, Legleye, Falissard & Chau, 2012; Secades-Villa, Garcia-Rodríguez, Jin, Wang & Blanco, 2015). In spite of this progression having been found to be stable over time in different countries and samples, two important aspects must be taken into account. First, heavy drug-users are less likely to follow the typical sequence of use (Mackesy-Amiti, Fendrich & Goldstein, 1997), this population being particularly relevant when it comes to establishing preventive measures: those youths who are most at risk of becoming serious drug users may be the ones who are least likely to follow the typical sequence of drug use initiation (Mackesy-Amiti, Fendrich & Goldstein, 1997). Second, initiation sequences, despite having a more or less defined pattern, have been shown to vary with the age when the initiation occurs (Patrick et al., 2011), especially true for the earlier ages (Moss, Chen & Yi, 2014).

The drugs scene in Spain has changed in the last two decades. Incidence rates for heroin use have decreased and have remained very low in recent years (Sánchez-Niubò et al., 2009; Sánchez-Niubò et al., 2013). However, life-time prevalence of cannabis and cocaine use are among the highest in the European Union –EU– (European Monitoring Centre for Drugs and Drug Addiction, 2016). Moreover, last year use of cannabis increased from 14.5% in 1995 to 32.1% in 2009, and that for cocaine from 3.4 to 10.2% over the same period (Observatorio Español de la Droga y las Toxicomanías, 2014). Nevertheless, incidences of cocaine and cannabis although very high, seemed stable since the year 2000 (standardized rates: around 9 per 1,000) (Sánchez-Niubò, Sordo, Fortiana, Brugal & Domingo-Salvany, 2013). More specifically, the highest incidences were for those aged 15-19 both in males and females (Sánchez-Niubò, Sordo, Fortiana, Brugal & Domingo-Salvany, 2013), and the differences between sexes have been narrowing in recent birth cohorts (Colell, Sánchez-Niubò & Domingo-Salvany, 2013). Tobacco incidence rates are not available, nevertheless the slight decrease of prevalence

between 2003 and 2009 may indicate a possible decrease of incidence (Observatorio Español de la Droga y las Toxicomanías, 2014). Of interest, women have experienced a growing and earlier incorporation to tobacco use in recent cohorts achieving the rates in men (Colell, Sánchez-Niubò & Domingo-Salvany, 2013).

These changes, also observed in neighboring countries (European Monitoring Centre for Drugs and Drug Addiction, 2016), have not been followed by any research on age of onset and progression patterns. Identifying onset of drug use would be helpful to indicate prevention efforts as well as its relation with future drug use.

Therefore, the main aim of the present work was to retrospectively study the onset and progression sequence of the most frequent pathways of drug use initiation in a sample of the Spanish general population and observe their evolution in different birth cohorts.

Material and Methods

All data were drawn from the Household Survey on Alcohol and Drugs (EDADES) 2011 (Delegación del Gobierno para el Plan Nacional sobre Drogas, 2011). EDADES is a biennial nationwide representative household survey carried out since 1995 to monitor use, perceptions and opinions of non-institutionalized 15–64-year-old residents in Spain with respect to alcohol and drug consumption. This study used the information obtained in Catalonia, the second largest region of Spain. Sampling followed a three-stage clustering design (census tract, household and random individual) without substitution in urban and rural populations. Participation rates were over 50%, samples being previously oversized to achieve desired effective numbers. The survey was self-administered and collected through a household survey. The final sample was of 2,069 individuals and had the same age distribution as the general population.

For the purposes of this study, we considered the age of onset of four behaviors: tobacco use (range: 6-48), daily tobacco use (range: 10-49), cannabis use (range: 11-45) and cocaine use (range: 12-40). All analyses were adjusted by sex and the following year birth cohorts: <1965, 1965-1974, 1975-1984 and 1985-1996. These birth cohorts correspond to the following ages at the time of the survey: >46, 37-46, 27-36 and 15-26. For inference to the whole population, individuals were weighted according to sampling design.

Age at first alcohol use was not included due to the high prevalence of ever alcohol use in Spain (91% in 2011), and because the association with initiation of other substances could be rather vague and uninformative (Golpe, Isorna, Barreiro, Braña & Rial, 2017; Teixidó-Compañó et al., 2019). On the other hand, as information about onset age of daily tobacco use was available, tobacco use ever, despite being prevalent (72% in 2011), was considered for comparisons.

Descriptive analyses were performed with medians of ages of drug initiation by sex and birth cohorts. Progressions of drug initiation were pictured by quantifying the transitions from a previous state in terms of the number of individuals and weighted percentages. As ages of onset are discrete integer values, coincidences were found between the ages of onset of different substances. To solve this problem, we considered the following ordered pattern: tobacco, daily tobacco, cannabis and cocaine; i.e., if onset age of tobacco use coincided with cannabis, we considered tobacco use earlier than cannabis. These assumptions were based on National data (Observatorio Español de la Droga y las Toxicomanías, 2014). Nevertheless, ties following other ordering patterns were checked.

