Tobacco and cannabis use trajectories from adolescence to young adulthood

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INTRODUCTION

Adolescence is no longer described exclusively as an inevitable period of storm and stress(1). Even so, substance use and its related disorders are significant problems appearing mostly during adolescence and young adulthood(2). Being a public health issue of great concern, substance use is also one of the major social and legal challenges of our modern world(3). The possible adverse consequences related to the use or abuse of any drug are global and touch individuals physically, socially and psychologically(3). Because key determinants of later adult health develop during the teenage years, substance use is therefore a subject of utmost importance during this period(4).

As adolescents continue to use illicit and legal substances at alarming rates(4;5), the investigation of the recent changes in the prevalence of their use continues to be necessary. Thus, several surveys keep tracking those trends internationally(6;7). Switzerland, in regard to substance use, seems to exhibit a particular status. In fact, despite the recent reduction seen in the use of several substances, Swiss adolescents remain among the highest cannabis users in Europe. This observation is however not valid regarding all drugs as rates of other substances usually initiated during adolescence, such as tobacco and alcohol, are positioned near international average.

Differing by their singular psychoactive effects and by their health consequences, some significant relations have however been found between many substances used during adolescence. Indeed, substances such as tobacco and cannabis seem intrinsically linked on many aspects. The fact that both substances are smoked(8), their pattern of use across adolescence(2) and their level of dependence being influenced when concomitantly used(9) are only some examples of those significant connections. In addition, consumption of both tobacco and cannabis are associated with alcohol and ecstasy use and to other drugs as well(10). As concurrent use of multiple drugs is now becoming relatively common(11), growing attention is oriented to predict the course over time of their use and possible interactions. Common risk and protective factors for substance use are also being closely examined to better understand which adolescents are at risk for adverse health outcomes.

As prevention and early intervention programs continue to be the most cost-effective solutions regarding substance use and its related problems(5), research examining the epidemiology of legal and illegal drug use, and the complex associations existing between them, remains of main interest. As not every adolescent having used substances still uses them at an older age, understanding substance use trajectories and factors influencing their courses are imperative to plan adequate interventions and, consequently, improve adolescent health.

Relationship between substances

Several associations have been found between substances of possible abuse (12). In particular, there is a significant relationship linking cannabis and tobacco(13-22). In addition, associations between those two substances and the use of other substances during adolescence has been proven as well(10;23;24).

Association between tobacco and cannabis

Cannabis and tobacco usually share the same route of administration(25) and, as a result, the gestures related to their consumption are similar(8;16;26). In a recent study by Agrawal and Lynskey, the association between cannabis and tobacco use has been found to be only significant when tobacco was smoked in comparison to smokeless tobacco use(27), adding to the notion that part of the relationship between those two substances comes from the act of smoking. Yet, tobacco and cannabis smoking have distinct smoking topography as marijuana smoking involves deeper inhalation and longer breath holding(28).

The association between tobacco and cannabis is also observed when, even among non-tobacco smokers, some tobacco is usually used to prepare cannabis cigarettes(8), a process called mulling (29), to ensure a smooth combustion of the preparation(30). This method has been proven to increase the amount of Tetrahidrocannabinol (THC) inhaled per gram of cannabis used by as much as 45% under certain conditions(31). This act of mixing cannabis and tobacco therefore increases the psychoactive effects of cannabis and is also, for some adolescents, a first exposition to tobacco(30).

Manifesting very different effects, active ingredients in tobacco and cannabis, respectively nicotine and THC, have been shown to have common neurological results, mostly via the dopaminergic system(30;32). Never been proven to our knowledge, cross-sensitization between nicotine and THC stays however plausible in light of former animal studies(32). As the adolescent brain continues to evolve with age until adulthood(33), the use of one substance during that critical period could then predispose to the consumption of other drugs due to prior sensitization(32).

Craving symptoms and even cessation attempts, when both substances are used simultaneously, seem also to display the firm link existing between tobacco and cannabis. Using tobacco in combination with cannabis contributes to cannabis dependence symptoms(9). Moreover, withdrawal symptoms during simultaneous cessation of both substances are more severe than for each substance separately(34). In the same way, treatment of cannabis dependence may be more effective if it addresses the issue of concurrent tobacco use(9).

It is noteworthy that cannabis use is almost systematically accompanied by tobacco use at some point during adolescence. French data indicate that the co-consumption of tobacco and cannabis is even on the rise(35). A recent Swiss report indicates that 4 out of every five current cannabis users are also cigarettes smokers(36). As tobacco use usually precedes the onset of cannabis use, research has mainly looked at tobacco as a risk factor for cannabis use(25). In fact, Kandel's gateway theory(37;38) postulates that both tobacco and alcohol use are the previous necessary steps to cannabis use, and then to other illegal drugs such as cocaine and heroin. This hypothesis implies 3 interrelated propositions(39): (1) sequencing implies that there is a common fixed sequence of substance initiation; (2) association of initiation implies that the use of one substance increases the likelihood of initiation of the other, and (3) causation, that the first substance causes the use of the second. Causation, a controversial proposition, has never been unequivocally proven. Consequently, the gateway theory stays for many authors a controversial hypothesis(32). However, drug policies in many countries are partly based on that assumption(40).

In contrast, recent research also indicates that cannabis use may precede(10;30) or be simultaneous(41) to tobacco use and that, in fact, its use may reinforce cigarette smoking(16;26) or lead to nicotine addiction independently of smoking status(25;30). This is defined as the reverse gateway theory(30). An Australian study(30) found that among non-smoking teens, at least one report of weekly cannabis use in adolescence predicted a more than eightfold increase in the odds of later initiation of tobacco use and that for 21-year-old smokers not yet nicotine-dependent, daily cannabis use raised the odds of nicotine dependence at the age of 24 years more than threefold after controlling for possible confounders. These data evidence that cannabis use during adolescence and young adulthood is associated with higher risk of tobacco initiation. Moreover, data from young adult American females (aged 18-29 years) show that women with a prior history of cannabis use are significantly more likely to transition from initiation to regular smoking, and from regular smoking to nicotine dependence(25). For some adolescents smoking cannabis has literally been described as having been either an introduction to smoking cigarettes, a reinforcement of their cigarette use or a barrier to quit tobacco(16). Most importantly, evidence now indicates that nicotine dependence and persistent cigarette smoking may be the main public health consequences of cannabis use(25). While US data report that only 7% of young adult females had used cannabis before tobacco(25), Swiss data among adolescents aged 16-20 years indicate that among current cannabis users 21% declare never having smoked a cigarette(36).

Association of tobacco and cannabis use with alcohol

The associations found among substances used during adolescence are not limited to the relation between tobacco and cannabis. In fact, alcohol use is predominant among adolescents smoking those substances. The majority of adolescent tobacco smokers also consume alcohol. In 2006, 25% of all adolescents aged 15 in a German sample reported recent concurrent use of both substances. Compared to consumers of alcohol only, those adolescents using both substances during the same period had significantly higher levels of consumption, more excessive use of alcohol, started to drink at an earlier age and showed a higher dependence score to nicotine(42). In addition, adolescent smokers are also known to have a 4.5-fold higher odds of alcohol use disorders than never smokers(43). Problematic drinking among adolescents is also associated with cannabis use(44;45). American longitudinal data even reported that use of cigarettes and marijuana at age 18 predicted heavy drinking at age 35(45).

Trajectories in substance use

Substance use along lifetime is not static. Some pathways of use are well known to exist for specific substances and recent studies continue to add knowledge on the influence that substances have on their trajectories when used concurrently. For instance, 95% of tobacco and cannabis users started to use the substance before the age of 20 years and their use seems to peak at age 19-21 to decrease afterwards(2;46). In addition, timing of initiation of one substance seems not only to influence its own use but the use of other substances too. As cannabis onset before late-adolescence predisposes to cannabis dependence (47), early cannabis use predicts other substance-related problems as well such as nicotine dependence(25;30). Similarly, early tobacco use is associated to the use of both alcohol(42;48) and illegal drugs such as ecstasy, cocaine or amphetamines at an older age(2). As timing of initiation of one drug influences diverse courses of substance use, intensity of use also seems to have a major importance on further consumption.

Being initiated on diverse moments and used at various intensities, substances used during adolescence and young adulthood may be examined within diverse pathways which can predict further type of use as outcomes. For instance, cannabis use initiated during early adolescence is associated to heavy cannabis use afterwards(2;49). When examined more closely, considerable heterogeneity exists in the developmental trajectories of substance use. Ellickson et al. reported that, using a sample of 5883 adolescents aged 13 who were followed until young adulthood (age 23), 4 trajectory groups were identified for cannabis use, after removal of abstainers: early high users, stable light users, steady increasers and occasional light users. Among those, abstainers consistently had the most favorable behavioral, socioeconomic and health outcome by age 29, whereas early high users, the least(46).

When several drugs are used at the same time, trajectories of use seem to become intrinsically joint. A recent examination of the co-occurrence of at least weekly cannabis use among low risk teenage alcohol users in an Australian cohort predicted a sevenfold higher rate of daily cannabis use in young adults and a twofold increase in high-risk alcohol use(23). Identification of those specific jointed trajectories, with substances sequencing of initiation and intensity of use turns out to be a complex task but also has some benefits. A study carried out in the United States, has evidenced that having maintained smoking cessation more than 12 months during adolescence was associated with significantly lower rates of future alcohol use disorders in young adults(24). Thus, the introduction of a change in the use of one substance may therefore be associated with a significant evolution on the consumption of concurrent substances. Additionally, the study of those concurrent consumptions is more than theoretical given the evidence that interventions such as policies affecting the use of one substance may affect the use of another substance (for example, the effect of pricing and age of legal use of alcohol reduces its consumption and influences cannabis use in the same direction) (50).

Trajectories of substance use are also influenced by crucial events happening during adolescence and young adulthood. In this sense, data from the US-based project *Monitoring The Future* show that life events such as being married, becoming a parent, being employed or attaining higher education are

associated to lower rates of cannabis use in young adulthood(51). The same can be said for cigarette smoking and heavy drinking(52;53). A Norwegian study(54) also found that, among adolescent and young adult women, life events such as childbirth, abortion or living with the father of the child have an influence on subsequent substance use.

It is also worth noting that adolescents using substances are at higher risk to become substance dependent as adults(52;55;56). Consequently, substance use also affects educational attainment and professional development. Smokers have lower academic aspirations than non-smokers(57) and young adults not enrolled in school are more likely to smoke(58). Cannabis use seems to decrease educational achievement in young people(59), and early marijuana users are more likely to have problems that limit the acquisition of skills necessary for employment(20). Early tobacco use(60) and the use of cannabis(61) or illegal drugs(62) have also been related to higher rates of school drop-out. Actually, school dropouts and unemployed adolescents are more likely to be using substances(63;64). Substance users are also more likely to skip classes(65). In fact, reducing substance use is associated with increased likelihoods of school attendance(66). Overall, adolescent substance use disorder is associated with less education and recent unemployment at age 30(56). Accordingly, cannabis abstainers from early adolescence through adulthood have the most favorable outcomes on behavioral, socioeconomic and health outcomes whereas early high users consistently have the least favorable outcomes(46). However, not all studies regarding adolescents and young adults who use substances confirm that substance use is solely associated with adverse outcomes. In fact, several studies reported that cannabis-only users, compared with abstainers, among a nationally representative sample of Swiss adolescents aged 16-20 years-old, reported similar academic performances(36) and were more socially driven(36;67). However, other results refute the idea that adolescents who abstain from substance use are socially maladjusted, and suggest instead that they function better than cannabis experimenters later in life(67).

A complete review of the literature can be found in Annex 1.

AIMS

The main objective of this longitudinal research is to answer the following question:

What is the relationship between tobacco and cannabis use trajectories from adolescence to young adulthood?

And more specifically we are interested in:

A. If the use of one of the substances (tobacco or cannabis) decreases overtime, does the use of the other one increase to compensate? Are other substances (such as alcohol, for example) also used to compensate in these cases?

B. Does the probability to become a tobacco smoker increase when cannabis use is heavier or has lasted longer?

C. What are the risk and protective factors that can predict that the use of tobacco and/or cannabis will increase or decrease overtime?

METHODS

Data

This project uses the TREE (Transitions from Education to Employment) data. This is a longitudinal survey based on a sample of more than 6000 young people living in Switzerland who participated in the PISA survey of the year 2000 and left compulsory school the same year. This sample has been followed up each year since then, for a total of seven waves (from T1:2001 to T7:2007). More information about the data and their use can be found on the project's home page (http://tree.unibas.ch).

Imputation of missing data

The analysis of substance use from the TREE database is especially difficult, because if only youths having responded to the substance use questions at every wave are taken into account, the remaining sample is quite small (n=1131) and little comparisons would be possible. The reason for having small numbers regarding substance use is due to the way TREE is run. At each wave, all youths receive a written questionnaire. If they do not respond, they answer a shorter telephone questionnaire. As the main goal of TREE is to assess the academic and professional trajectories of youths, substance use is omitted from the telephone questionnaire. This is the reason for missing data.

For the reason mentioned above, we decided to input missing data in order to have a larger sample to work on. Data imputation has been difficult because, to date, none of the other groups working on the TREE database had done so and no guidelines as how to do it had been set.

The TREE project being inscribed in a longitudinal framework, data of each wave are certainly not independent. It is then necessary to take their possible relations into account and to provide estimated values of missing data coherent not only in regard to other variables of the same wave (some values of these variables being maybe also missing), but also from one wave to another. Moreover, many of the variables are categorical rather than continuous. This is an additional level of difficulty, since the majority of models for missing data have been developed more specifically for continuous data.

Missing data can be of three different types: *Missing Completely At Random* (MCAR), *Missing At Random* (MAR), and *Missing Not At Random* (MNAR). We speak of MCAR when the missing data are a random sample of the entire dataset. This situation is very rare in practice. MAR means that the probability a particular data is missing does not depend on the missing data, but only on other variables of the dataset. For instance, if we know the sex of each subject, but if the weight of some subjects is missing, we could hypothesize that girls refuse to report their weight more often than boys, but that the fact to report or not the weight is independent from the weight itself. Finally, MNAR data are data whose probability of missing is influenced by the real non-observed value of the data. For instance, the probability of not reporting income could be positively correlated with the level of income. From a practical point of view, if the general mechanism of missing data if MAR, then it is possible to build statistical models for the relation between several variables, and then to use these models to obtain unbiased estimations of the missing data. Diagnostics exist to assess the missing data mechanism, but in practice we hypothesized that missing data in TREE are of the MAR kind.