Survival analyses were employed to assess the most prevalent pathways found in the descriptive analysis, while taking into account censures for individuals who have not yet had a chance to start using a drug. Specifically, we used additive hazard regression which can provide a better picture of how effects of covariates develop over time than Cox regression models (Aalen, Borgan & Gjessing, 2008). Parameters of these models are arbitrary cumulative regression functions that represent the cumulative excess risk at each unit of time and are useful to assess changes over time graphically (Xie et al., 2013). Events in each survival analysis were the ages at first use of cannabis and of cocaine. People not reporting the event in the period of observation were considered censures at the age of the survey. In the analyses for both substances, cumulative excess risk estimates were obtained for the categories: having never smoked tobacco (reference category), having ever

smoked but not daily, and having ever smoked daily, always previous to the event. Also for cocaine, cumulative excess risk estimates were obtained from those having never used cannabis (reference category) to having ever used cannabis, previous to the event. Note that onset ages for tobacco and cannabis were treated as time-varying covariates.

All analyses were done with R (R Foundation for Statistical Computing, 2015) and survival analyses with the R package “survival” (Therneau & Grambsch, 2000).

Results

1,498 (72.4%) individuals reported at least one behavior: 1,473 tobacco use, 947 of them being daily tobacco users, 631 cannabis use and 183 cocaine use. Weighted medians and confidence interval of age of onset by behaviour and stratified by sex and birth cohorts are shown in table 1. We observe that onset age medians were ordered by tobacco, daily tobacco, cannabis and cocaine and have decreased over the years since 1965. Furthermore, age ranges differ between birth cohorts, median age in more recent cohort tending to be lower than those in older cohorts. Median ages for tobacco use ever and daily, were equal for males and females, whereas for cannabis and cocaine, those for males were lower, although in general not significantly.

Figure 1 shows all possible pathway combinations of the progression of drug use initiation found in the sample. Among the 143 individuals who had initiated all four considered behaviors, the most frequent pathway was tobacco- daily tobacco- cannabis- cocaine (92 individuals). The

Table 1. Age of first use of selected behaviors by birth cohort and sex.

Weighted Median Age (CI 95%)	Females				Males				TOTAL
	Birth cohorts								
	> 1965 n med. CI95%	1965 - 1974 n med. CI95%	1975 - 1984 n med. CI95%	1985 - 1996 n med. CI95%	> 1965 n med. CI95%	1965 - 1974 n med. CI95%	1975 - 1984 n med. CI95%	1985 - 1996 n med. CI95%	
Age of survey	250 55 (54, 56)	239 41 (40, 42)	285 32 (31, 32)	247 22 (21, 23)	241 55 (54, 57)	247 41 (40, 41)	299 32 (31, 32)	261 22 (20, 23)	2069
1 st tobacco use	155 17 (16, 18)	165 16 (16, 16)	186 16 (16, 16)	141 15 (15, 16)	209 16 (15, 16)	210 16 (16, 17)	231 16 (16, 16)	176 15 (15, 16)	1473
1 st tobacco use non daily users ever	68 16 (16, 18)	57 17 (15, 18)	84 16 (16, 17)	54 15 (15, 16)	46 17 (15, 18)	63 17 (16, 18)	71 16 (15, 17)	83 16 (15, 16)	526
1 st tobacco use daily users ever	87 18 (18, 20)	108 18 (17, 18)	102 17 (16, 18)	87 16 (15, 17)	163 18 (17, 18)	147 18 (17, 18)	160 17 (17, 18)	93 16 (16, 17)	947
1 st cannabis use	27 20 (18, 24)	42 20 (18, 22)	64 18 (17, 18)	83 17 (16, 17)	52 19 (18, 21)	108 18 (18, 18)	139 17 (17, 18)	116 16 (16, 17)	631
1 st cannabis use non-tobacco users	4 23 (17, 29)	7 17 (16, 20)	16 17 (16, 18)	20 16 (15, 18)	10 18 (17, 18)	26 17 (15, 18)	48 16 (16, 17)	36 15 (15, 17)	167
1 st cannabis use tobacco users non daily ever	4 24 (18, 54)	7 18 (16, 25)	19 18 (16, 19)	20 16 (15, 17)	8 20 (15, 23)	15 18 (17, 20)	20 17 (16, 19)	34 16 (16, 17)	127
1 st cannabis use tobacco users daily ever	19 19 (18, 20)	28 20 (18, 24)	29 18 (16, 19)	43 17 (16, 17)	34 20 (18, 21)	67 18 (18, 20)	71 18 (17, 18)	46 17 (16, 17)	337
1 st cocaine use	9 20 (18, 24)	10 25 (20, 30)	18 20 (20, 21)	16 18 (17, 20)	13 21 (18, 26)	41 20 (20, 22)	58 19 (18, 20)	18 18 (17, 19)	183
1 st cocaine use non-tobacco users	1 32 n/a	0 n/a	1 22 n/a	2 16 (16, 18)	2 18 (18, 40)	3 17 (14, 25)	8 18 (15, 20)	2 17 (17, 19)	19
1 st cocaine use tobacco users non daily ever	2 21 (20, 24)	1 25	6 20 (18, 24)	1 20 n/a	2 26 (26, 28)	4 21 (20, 25)	7 20 (15, 25)	5 18 (18, 18)	28
1 st cocaine use tobacco users daily ever	6 20 (18, 23)	9 25 (19, 31)	11 20 (19, 20)	13 18 (17, 20)	9 20 (18, 24)	34 20 (20, 22)	43 19 (18, 20)	11 17 (16, 19)	136
1 st cocaine use non-cannabis users	4 21 (18, 24)	2 25 (22, 35)	2 19 (18, 23)	1 15 n/a	1 40 n/a	4 23 (14, 23)	3 21 (20, 24)	0 n/a	17
1 st cocaine use cannabis users	5 20 (18, 30)	8 25 (20, 25)	16 20 (20, 20)	15 18 (17, 20)	12 20 (18, 25)	37 20 (20, 22)	55 18 (18, 20)	18 18 (17, 19)	166

second most frequent pathway was tobacco- cannabis- daily tobacco- cocaine (26 individuals).