Old approaches including complete-case analysis and replacement by the mean or the median are still used to deal with missing data, but they are acceptable only when the number of missing data is very small in regard of the total sample size, what is not the case here. Complete case analysis means that only subjects without any missing data on the variables of interest are included in the analysis, but as noted before, since many subjects have missing data regarding substance use, this approach is not feasible here. The replacement of missing observations by the mean or the median of available data reduces the diversity of observations, leading to an underestimation of the variance with known consequences such as wrong p-values and too narrow confidence intervals (68).

Among modern methods for handling missing data, we can distinguish between two approaches: model-based maximum likelihood (ML) estimation and multiple imputation. In the first approach, missing data are replaced by values maximizing the likelihood of a statistical model. The traditional algorithm to do so is the Expectation-Maximization (EM) algorithm (69), which converges surely to a maximum of the log-likelihood. The main drawback of this method is that if each missing data is replaced by only one estimated value, the result being a unique completed dataset *D1,* statistical results computed from this dataset can be biased if the estimated values are biased (for instance the estimated values tend to systematically overestimate the real non-observed value), and the variance of the statistics can be underestimated when the estimated values are less variable than the real non-observed values. We faced then the same problems already described in the case of a replacement by the mean or the median.

One of the best approaches to overcome this issue is currently the multiple imputation proposed by Rubin (70). This is a general procedure designed to respect the variability of data. Its principle is to independently generate not one, but *m* completed datasets *D1, …, Dm*. The statistics of interest are then computed on the *m* datasets and the results are combined in a straightforward manner into a single final statistics. It has been shown that the number *m* of completed datasets has not to be very large. Very good results can be achieved with *m* as low as 5.

Based on the general idea of multiple imputation, different procedures can be used for the practical estimation of the missing values. There is not an overall best method, the chosen one being directly related to the kind of missing data and the nature of the dataset itself. In practice, multiple imputation works well with MAR data, but this assumption is not absolutely required and correct results can be achieved even in the MNAR case. Moreover, if the MAR assumption is violated, not only the multiple imputation method will be affected, but the majority of missing data treatments, so it is absolutely not proven that another technique would lead to better results than multiple imputation do.

Among the available methods which can be used to generate the *m* imputed datasets, and after considering several alternative including data augmentation (71) and bootstrap (72), we finally chose to use the chained equations method developed among others by Raghunathan, Lepkowski, Van Hoewyk, & Solenberger (73) and Van Buuren, Boshuizen, & Knook (74). Several variables with missing data can be considered simultaneously. The process is initialized by replacing each missing data on each variable by a random value. A regression model is then used to estimate successively the missing data of each variable, using the other variables and covariates as predictors. The full process is then repeated until obtaining *m* imputed datasets.

The chained equations method is perfectly suited to the TREE data, since a variable such as cannabis consumption observed each year from T1 to T7 can be simultaneously imputed in only one run of the algorithm, keeping a strong dependency between the waves. Moreover, the regression model can be either, linear, logistic, multinomial, or ordinal, opening the way to the imputation of any kind of variables.

In practice, in addition to the variables describing the use of cannabis and tobacco overtime, which are the main variables used in this study, we imputed more than 90 other variables related to the health, professional achievement and well-being of the sampled adolescents. These variables were then used as predictors in survival analysis models.

A more detailed description of the principles of multiple imputation and chained equations can be found in Annex 2.

Substance use groups

From a complete weighted sample of 2954 subjects, four groups of substance users have been created as follows:

1. Cannabis only: adolescents reporting that they use cannabis but do not smoke tobacco (weighted n= 68.6).

2. Cannabis & tobacco: adolescents reporting that they use both substances (weighted n= 544.7).
3. Tobacco only: adolescents reporting that they smoke tobacco but do not use cannabis (weighted n= 781.9).
4. No substance (abstinent): adolescents reporting that they do not use neither cannabis nor tobacco (weighted n= 1558.8).

Explanatory variables

- **Region**: Linguistic region at the time of the PISA 2000 survey (German / French / Italian).
- **Compulsory school**: Compulsory school track at the time of the PISA 2000 survey (pre-gymnasium / extended requirements / basic requirements / other).
- **Gender**: Gender (male / female).
- **Country of birth**: Country of birth (Swiss / other).
- **Age**: Age in months at the time of the PISA 2000 survey.
- **Family wealth**: Family wealth as evaluated at the time of the PISA 2000 survey. This is a scale computed from the answers to the following questions:
    - In your home, do you have:
        - A dishwasher?
        - A room of your own?
        - Educational software?
        - A link to the internet?
    - How many of these do you have at your home?
        - Cellular phone
        - Television
        - Computer
        - Motor car
        - Bathroom
- **Socioeconomic status**: Socioeconomic situation as determined each year of the survey (student / apprentice / worker / other).
- **Employed**: To have a job (yes / no).
- **Level of alcohol use**: Level of alcohol use evaluated each year of the survey (none / occasional (<3x/week) / regular (>=3x/week)).
- **Level of tobacco smoking**: Level of tobacco smoking evaluated each year of the survey (none / occasional (<3x/week) / regular (>=3x/week)).
- **Level of cannabis use**: Level of cannabis use evaluated each year of the survey (none / occasional (<3x/week) / regular (>=3x/week)).
- **Evolution of alcohol use**: Evolution of the level of alcohol use between two successive waves of the survey (none (no consumption of this substance) / stable (no change since the preceding wave) / augmentation (increase of the consumption since the preceding wave) / diminution (decrease of the consumption since the preceding wave).
- **Evolution of tobacco smoking**: Evolution of the level of tobacco smoking between two successive waves of the survey (none (no consumption of this substance) / stable (no change since the preceding wave) / augmentation (increase of the consumption since the preceding wave) / diminution (decrease of the consumption since the preceding wave).

- **Evolution of cannabis use**: Evolution of the level of cannabis use between two successive waves of the survey (none (no consumption of this substance) / stable (no change since the preceding wave) / augmentation (increase of the consumption since the preceding wave) / diminution (decrease of the consumption since the preceding wave).
- **Negative life events**: Number of significant life events during the last year in 4 categories (none / 1 / 2 / >2). The life events considered are
    - My family moved house.
    - I have left my family home.
    - My parents got separated or divorced.
    - I got married.
    - I had a grave accident or got a grave illness.
    - A person, who was close to me, died.
    - I had problems with the police.
    - I went through an unhappy relationship.
    - I had a big bust-up at school or at work.
    - I had a big bust-up with friends or family.
    - I became a mum/dad.
    - I fell pregnant/I got a girl pregnant.
    - I moved house.
    - I (myself) have gone through a separation or divorce.
    - Somebody who I am very close to fell very sick or had a grave accident.
    - Somebody who I am very close to lost his/her job.
    - Other.

    Some of the questions were not asked continuously from wave 1 to wave 7.

- **At least one postulation**: At least one postulation to a new school or apprenticeship during the preceding year. True if at least one of the five following events did occur at least once during the preceding year:
    - I applied for an apprenticeship training position.
    - I enrolled in a school.
    - I sought advice from a career counsellor.
    - I sat an entrance examination in order to be admitted at a particular school or in an apprenticeship.
    - I went on a 'work experience week'.
- **Educational/work drawback**: At least one educational or work drawback during the preceding year. True if at least one of the seven following events did occur at least once during the preceding year:
    - I did not get an apprenticeship position for which I had applied.
    - I was not taken at a school at which I had enrolled.
    - I have quit a school or an apprenticeship.
    - I have been unemployed for a while.
    - I have quit a job or was made redundant at a job.
    - I was made redundant.
    - I quit my job.

    Some of the questions were not asked continuously from wave 1 to wave 7.
- **Changing school/work**: At least one change in the educational or work position during the preceding year. True if at least one of the five following events did occur at least once during the preceding year:
    - I have started at another school or apprenticeship.
    - I have changed to another training company.

- I have changed the occupation I am trained in.
- I have started a job (paid employment).
- I have changed my job.

Some of the questions were not asked continuously from wave 1 to wave 7.

- **Low grades**: At least one failure at school or in apprenticeship during the preceding year. True if at least one of the three following events did occur at least once during the preceding year:
  - At the moment I am repeating a school or training year.
  - I did not pass an important intermediate or entrance examination.
  - In your last school reports, did you have insufficient grades or did you get a bad report?

  Some of the questions were not asked continuously from wave 1 to wave 7.
- **Psychosomatic symptoms**: At least one of the following symptoms more than 2 times per week during the last month:
  - Stomach-ache.
  - Lack of appetite.
  - Lack of concentration.
  - Dizziness.
  - Sleeping disorder.
  - Nervousness.
  - Tiredness.
  - Headaches.
- **Faith in future**: Scale of confidence in the future computed as the average of the 5 following questions which answers were given on a 6-point scale (1: totally wrong to 6: totally right):
  - My future looks bright.
  - I am happy to live.
  - I am happy with the way my life plan unfolds.
  - Whatever happens, I can see the positive side of it.
  - My life seems to be meaningful.

  Cronbach's alpha ranges from 0.7579 in wave 5 to 0.8559 in wave 6.
- **Very satisfied with training**: Very satisfied with education (apprenticeship, pre-apprenticeship, school, etc.) (<= rather satisfied / >=very satisfied).
- **Social support**: Scale of availability of social support computed as the average of the 4 following questions which answers were given on a 4-point scale (1: not at all true, to 4: exactly true):
  - There are persons on who I can always rely.
  - If there is too much for me to cope with, others help me.
  - There are persons who offer me help if I need some.
  - If I am worried there is someone who supports me.

  These questions were available only from wave 5 to wave 7. Cronbach's alpha ranges from 0.8036 in wave 5 to 0.8195 in wave 6.
- **Self-esteem**: Scale of self-esteem computed as the average of the 8 following questions which answers were given on a 5-point scale (1: not at all accurate, to 5: very accurate):
  - On the whole, I am satisfied with myself.
  - I feel that I have a number of good qualities.
  - I am able to do things as well as most other people.
  - I feel that I am a person of worth, at least on an equal plane with others.

- At times, I think I am no good at all.
- I certainly feel useless at times.
- I wish I could have more respect for myself.
- All in all, I am inclined to feel that I am a failure.

The answers to the last 4 questions have been reversed before computing the scale. Cronbach's alpha ranges from 0.7799 in wave 5 to 0.8581 in wave 4.

- **Positive affectivity**: Scale of positive affectivity computed as the average of the 5 following questions which answers were given on a 5-point scale (1: not at all, to 5: very):
  - Over the last month, how did you generally feel? Active?
  - Over the last month, how did you generally feel? Strong?
  - Over the last month, how did you generally feel? Enthusiastic?
  - Over the last month, how did you generally feel? Determined?
  - Over the last month, how did you generally feel? Interested?

  These questions were available only from wave 2 to wave 7. Cronbach's alpha ranges from 0.8072 in wave 3 to 0.8182 in wave 4, with the exception of wave 5 (0.6851).
- **Negative affectivity**: Scale of negative affectivity computed as the average of the 5 following questions which answers were given on a 5-point scale (1: not at all, to 5: very):
  - Over the last month, how did you generally feel? Irritable?
  - Over the last month, how did you generally feel? Distressed?
  - Over the last month, how did you generally feel? Annoyed?
  - Over the last month, how did you generally feel? Anxious?
  - Over the last month, how did you generally feel? Guilty?

  These questions were available only from wave 2 to wave 7. Cronbach's alpha ranges from 0.7327 in wave 7 to 0.7816 in wave 4, with the exception of wave 5 (0.6611).
- **Perseverance in training**: Willingness to finish the educational training (<= very often / almost ever).

Description of the survival analysis regression models

Since the TREE survey provides discrete time data (from wave 1 (2001) to wave 7 (2007), the survival models described here are implemented as logistic regressions.

Models of consumption

- **Model 1: Cannabis only users:** In this model we explain using a set of categorical and continuous predictors the fact of becoming for the first time a cannabis only consumer, whatever the consumption level of tobacco the preceding years.
- **Model 2: Tobacco only smokers:** In this model we explain using a set of categorical and continuous predictors the fact of becoming for the first time a tobacco only smoker, whatever the consumption level of cannabis the preceding years.
- **Model 3: Cannabis & tobacco users:** In this model we explain using a set of categorical and continuous predictors the fact of becoming for the first time a co-consumer of cannabis and tobacco, whatever the substances consumed during the preceding waves.
- **Model 4: Abstinent:** In this model we explain using a set of categorical and continuous predictors the fact of becoming abstinent for the first time, whatever the substances consumed during the preceding waves.
- **Model 5: Cannabis users with or without tobacco smoking:** In this model we explain using a set of categorical and continuous predictors the fact of becoming for the first time a cannabis consumer, with

or without simultaneously smoking tobacco, whatever the consumption level of tobacco the preceding years.

- **Model 5b: Cannabis users with or without tobacco smoking (including tobacco):** This model is similar to model 5, except that the level of tobacco smoking is added to the predictor list.
- **Model 6: Tobacco smokers with or without cannabis use:** In this model we explain using a set of categorical and continuous predictors the fact of becoming for the first time a tobacco smoker, with or without using simultaneously cannabis, whatever the consumption level of cannabis the preceding years.
- **Model 6b: Tobacco smokers with or without cannabis use (including cannabis):** This model is similar to model 6, except that the level of cannabis use is added to the predictor list.
- **Model 7: Cannabis users, tobacco smokers or both:** In this model we explain using a set of categorical and continuous predictors the fact of becoming for the first time a consumer or either cannabis or tobacco, or even both.
- **Model 8: Becoming an abstinent:** In this model we explain using a set of categorical and continuous predictors the fact of quitting for the first time the consumption of both tobacco and/or cannabis to become abstinent. This model is similar to model 4, except that it was computed only for subjects not abstinent in wave 1.
- **Model 9: Becoming a consumer:** In this model we explain using a set of categorical and continuous predictors the fact of quitting abstinence for the first time to start any consumption of tobacco, cannabis, or both. This model is similar to model 7, except that it was computed only for subjects abstinent in wave 1.