Coincidences in the age of onset of some behaviors were relatively frequent, such as tobacco and cannabis use (n = 117, 19% of people with both behaviors), daily tobacco and cannabis use (n=111, 24% of cannabis users) and ever tobacco, daily tobacco and cannabis use (n=56, 12% of people with the three behaviors). Ties with cocaine were with cannabis (n=24, 14% of cocaine users), tobacco (n=6, 3%) and daily tobacco (n=8, 5%). As a sensitivity study, when the age of onset in both behaviors was coincident the assumption that cannabis had been used before tobacco was considered. In that case, the number of individuals in the pathway tobacco- daily tobacco- cannabis- cocaine would have decreased from 92 to 57 individuals, still remaining as the most frequent pathway. Also, the second most frequent pathway would have increased from 26 to 35 individuals, and the third most frequent pathway would have been cannabis- tobacco- daily tobacco- cocaine increasing from 7 to 33 individuals.

The additive hazard regression model with the age at first cannabis use as outcome was used to obtain the cumulative excess risk estimates and 95% confidence intervals over time in terms of age for the variables sex, birth cohort and previous tobacco use. The most relevant results were the following: males had a steep significant slope between 16 and 25 years old maintained afterwards as a cumulative

excess risk of around 0.12 over females. Compared to never smoked tobacco, ever smoked tobacco (but never daily) had a significant slope from age 15 to 18 reaching a cumulative excess risk of around 0.12 maintained afterwards; and, ever daily tobacco use surpassed the previous category in the age of 19 to a cumulative excess risk of around 0.2, following a smooth slope afterwards. Each younger cohort had a significant higher slope reaching cumulative excess risks of around 0.15, 0.2 and 0.45, respectively, over the oldest cohort (see figure 2).

Regarding the results of the additive regression model with age of first cocaine use as outcome, and variables sex, birth cohort, and previous tobacco and cannabis use, the most relevant results were the following: males had a significant but very low cumulative excess risk between 18 and 21 years old, and later, between 27 and 35 years old had a cumulative excess risk of around 0.03. Ever smoked tobacco (but never daily) had a similar effect to never smoked; in contrast, ever daily tobacco and ever cannabis use had higher and significant slopes, between 17 and 24 years old for daily tobacco (a cumulative excess risk of around 0.03), and 26 years old for cannabis (around 0.17). Regarding birth cohorts, the one for 1965-1974 had a non-significantly different cumulative excess risk compared to the oldest cohort (see figure 3); the 1975-1984 birth cohort had a significant steep slope between 18 and 25 years old reaching a cumulative excess risk of around 0.06; the more recent cohort had a significant

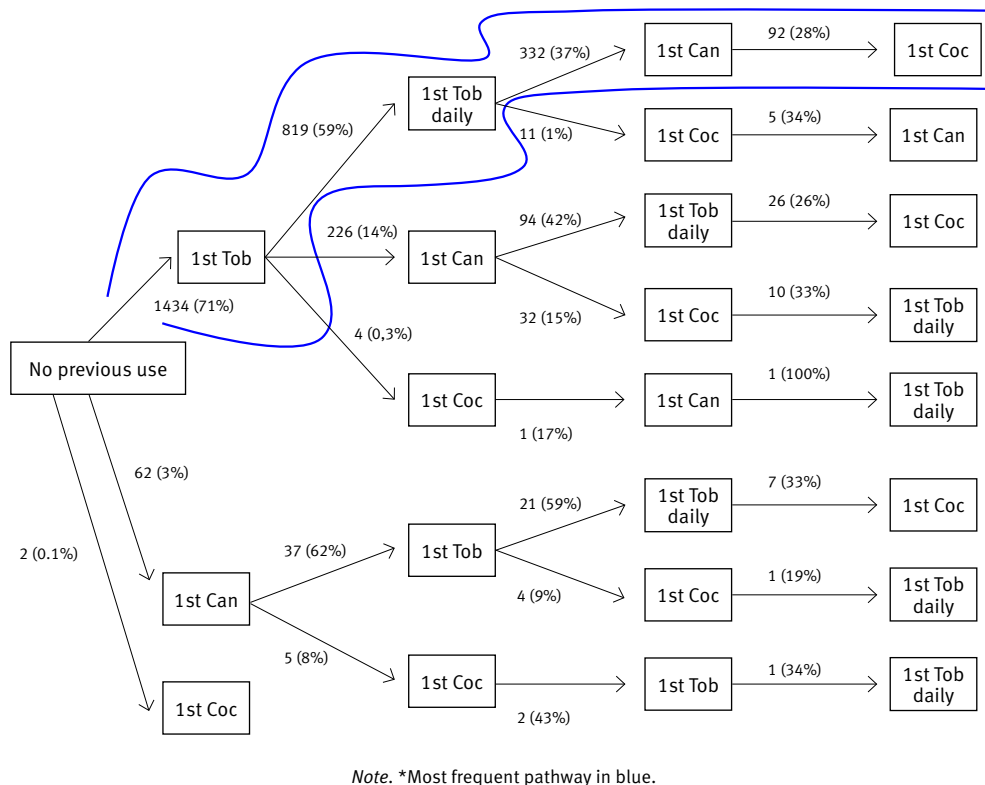
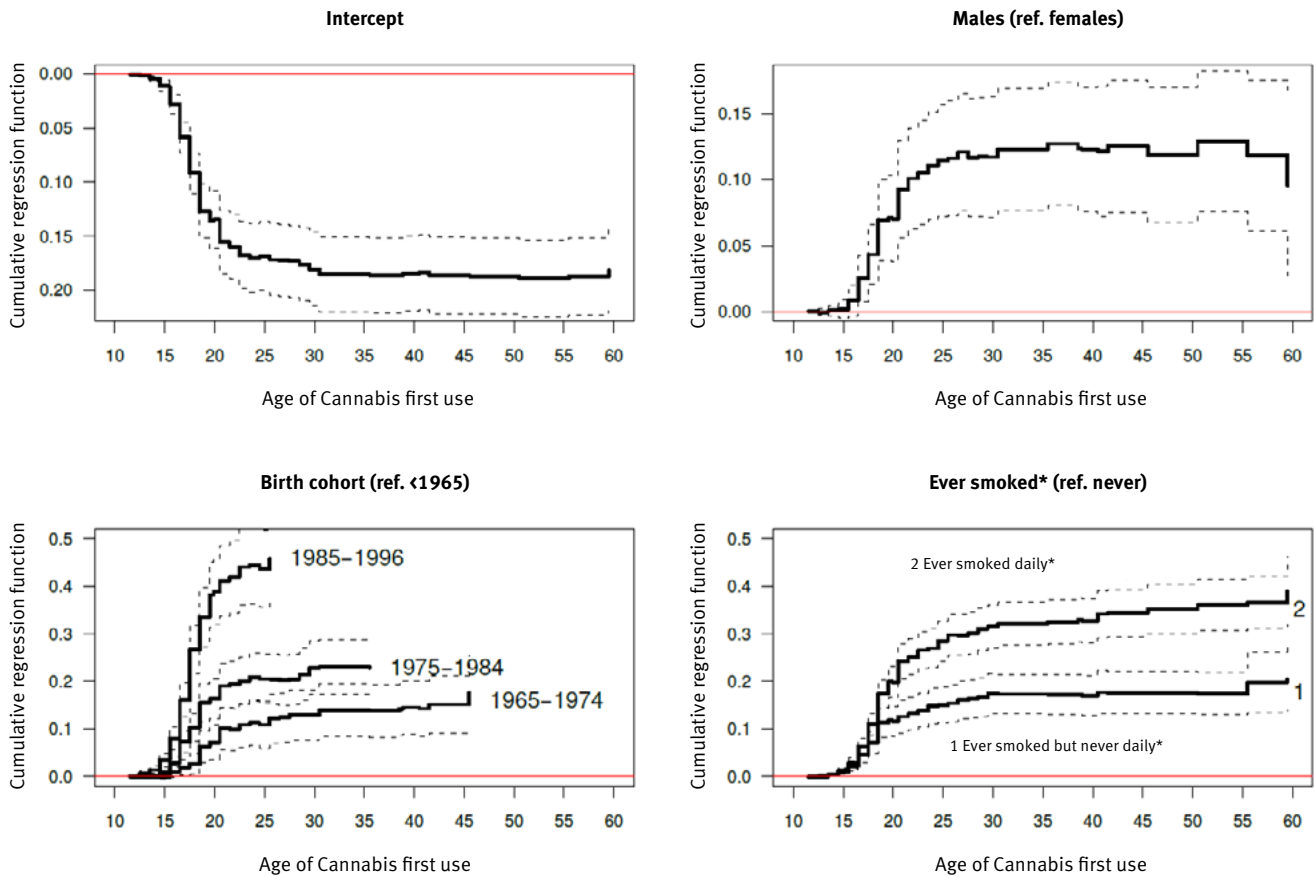


Figure 1. Progression of drug use initiation of 2,069 individuals: pathway combinations and their sample sizes and weighted percentages.



Note. *Previous first cannabis use.

Figure 2. Cumulative excess of risk for cannabis first use by sex, birth cohort and previous tobacco first use.

but lower slope than the previous cohort between 17 and 21 years old with a cumulative excess risk of around 0.03, but was not significant afterwards (see figure 3).