Models of change in substance use

- **Increase in cannabis use:** In this model we explain using a set of categorical and continuous predictors the fact of increasing the level of cannabis use compared to the level observed the preceding year.
- **Decrease in cannabis use:** In this model we explain using a set of categorical and continuous predictors the fact of decreasing the level of cannabis use compared to the level observed the preceding year.
- **Increase in tobacco smoking:** In this model we explain using a set of categorical and continuous predictors the fact of increasing the level of tobacco smoking compared to the level observed the preceding year.
- **Decrease in tobacco smoking:** In this model we explain using a set of categorical and continuous predictors the fact of decreasing the level of tobacco smoking compared to the level observed the preceding year.
- **Increase in alcohol use:** In this model we explain using a set of categorical and continuous predictors the fact of increasing the level of alcohol use compared to the level observed the preceding year.
- **Decrease in alcohol use:** In this model we explain using a set of categorical and continuous predictors the fact of decreasing the level of alcohol use compared to the level observed the preceding year.

Statistical analysis

All statistical analysis performed in this project rely on the subset of 2954 weighted subjects for whom, after imputation, we have complete information about their substance use trajectory from 2001 to 2007.

Two different kind of statistical analyses were used to answer to the research questions. First of all, frequency distributions and cross-tables were used to describe the evolution of consumption year after

year, and the association between consumption groups at T1 and T7. Then, particular events of interest (beginning of cannabis consumption, end of cannabis consumption, beginning of co-consumption cannabis & tobacco, …) were defined and statistical models were computed in order to identify the factors (risk and protective) potentially explaining their occurrence.

The events we are interested in can occur anytime during the analyzed period (2001-2007), and they are likely not to occur for many subjects. For instance, the majority of the sample never began to consume cannabis. In statistics, such events can be described using *survival analysis* models (75). In the discrete time case, these models are formulated as logistic regressions, the dependent variable being the fact to experience the event of interest.

All computations were performed using Stata 10.1. The *ice* function was used for the imputation of missing data, and the *mim* prefix was used for combining the statistics computed individually on each of the 20 replications of the original dataset into a single final result.

RESULTS

Descriptive

Cannabis use by wave

Overall, cannabis use decreases overtime, with non-users grossly increasing from79 to 85% between T1 and T7. Occasional users decrease overtime: they represent 15% of the sample at T1 and only 9% at T7. However, regular users show a somehow different pattern: the percentages are quite similar at T1 (6.1%) and T7 (5.6%) but they increase and remain stable at 8% between T2 and T5.

Two main differences can be observed by gender. On the one side, at each wave there are more males using cannabis than females. On the other, the percentages of male regular users at least double females' percentages at each wave, while the difference for occasional users is quite minimal (Table 1).

Table 1. Cannabis use by wave. Global and by gender

	Global			Females			Males		
	Never	Occasional	Regular	Never	Occasional	Regular	Never	Occasional	Regular
T1	79.3%	14.6%	6.1%	82.5%	13.7%	3.8%	75.8%	15.6%	8.2%
T2	78.6%	13.3%	8.1%	82.5%	13.1%	4.4%	74.3%	13.5%	12.2%
T3	78.2%	13.4%	8.4%	82.5%	11.6%	5.9%	73.4%	15.4%	11.2%
T4	81.4%	10.2%	8.4%	86.4%	9.1%	4.5%	75.9%	11.4%	12.7%
T5	79.7%	12.3%	8.0%	85.5%	10.3%	4.2v	73.2%	14.7%	12.1%
T6	86.0%	8.7%	5.3%	90.6%	6.4%	3.0%	81.1%	11.2%	7.7%
T7	85.4%	9.0%	5.6%	89.0%	8.2%	2.8%	81.3%	10.0%	8.7%

Tobacco use by wave

Although the rate of non-smokers remains around 50%, a decrease can be observed overtime, from 55% at T1 to 49% at T7. While the percentage of occasional smokers diminishes slightly overtime (from 17% at T1 to 14% at T7), the main change across waves is the increase in the percentage of regular smokers: while they represent a little more than a quarter of all subjects at T1, they are over one third at T7.

By gender, the results are relatively similar with some exceptions. Occasional smokers are quite stable among females while they decrease among males. Although they decrease in both genders, non-smokers are more frequent among females. As a consequence, regular smokers increase overtime and, with the exception of T1, are more frequent among males than among females (Table 2).

Table 2. Tobacco use by wave, global and by gender

	Global			Females			Males		
	Never	Occasional	Regular	Never	Occasional	Regular	Never	Occasional	Regular
T1	55.2%	17.2%	27.6%	56.2%	15.8%	28.0%	54.1%	18.7%	27.2%
T2	53.7%	13.1%	33.2%	53.9%	14.5%	31.6%	53.4%	11.6%	35.0%
T3	53.3%	12.0%	34.7%	55.0%	11.6%	33.4%	51.3%	12.4%	36.3%
T4	49.7%	14.2%	36.1%	51.1%	14.3%	34.6%	48.3%	14.2%	37.5%
T5	49.9%	13.4%	36.7%	52.7%	12.2%	35.1%	46.8%	14.7%	38.5%
T6	51.2%	12.7%	36.1%	52.9%	11.4%	35.7%	49.4%	14.0%	36.6%
T7	48.9%	14.2%	36.9%	50.5%	14.1%	35.4%	47.2%	14.2%	38.6%

Alcohol use by wave

Whether occasionally or regularly, the vast majority of adolescents use alcohol and its use increases with time. Especially important is the fact that between T3 (age 18) and T4 (age 19) the rate of regular users doubles (from 4.5% to 9%).

Some differences can be noted between genders. First, while occasional alcohol users increase among females overtime, they remain quite stable among males. Second, at any wave, there are more male than

female drinkers. And third, there is a huge gender difference in the percentages of regular drinkers: males outnumber females by two to three-fold (Table 3).

Table 3. Alcohol use by wave, global and by gender

	Global			Females			Males		
	Never	Occasional	Regular	Never	Occasional	Regular	Never	Occasional	Regular
T1	26.5%	70.0%	3.5%	29.3%	68.1%	2.6%	23.3%	72.1%	4.6%
T2	22.4%	73.5%	4.1%	24.1%	73.1%	2.8%	20.5%	73.9%	5.6%
T3	18.7%	76.8%	4.5%	21.7%	76.3%	2.0%	15.3%	77.4%	7.3%
T4	19.0%	72.0%	9.0%	22.5%	73.4%	4.1%	15.2%	70.5%	14.3%
T5	15.4%	75.1%	9.5%	18.9%	77.2%	3.9%	11.5%	72.7%	15.8%
T6	17.1%	74.7%	8.2%	19.2%	77.0%	3.8%	14.9%	72.0%	13.1%
T7	15.2%	73.5%	11.3%	17.9%	76.3%	5.8%	12.2%	70.3%	17.5%

Substance use group by wave

The percentage of those using *cannabis only* is small and diminishes overtime, from 2.3% at T1 to 1.6% at T7.