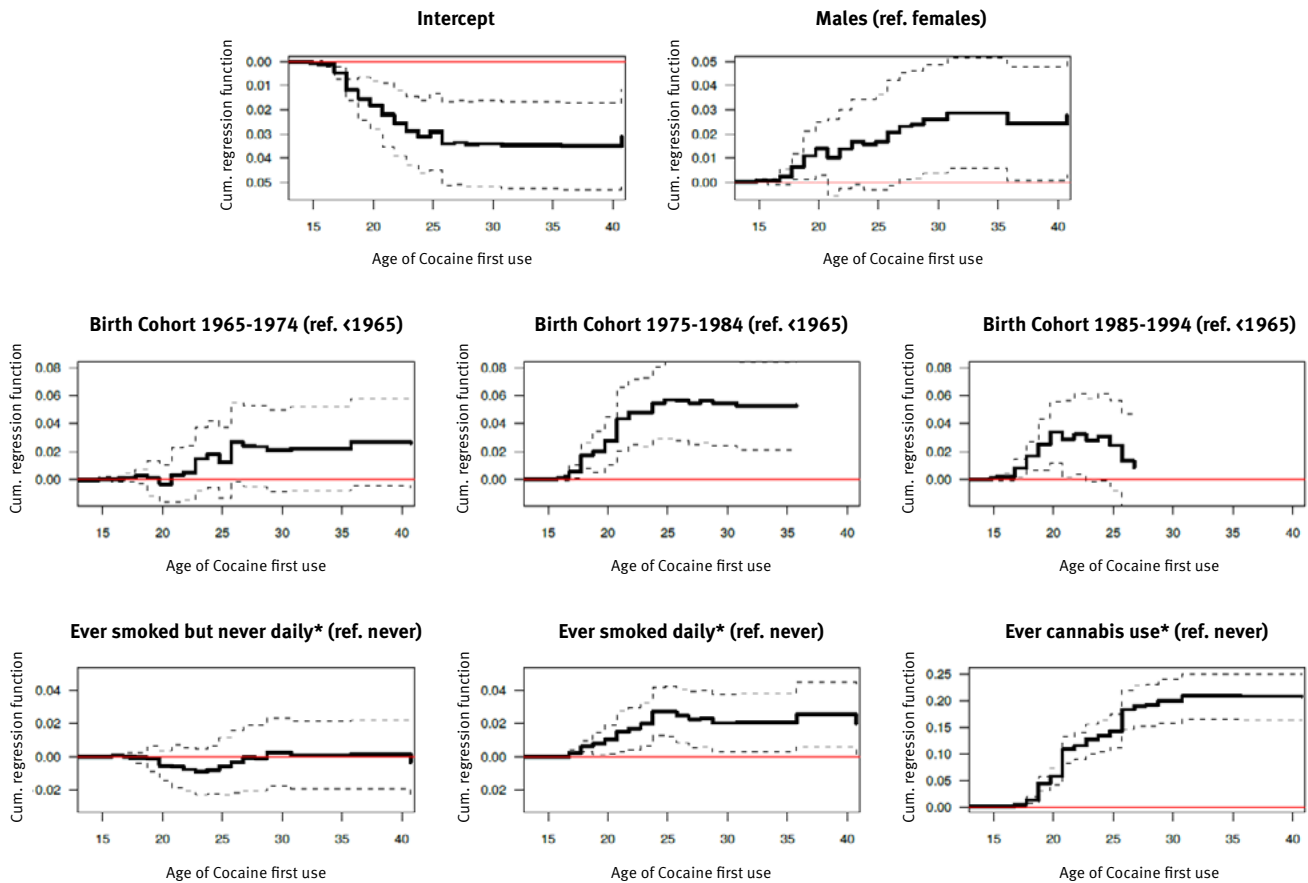
Discussion

Study findings show the expected usual progression in the age of starting use of different drugs: the most frequent progression in our sample is from first tobacco use to daily tobacco use, then to cannabis use and in a small proportion to cocaine use. Onset of consumption has changed over the years studied, being especially relevant the drop in age of onset, and the progressive acquisition by women of patterns considered masculine in previous generations.

Regarding progression of consumption, their interpretation under the Gateway theory (tobacco and alcohol could be considered as gateway substances to the use of certain other illicit drugs) should be done with caution. This theory has been heavily criticized and alternative theories have tried to address the development of involvement with psychoactive substances in the young: from the fact that what we call gateway substances are merely those substances which are most prevalent and hence accessible, to the fact that individual characteristics or environmen-

tal factors could explain the sequence better than the legal/illegal explanation (Mayet, Legleye, Beck, Falissard & Chau, 2016; Otten, Mun & Dishion, 2017; Vanyukov et al., 2012). Nevertheless, what nobody denies is the potential relevance of these repeatedly observed sequences in drug use initiation and the need for a better analysis of this phenomena. Some substances are consumed before others and a deeper study of their relationship would allow us to understand better drug use patterns and to provide adequate prevention and early intervention services for young people, especially youth at high-risk.

One of the most interesting findings of this study is the correlation between smoking and consumption of other drugs. Tobacco is not only the drug most used initially, but also its consumption is related with the subsequent increase in the consumption of other drugs. In this sense, this study shows an excess of risk in the relationship between tobacco and cannabis that had been pointed out before (Degenhardt et al., 2010; Mayet et al., 2012). In the specific case of Spain, the fact that the usual way to consume cannabis is smoking mixed with tobacco, could facilitate such an experience. Moreover, recent reports of the National Plan on Drugs for Spain have pointed out that incidence of cannabis is overtaking tobacco (Observatorio Español de la Dro-



Note. * Previous first cocaine use.

Figure 3. Cumulative excess of risk for cocaine first use by sex, birth cohort, previous tobacco and cannabis first use.

ga y las Toxicomanías, 2014). All this suggests, in line with findings of recent surveys conducted in Spain (Delegación del Gobierno para el Plan Nacional sobre Drogas, 2011), that people’s perceptions of the risks of tobacco and cannabis use are similar.

This study shows that the age of initiation of cannabis use has been decreasing in recent birth cohorts in both genders and among daily smokers. This trend has been reported previously in the European context in those countries that have produced a recent survey estimate (since 2013) (European Monitoring Centre for Drugs and Drug Addiction, 2016). This fact is important by itself (younger, more vulnerable, people starting earlier) as well as for its implications for the future: there is a relationship between early age of onset of a substance with more persistence of its use and more severe behavioural problems related to it (Poudel & Gautam, 2017).

For first ever cocaine use, the two more recent birth cohorts had a substantial excess of risk over the previous birth cohorts, also a significant increase for cannabis smokers, and a small but significant increase in risk from never to daily tobacco smokers. Once initiated in the illicit use of cannabis, the risk of initiating cocaine seems to be substantial. Initiating cannabis use may not be a direct cause of on-

set of cocaine use but rather a mediator that increases the risk of cocaine use. This could be explained by factors such as substance availability and also selection of drug-using friends contributing to the progression to potentially more rewarding and damaging illicit drugs as well as a reduction in risk perception (Otten et al., 2017).

In short, this study indicates (especially in older cohorts) that the ages of onset of consumption vary depending on whether other substances have been consumed previously (Patrick et al., 2011). Tobacco over cannabis and both over cocaine, appear to have the capacity to modify the onset and progression of drug use. For this reason, it is necessary to emphasize the need to make an effort to prevent (or delay) initiation of drugs, especially that of cannabis.

Our findings also highlighted the fact that the gender-gap in lifetime occurrence of substance use is narrowing (cannabis and cocaine) and even reversing (tobacco) in the more recent cohorts. This has been pointed out by a previous study in a wider context (Colell et al., 2013). Also outside of Spain or even Europe, similar results have been observed (Degenhardt, Lynskey & Hall, 2000; Degenhardt, Chiu, Sampson, Kessler & Anthony, 2007; Johnson & Gerstein, 1998; Johnson & Gerstein, 2000; Kerr, Greenfield, Bond, Ye & Rehm, 2004). This trend is parallel to the

change of roles of women in society, with evidence about possible specific preventive interventions being very limited (Stockings et al., 2016). More research along these lines is needed.

The findings of this study should be interpreted in the light of its limitations. As we are dealing with data from a cross-sectional study to build a retrospective cohort, selection bias should be taken into account. We handled data from birth cohorts that have been followed up to 2011. Moreover, the survey was home-based, so institutionalized and homeless people were not included. So, deaths previous to 2011 and institutionalized or homeless people were not considered even as censures in the survival analysis; this can lead to a selection bias if these people are not represented in the observed sample. Furthermore, we shouldn't forget the difficulty to include subjects with more extreme patterns of substance use as they are likely not to be considered in the Census and probably exhibit atypical initiation sequences (Mackesy-Amiti et al., 1997).

Regarding coincidences between age of onset for the different substances, we found that even assuming cannabis use prior to tobacco use in all cases, the most frequent pattern remained the same. Adding the fact that we are dealing with the general population, our results support previous studies that showed a similar sequence in drug use initiation. But some considerations should be taken into account: in most of the cases their first use was just mixing tobacco and cannabis, and this could lead to later daily tobacco use and subsequently use of cocaine. So, it is of concern that using the same route of administration may lead to a higher risk of subsequent dependence on tobacco and to trying other illicit drugs. Besides our analysis could not take into account how many were experimental users, and how many became regular cannabis or cocaine users, since the only data available for these substances was whether they had ever been used. Finally, it is important to point out that the sample of 2,069 individuals may be considered representative of the autonomous region of Catalonia, but its extrapolation to other communities is questionable due to different regional plans of addiction disorders.

The present study describes and reinforces the commonly accepted sequence pattern of drug use initiation for Catalonia, which has not changed recently, although we do observe a drop in age of onset, and certain changes in patterns of relationship between different substances. There is a need to promote studies analysing the underlying mechanisms of the progression and its real causes through the incorporation of appropriate questions in surveys, for example, about social habits, risk perceptions and mental disorders. Health policies and prevention strategies should try to act in three different areas: 1) Raising risk perception of legal substances; 2) Delaying age of onset of consumption of all drugs (legal and illegal) using effective measures; and 3) Separating cocaine from cannabis, giv-

en the difference in magnitude of harm related with each substance: separation of the information provided about them, as well as their markets.

Funding

Funding for this study was provided by Spanish Government Grant: Instituto de Salud Carlos III -FIS PI11/01358. Further financial support was provided by the Spanish Network on Addictive Disorders, grant numbers RD12/0028/0018 and RD16/00170013.

Writing of the paper was partially supported by Rio Hortega contract (CM14/00012).

Competing interests

All authors have no relationships or activities that could appear to have influenced the submitted work.