The percentage of those using both *tobacco and cannabis* also diminishes as waves advance. At T1 it corresponds to almost one fifth (18.4%) of all cases, while at T7 it represents 13%.

On the contrary, those smoking *tobacco only* increase overtime, from 26.4% at T1 to 38.1% at T7.

In the three above-mentioned cases, whether increasing or decreasing, the main change seems to occur between waves 5 and 6, representing the ages of 20-21 years.

Finally, the group of youths declaring being abstinent remains relatively stable around 50% at each wave, although with a small decrease, from 52.9% at T1 to 47.3% at T7. (Table 4)

Table 4. Percentages of substance (cannabis and/or tobacco) use at each wave.

	Cannabis only	Tobacco & Cannabis	Tobacco only	No substance
T1	2.33%	18.39%	26.39%	52.90%
T2	3.22%	18.16%	28.18%	50.43%
T3	3.71%	18.11%	28.64%	49.54%
T4	2.41%	16.14%	34.12%	47.33%
T5	3.09%	17.23%	32.90%	46.79v
T6	1.88%	12.08%	36.67%	49.37%
T7	1.63%	12.99%	38.08%	47.30%

By gender, the trends are very similar, although while females are more likely to be tobacco only smokers (from 27.9% at T1 to 39.4% at T7) than males (from 24.7% to 36.6%) the latter are more likely to use cannabis only (from 3.1% to 2.6%, vs. 1.7% to 0.8% among females) or tobacco and cannabis combined (from 21.2% to 16.1%, vs. 15.9% to 10.2% among females). The percentage of abstinent youth is also slightly higher among females (from 54.6% at T1 to 49.7% at T7) than among males (51% and 44.7%, respectively). (Table 5)

Table 5. Percentages of substance (cannabis and/or tobacco) use at each wave, by gender.

Females	**Cannabis only**	**Tobacco & Cannabis**	**Tobacco only**	**No substance**
T1	1.67%	15.85%	27.91%	54.58%
T2	2.26%	15.19%	30.94%	51.61%
T3	3.76%	13.72%	31.28%	51.23%
T4	1.78%	11.79%	37.15%	49.28%
T5	2.15%	12.32%	35.00%	50.53%
T6	1.27%	8.17%	38.90%	51.66%
T7	0.78%	10.16%	39.40%	49.66%
Males	**Cannabis only**	**Tobacco & Cannabis**	**Tobacco only**	**No substance**
T1	3.06%	21.19%	24.71%	51.04%
T2	4.29%	21.45%	25.13%	49.13%
T3	3.65%	22.96%	25.73%	46.67%
T4	3.11%	20.95%	30.76%	45.18%
T5	4.13%	22.65%	30.57%	42.66%
T6	2.56%	16.40%	34.20%	46.85%
T7	2.56%	16.11%	36.63%	44.69%

Trajectories

When looking at the trajectories of substance users between T1 (age 16) and T7 (age 22) according to their starting point (Non users / Cannabis only / Tobacco only / Tobacco & Cannabis) and using *non users* as the reference group, several differences between groups can be observed:

Table 6. Tobacco, cannabis and both substances' trajectories between T1 and T7.

T7 \ **T1**	**Cannabis only**	**Tobacco only**	**Tobacco and cannabis**
Cannabis, occasional	**4.66 [1.67/12.96]**	1.31 [0.55/3.11]	**4.70 [1.76/12.55]**
Cannabis, regular	**4.88 [1.56/15.27]**	1.40 [0.53/3.72]	**11.89 [4.55/31.03]**
Tobacco, occasional	1.42 [0.65/3.08]	**4.43 [2.81/6.97]**	**6.50 [3.30/12.79]**
Tobacco, regular	**2.19 [1.05/4.58]**	**19.49 [12.37/30.70]**	**19.53 [10.33/36.90]**

(Note: data are expressed as Relative Risk Ratio with [95% confidence interval]. Significant results are in bold type)

Those using *cannabis only* (and not tobacco) at T1 are 4 to 5 times more likely to be either occasional or regular cannabis users at T7. Although they are not more likely to be occasional tobacco smokers, they have twice the chances to be regular smokers (Table 6). Almost half those using cannabis only at T1 (49.3%) will not be using cannabis or tobacco at T7. However, 6.6% will continue to use cannabis only, 28% will switch to tobacco only and 16.1% to both substances (Table 7).

Interestingly, the vast majority (96%) of cannabis only users at T1 that became abstinent at T7 were occasional users. The same was true (98%) for those switching to tobacco only, while 40% of those using both substances at T7 were regular cannabis users at T1.

Those using *tobacco only* (and not cannabis) at T1 are over 4 times more likely to be occasional smokers and 19 times more likely to be regular smokers at T7. However, they are not more likely to use cannabis (either occasionally or regularly) at T7 than non users (Table 6). The vast majority of tobacco only smokers at T1 (65.8%) will continue to smoke tobacco only at T7. Very few (0.6%) will switch to cannabis only and 12.3% to both substances. Finally, 21.2% will become abstinent (Table 7).

Two-thirds of those becoming abstinent at T7 were occasional smokers at T1. On the contrary, the majority (61% in both cases) of those who continue to smoke or who switch to tobacco and cannabis were regular smokers at T1.

Those using *tobacco & cannabis* at T1 are over 6 and 19 times more likely to be, respectively, occasional and regular smokers. Additionally, they are also almost 5 and 12 times more likely to be occasional and regular cannabis users (Table 6). Similar percentages of those using both substances at T1 will continue to use both substances (41.8%) or tobacco only (43.7%) at T7. Very few (3.9%) will use cannabis only and one tenth (10.6%) will become abstinent (Table 7).

Almost half (48%) of those who continue to use both substances at T7 were already regular users of both substances at T1, while 52% of those who switched to tobacco only at T7 were regular smokers but occasional cannabis users at T1. The majority (63%) of the few becoming abstinent at T7 were occasional users of tobacco and cannabis at T1.

Finally, 73% of abstinent at T1 will continue to be so at T7. The rest of them will be distributed between tobacco smokers (22.8%), cannabis users (1.1%) and those using both substances (3.2%) (Table 7).

Table 7. Tobacco, cannabis and tobacco & cannabis trajectories between T1 and T7.

T7 \ T1	Abstinent	Cannabis only	Tobacco only	Tobacco and cannabis
Abstinent	72.96%	49.29%	21.24%	10.61%
Cannabis only	1.12%	6.64%	0.64%	3.86%
Tobacco only	22.77%	28.01%	65.77%	43.69%
Tobacco & cannabis	3.15%	16.06%	12.34%	41.84%

In summary, whatever the substance(s) used at age 16, the probability to continue to use them 6 years later at young adulthood is very high, especially when tobacco is involved. Interestingly, although some cannabis only users at age 16 will become tobacco smokers overtime, the same is not true the other way around: tobacco smokers at age 16 are not more likely to become cannabis users. It is also worth noting that subjects consuming both substances at age 16 have higher chances to be using any of the 2 substances at age 22 than those using only one of them.