References

- Aalen, O. O., Borgan, Ø. & Gjessing, H. K. (2008). Survival and event history analysis: a process point of view. New York, NY: Springer. Retrieved at <https://www.springer.com/la/book/9780387202877>.
- Anthony, J. C. (2012). Steppingstone and gateway ideas: a discussion of origins, research challenges, and promising lines of research for the future. *Drug and Alcohol Dependence*, 123, S99-S104. doi:10.1016/j.drugalcdep.2012.04.006.
- Baggio, S., Studer, J., Deline, S., N'Goran, A., Dupuis, M., Henchoz, Y. & Gmel, G. (2014). Patterns and Transitions in Substance Use Among Young Swiss Men: A Latent Transition Analysis Approach. *Journal of Drug Issues*, 44, 381-393. doi:10.1177/0022042614526996.
- Choo, T., Roh, S. & Robinson, M. (2008). Assessing the "Gateway Hypothesis" among Middle and High School Students in Tennessee. *Journal of Drug Issues*, 38, 467-492. doi:10.1111/j.1467-9507.2008.00459.x.
- Colell, E., Sánchez-Niubò, A. & Domingo-Salvany, A. (2013). Sex differences in the cumulative incidence of substance use by birth cohort. *The International Journal on Drug Policy*, 24, 319-325. doi:10.1016/j.drugpo.2012.09.006.
- Degenhardt, L., Chiu, W. T., Sampson, N., Kessler, R. C. & Anthony, J. C. (2007). Epidemiological patterns of extra-medical drug use in the United States: evidence from the National Comorbidity Survey Replication, 2001-2003. *Drug and Alcohol Dependence*, 90, 210-223. doi:10.1016/j.drugalcdep.2007.03.007
- Degenhardt, L., Dierker, L., Chiu, W. T., Medina-Mora, M. E., Neumark, Y., Sampson, N., Kessler, R. C. (2010). Evaluating the drug use «gateway» theory using cross-national data: consistency and associations of the order of initiation of drug use among participants in the WHO

- World Mental Health Surveys. *Drug and Alcohol Dependence*, 108, 84-97. doi:10.2105/ajph.88.1.27.
- Degenhardt, L., Lynskey, M. & Hall, W. (2000). Cohort trends in the age of initiation of drug use in Australia. *Australian and New Zealand Journal of Public Health*, 24(4), 421-426. doi:10.1111/j.1467-842X.2000.tb01605.x.
- Delegación del Gobierno para Plan Nacional sobre Drogas. (2011). Encuesta sobre alcohol y drogas en España (EDADES) 2011/12. Madrid: Ministerio de Sanidad, Servicios Sociales e Igualdad. Retrieved at <http://www.pnsd.mssi.gob.es/profesionales/sistemasInformacion/sistemaInformacion/pdf/EDADES2011.pdf>.
- DuRant, R. H., Smith, J. A., Kreiter, S. R. & Krowchuk, D. P. (1999). The relationship between early age of onset of initial substance use and engaging in multiple health risk behaviors among young adolescents. *Archives of Pediatrics & Adolescent Medicine*, 153, 286-291. doi:10.1016/j.dcn.2015.07.002.
- European Monitoring Centre for Drugs and Drug Addiction (2016), European Drug Report 2016: Trends and Developments, Publications Office of the European Union, Luxembourg. (s. f.). Retrieved at http://www.emcdda.europa.eu/publications/edr/trends-developments/2016_en.
- Fergusson, D. M. & Boden, J. M. (2014). Commentary on Prince van Leeuwen et al. (2014): Tobacco and cannabis use. *Addiction*, 109, 312-313. doi:10.1111/add.12417.
- Golpe, S., Isorna, M., Barreiro, C., Braña, T. & Rial, A. (2017). Binge drinking among adolescents: prevalence, risk practices and related variables. *Adicciones*, 29, 256-267. doi:10.20882/adicciones.932.
- Hser, Y.-I., Grella, C. E., Collins, C., & Teruya, C. (2003). Drug-use initiation and conduct disorder among adolescents in drug treatment. *Journal of Adolescence*, 26, 331-345. doi:10.1016/S0140-1971(03)00012-5.
- Johnson, R. A. & Gerstein, D. R. (1998). Initiation of use of alcohol, cigarettes, marijuana, cocaine, and other substances in US birth cohorts since 1919. *American Journal of Public Health*, 88, 27-33. doi:10.1177/002204260103100412.
- Johnson, R. A. & Gerstein, D. R. (2000). Age, period, and cohort effects in marijuana and alcohol incidence: United States females and males, 1961-1990. *Substance Use & Misuse*, 35, 925-948. doi:10.3109/10826080009148427.
- Kerr, W. C., Greenfield, T. K., Bond, J., Ye, Y. & Rehm, J. (2004). Age, period and cohort influences on beer, wine and spirits consumption trends in the US National Alcohol Surveys. *Addiction*, 99, 1111-1120. doi:10.1111/j.1360-0443.2004.00820.x.
- Mackesy-Amiti, M. E., Fendrich, M. & Goldstein, P. J. (1997). Sequence of drug use among serious drug users: typical vs atypical progression. *Drug and Alcohol Dependence*, 45, 185-196. doi:10.1016/S0376-8716(97)00032-X.
- Mayet, A., Legleye, S., Beck, F., Falissard, B. & Chau, N. (2016). The Gateway Hypothesis, Common Liability to Addictions or the Route of Administration Model A Modelling Process Linking the Three Theories. *European Addiction Research*, 22, 107-117. doi:10.1159/000439564.
- Mayet, A., Legleye, S., Chau, N. & Falissard, B. (2010). The mediation role of licit drugs in the influence of socializing on cannabis use among adolescents: A quantitative approach. *Addictive Behaviors*, 35, 890-895. doi:10.1016/j.addbeh.2010.06.001.
- Mayet, A., Legleye, S., Chau, N. & Falissard, B. (2011). Transitions between tobacco and cannabis use among adolescents: a multi-state modeling of progression from onset to daily use. *Addictive Behaviors*, 36, 1101-1105. doi:10.1016/j.addbeh.2011.06.009.
- Mayet, A., Legleye, S., Falissard, B. & Chau, N. (2012). Cannabis use stages as predictors of subsequent initiation with other illicit drugs among French adolescents: use of a multi-state model. *Addictive Behaviors*, 37, 160-166. doi:10.1016/j.addbeh.2011.09.012.
- Moss, H. B., Chen, C. M. & Yi, H.-Y. (2014). Early adolescent patterns of alcohol, cigarettes, and marijuana polysubstance use and young adult substance use outcomes in a nationally representative sample. *Drug and Alcohol Dependence*, 136, 51-62. doi:10.1016/j.drugalcdep.2013.12.011.
- Observatorio Español de la Droga y las Toxicomanías (Ed.). (2014). Informe 2013. Alcohol, tabaco y drogas ilegales en España. Retrieved at http://www.pnsd.mssi.gob.es/profesionales/sistemasInformacion/informes-Estadisticas/pdf/2_Informe_2013.pdf.
- Otten, R., Mun, C. J. & Dishion, T. J. (2017). The social exigencies of the gateway progression to the use of illicit drugs from adolescence into adulthood. *Addictive Behaviors*, 73, 144-150. doi:10.1016/j.addbeh.2017.05.011.
- Patrick, M. E., Schulenberg, J. E., O'Malley, P. M., Maggs, J. L., Kloska, D. D., Johnston, L. D. & Bachman, J. G. (2011). Age-related changes in reasons for using alcohol and marijuana from ages 18 to 30 in a national sample. *Psychology of Addictive Behaviors: Journal of the Society of Psychologists in Addictive Behaviors*, 25, 330-339. doi:10.1037/a0022445.
- Poudel, A. & Gautam, S. (2017). Age of onset of substance use and psychosocial problems among individuals with substance use disorders. *BMC Psychiatry*, 17, 10. doi:10.1186/s12888-016-1191-0.
- R Foundation for Statistical Computing (Ed.). (2015). *R: A language and environment for statistical computing*. Vienna, Austria. Retrieved at <http://www.R-project.org/>.
- Sánchez-Niubò, A., Aalen, O. O., Domingo-Salvany, A., Amundsen, E. J., Fortiana, J. & Røysland, K. (2013). A multi-state model to estimate incidence of heroin use. *BMC Medical Research Methodology*, 13, 4. doi:10.1186/1471-2288-13-4.
- Sánchez-Niubò, A., Fortiana, J., Barrio, G., Suelves, J. M., Correa, J. F. & Domingo-Salvany, A. (2009). Problema-