It is worth noting that, apart from abstinent youths at T1, almost half of those using cannabis only will not be using any of these substances at T7, while the same is true for one fifth of those using tobacco only and, for those using both substances, it represents merely one tenth.

By model of consumption

In this part we describe the risk and protective factors independently influencing the chances that an individual will start or not some kind of substance use. For this purpose, we have used the 4 models already described (non users / Cannabis only / Tobacco only / Tobacco & Cannabis) and have added 5 more options: cannabis users with or without tobacco smoking; tobacco smokers with or without cannabis use; tobacco smokers or cannabis users or both; users of any of the two substances that become abstinent; and abstinent who become users of any of the two substances.

Cannabis only users (model 1)

The main factor that predicts starting to use cannabis only is alcohol use. Youths using alcohol occasionally (Odds Ratio [OR]: 2.81) or regularly (OR: 2.71) have more chances to start using cannabis. Additionally, male gender (OR: 1.58) is also a predictor of cannabis only use (Table 8).

Tobacco only smokers (model 2)

As it is the case for cannabis only, drinking occasionally (OR: 2.71) or regularly (OR: 3.08) increases significantly the odds to start smoking. Other factors also predict the risk of smoking: being younger (OR: 0.98), being in the basic requirements track in compulsory school (OR: 1.57), being non Swiss-born (OR: 1.60), from a wealthier family (OR: 1.17), and having lived 2 negative life events (OR: 1.42). Although not significant, a negative affectivity shows a clear trend (OR: 1.19; p=0.054). On the contrary, living in the Italian part of Switzerland (OR: 0.71) is a protective factor (Table 8).

Table 8. Variables predicting belonging to the cannabis only and tobacco only groups.

	Cannabis only users (model 1)			Tobacco only smokers (model 2)		
	OR	95%CI		OR	95% CI	
Region						
German (ref)	1			1		
French	1,11	0,71	1,74	0,81	0,64	1,03
Italian	1,17	0,61	2,24	**0,71**	**0,52**	**0,98**
Compulsory school						
Pre-gymnasium (ref)	1			1		
Extended requirements	1,10	0,67	1,80	1,14	0,87	1,48
Basic requirements	0,76	0,33	1,75	**1,57**	**1,13**	**2,18**
Other	0,60	0,25	1,43	1,48	0,95	2,30
Gender (male)	**1,58**	**1,02**	**2,45**	0,85	0,68	1,06
Country of birth (other)	0,70	0,31	1,56	**1,60**	**1,11**	**2,30**
Age	1,00	0,96	1,03	**0,98**	**0,96**	**1,00**
Family wealth	1,06	0,75	1,50	**1,17**	**1,03**	**1,33**
Socioeconomic status						
Student (ref)	1			1		
Apprentice	0,73	0,47	1,14	1,17	0,89	1,52
Worker	0,41	0,17	1,02	1,11	0,75	1,63
Nothing	0,22	0,03	1,88	1,30	0,54	3,16
Level of alcohol use						
no use (ref)	1			1		
occasional	**2,81**	**1,44**	**5,46**	**2,71**	**2,00**	**3,67**
regular	**2,71**	**1,07**	**6,87**	**3,08**	**1,77**	**5,36**
Employed (no)	1,22	0,65	2,29	1,06	0,78	1,44
Negative life events						
None (ref)	1			1		
1	1,18	0,72	1,92	1,12	0,89	1,40
2	1,08	0,59	1,96	**1,42**	**1,06**	**1,88**
>2	0,66	0,31	1,41	1,47	0,94	2,30
At least one postulation	0,89	0,45	1,76	1,14	0,84	1,54
Educational/work drawback	1,30	0,64	2,66	1,06	0,77	1,46
Changing school/work	1,29	0,59	2,83	1,15	0,86	1,54
Low grades	1,14	0,71	1,83	1,04	0,83	1,30
Psycosomatic symptoms	1,59	0,95	2,66	1,12	0,88	1,44
Faith in future	0,78	0,56	1,09	0,93	0,76	1,14
Very satisfied with training	0,93	0,56	1,55	1,05	0,84	1,32
Social support	0,94	0,37	2,35	0,85	0,48	1,50
Self-esteem	1,02	0,64	1,65	1,01	0,80	1,27
Positive affectivity	0,84	0,56	1,26	0,92	0,73	1,16
Negative affectivity	0,75	0,51	1,11	1,19	1,00	1,42
Perseverance in training	0,73	0,43	1,26	0,95	0,75	1,21

(Note: significant values are in bold type)

Tobacco and cannabis users (model 3)

As for the previous cases, occasional (OR: 5.59) and regular (OR: 14.65) alcohol use are important predictors. Having low academic grades (OR: 1.45) and less faith in the future (OR: 0.64) are also risk factors. As is the case for tobacco only smokers, living in the Italian part of the country is a protective factor (OR: 0.63) (Table 9).

Table 9. Variables predicting belonging to the cannabis & tobacco and abstinent groups.

	Cannabis & tobacco users (model 3)			Abstinent (tobacco & cannabis free) (model 4)		
	OR	95% CI		OR	95%CI	
Region						
German (ref)	1			1		
French	0,84	0,60	1,19	1,06	0,81	1,38
Italian	**0,63**	**0,40**	**0,99**	**1,78**	**1,17**	**2,71**
Compulsory school						
Pre-gymnasium (ref)	1			1		
Extended requirements	1,25	0,87	1,81	**0,71**	**0,53**	**0,96**
Basic requirements	0,98	0,57	1,71	**0,66**	**0,45**	**0,98**
Other	0,85	0,48	1,52	1,03	0,59	1,80
Gender (male)	1,19	0,87	1,62	0,81	0,62	1,07
Country of birth (other)	0,93	0,57	1,53	0,55	0,36	0,86
Age	0,99	0,97	1,01	1,02	1,00	1,03
Family wealth	1,05	0,89	1,25	0,86	0,73	1,01
Socioeconomic status						
Student (ref)	1			1		
Apprentice	0,80	0,53	1,20	0,77	0,58	1,03
Worker	0,86	0,39	1,87	0,64	0,38	1,08
Nothing	0,82	0,25	2,74	0,48	0,10	2,31
Level of alcohol use						
no use (ref)	1			1		
occasional	**5,59**	**2,90**	**10,77**	**0,25**	**0,18**	**0,35**
regular	**14,65**	**6,14**	**35,00**	**0,13**	**0,06**	**0,26**
Employed (no)	1,00	0,67	1,47	1,02	0,71	1,46
Negative life events						
None (ref)	1			1		
1	1,01	0,72	1,43	0,91	0,69	1,19
2	1,05	0,67	1,62	**0,65**	**0,46**	**0,92**
>2	1,25	0,78	1,99	**0,52**	**0,31**	**0,86**
At least one postulation	1,20	0,80	1,79	0,88	0,66	1,18
Educational/work drawback	1,16	0,72	1,87	1,01	0,70	1,46
Changing school/work	1,09	0,72	1,65	0,95	0,70	1,30
Low grades	**1,45**	**1,05**	**2,01**	0,85	0,65	1,11
Psycosomatic symptoms	1,17	0,85	1,60	0,78	0,59	1,04
Faith in future	**0,64**	**0,51**	**0,82**	1,22	0,97	1,52
Very satisfied with training	0,93	0,66	1,30	1,15	0,89	1,47
Social support	1,17	0,33	4,10	1,55	0,60	3,95
Self-esteem	1,19	0,92	1,55	0,93	0,71	1,23
Positive affectivity	0,92	0,70	1,22	0,93	0,70	1,23
Negative affectivity	0,98	0,75	1,27	1,09	0,83	1,43
Perseverance in training	1,01	0,70	1,45	1,07	0,79	1,43