- tic heroin use incidence trends in Spain. *Addiction*, *104*, 248-255. doi:10.1111/j.1360-0443.2008.02451.x.
- Sánchez-Niubò, A., Sordo, L., Fortiana, J., Brugal, M. T. & Domingo-Salvany, A. (2013). Incidence trends of cannabis and cocaine use from periodic Spanish general population surveys: effect of standardizing results by age structure. *Addiction*, *108*, 1450-1458. doi:10.1111/add.12170.
- Secades-Villa, R., Garcia-Rodríguez, O., Jin, C. J., Wang, S. & Blanco, C. (2015). Probability and predictors of the cannabis gateway effect: a national study. *The International Journal on Drug Policy*, *26*, 135-142. doi:10.1016/j.drugpo.2014.07.011.
- Stockings, E., Hall, W. D., Lynskey, M., Morley, K. I., Reavley, N., Strang, J., ... Degenhardt, L. (2016). Prevention, early intervention, harm reduction, and treatment of substance use in young people. *Lancet Psychiatry*, *3*, 280-296. doi:10.1016/S2215-0366(16)00002-X.
- Swift, W., Coffey, C., Degenhardt, L., Carlin, J. B., Romaniuk, H. & Patton, G. C. (2012). Cannabis and progression to other substance use in young adults: findings from a 13-year prospective population-based study. *Journal of Epidemiology and Community Health*, *66*, e26. doi:10.1136/jech.2010.129056.
- Teixidó-Compañó, E., Sordo, L., Bosque-Prous, M., Puigcorbó, S., Barrio, G., Brugal, M.T.,... Espelt A. (2019). Individual and contextual factors related to binge drinking among adolescents in Spain: a multilevel approach. *Adicciones*, *31*, 33-40. doi:10.20882/adicciones.975.
- Therneau, T. M. & Grambsch, P. M. (2000). *Modeling survival data: extending the Cox model*. New York: Springer.
- van Leeuwen, A. P., Verhulst, F. C., Reijneveld, S. A., Vollenbergh, W. A. M., Ormel, J. & Huizink, A. C. (2011). Can the gateway hypothesis, the common liability model and/or, the route of administration model predict initiation of cannabis use during adolescence? A survival analysis—the TRAILS study. *The Journal of Adolescent Health*, *48*, 73-78. doi:10.1016/j.jadohealth.2010.05.008.
- Vanyukov, M. M., Tarter, R. E., Kirillova, G. P., Kirisci, L., Reynolds, M. D., Kreek, M. J. & Ridenour, T. A. (2012). Common liability to addiction and «gateway hypothesis»: theoretical, empirical and evolutionary perspective. *Drug and Alcohol Dependence*, *123*, S3-17. doi:10.1016/j.drugalcdep.2011.12.018.
- Xie, X., Strickler H. D. & Xue, X. (2013). Additive Hazard Regression Models: An Application to the Natural History of Human Papillomavirus. *Computational and Mathematical Methods in Medicine*, 796270. doi:10.1155/2013/796270.