(Note: significant values are in bold type)

Abstinent (tobacco and cannabis free) (model 4)

As expected, those remaining abstinent are less likely to be occasional (OR: 0.25) or regular (OR: 0.13) alcohol users. Similarly, they are less likely to have been in an extended requirements (OR: 0.71) or basic requirements (OR: 0.66) academic track in compulsory school. Additionally, they are less likely to have lived 2 (OR: 0.65) or more (OR: 0.52) negative life events and reveal a trend (OR: 0.86; p=0.062) towards less family wealth. The chances to remain abstinent increase among those living in the Italian part of the country (OR: 1.78) (Table 9).

Cannabis users (with or without tobacco / models 5 & 5b)

The odds to use cannabis (independently of whether smoking tobacco or not) are much higher among occasional (OR: 5.08) and regular (OR: 11.59) alcohol users, those having low academic grades (OR:

1.37) and those with less faith in the future (OR: 0.62). Although not significant, male gender also shows a clear trend (OR: 1.32; p=0. 052) (Table 10).

Table 10. Variables predicting belonging to the cannabis users group independently of the use of the other substance.

	Cannabis users with or without tobacco smoking (model 5)			Cannabis users with or without tobacco smoking (including tobacco, model 5b)		
	OR	95% CI		OR	95% CI	
Region						
German (ref)	1			1		
French	0,83	0,61	1,14	0,83	0,60	1,16
Italian	0,73	0,49	1,11	0,85	0,55	1,30
Compulsory school						
Pre-gymnasium (ref)	1			1		
Extended requirements	1,15	0,83	1,59	0,96	0,69	1,34
Basic requirements	0,84	0,51	1,38	0,65	0,39	1,10
Other	0,75	0,42	1,34	0,66	0,38	1,17
Gender (male)	1,32	1,00	1,75	**1,43**	**1,06**	**1,94**
Country of birth (other)	0,97	0,63	1,52	0,78	0,48	1,26
Age	0,99	0,97	1,01	0,99	0,97	1,02
Family wealth	1,13	0,95	1,34	1,02	0,84	1,24
Socioeconomic status						
Student (ref)	1			1		
Apprentice	0,78	0,55	1,10	**0,62**	**0,44**	**0,89**
Worker	0,89	0,48	1,64	0,68	0,35	1,30
Nothing	0,75	0,22	2,54	0,52	0,14	1,96
Level of tobacco smoking						
no use (ref)	--	--	--	1		
occasional	--	--	--	**5,61**	**3,81**	**8,26**
regular	--	--	--	**8,15**	**5,53**	**12,00**
Level of alcohol use						
no use (ref)	1			1		
occasional	**5,08**	**2,94**	**8,77**	**2,98**	**1,74**	**5,10**
regular	**11,59**	**5,83**	**23,00**	**4,61**	**2,27**	**9,35**
Employed (no)	0,97	0,67	1,41	0,94	0,62	1,43
Negative life events						
None (ref)	1			1		
1	1,21	0,89	1,65	1,14	0,81	1,59
2	1,12	0,74	1,69	0,94	0,61	1,47
>2	1,26	0,81	1,96	0,95	0,59	1,51
At least one postulation	1,17	0,79	1,72	1,10	0,74	1,65
Educational/work drawback	1,31	0,84	2,06	1,32	0,83	2,10
Changing school/work	1,10	0,73	1,65	1,09	0,70	1,71
Low grades	**1,37**	**1,02**	**1,85**	1,18	0,86	1,61
Psycosomatic symptoms	1,20	0,89	1,61	1,12	0,81	1,55
Faith in future	**0,62**	**0,50**	**0,77**	**0,66**	**0,52**	**0,84**
Very satisfied with training	0,96	0,70	1,31	0,95	0,68	1,33
Social support	0,75	0,32	1,74	0,70	0,29	1,72
Self-esteem	1,22	0,96	1,56	1,13	0,88	1,46
Positive affectivity	0,89	0,68	1,17	0,90	0,67	1,21
Negative affectivity	0,98	0,78	1,23	0,92	0,72	1,16
Perseverance in training	0,93	0,68	1,29	0,91	0,64	1,28

(Note: significant values are in bold type)

When tobacco use is included in the equation (model 5b), both occasional (OR: 5.61) and regular (OR: 8.15) smoking becomes a risk factor that diminishes the odds of alcohol use (occasional: 2.98; regular: 4.61). Having low academic grades does not remain significant after adjusting for tobacco, but having less faith in the future continues to be significant (OR: 0.66). Male gender becomes significant (OR: 1.43) and, compared with students, apprentices are less likely to pertain to this group (OR: 0.62) (Table 10).

Tobacco smokers (with or without cannabis / models 6 & 6b)

Risk factors for tobacco use include occasional (OR: 4.25) and regular (OR: 9.30) alcohol use, having lived two (OR: 1.58) or more (OR: 2.02) negative life events, and having less faith in the future (OR: 0.77). Having been in an extended requirements track in compulsory school also reveals a trend (OR: 1.28; p=0.055). On the contrary, living in the Italian part of Switzerland is protective (Table 11).

Table 11. Variables predicting belonging to the tobacco smokers group independently of the use of the other substance.

	Tobacco smokers with or without cannabis use (model 6)			**Tobacco smokers with or without cannabis use (including cannabis, model 6b)**		
	OR	**95%CI**		**OR**	**95%CI**	
Region						
German (ref)	1			1		
French	0,82	0,65	1,03	0,80	0,62	1,02
Italian	**0,69**	**0,51**	**0,94**	**0,69**	**0,50**	**0,96**
Compulsory school						
Pre-gymnasium (ref)	1			1		
Extended requirements	1,28	0,99	1,65	**1,34**	**1,03**	**1,74**
Basic requirements	1,23	0,89	1,71	**1,49**	**1,06**	**2,08**
Other	1,32	0,83	2,11	1,57	0,97	2,55
Gender (male)	1,04	0,84	1,29	0,96	0,77	1,20
Country of birth (other)	**1,69**	**1,13**	**2,53**	**1,78**	**1,17**	**2,72**
Age	0,99	0,98	1,01	0,99	0,97	1,01
Family wealth	1,21	1,06	1,37	**1,17**	**1,02**	**1,35**
Socioeconomic status						
Student (ref)	1			1		
Apprentice	1,21	0,92	1,58	1,29	0,99	1,68
Worker	1,34	0,87	2,05	1,41	0,89	2,23
Nothing	1,38	0,54	3,53	1,70	0,66	4,40
Level of cannabis use						
no use (ref)	--	--	--	1		
occasional	--	--	--	**8,27**	**6,13**	**11,15**
regular	--	--	--	**19,61**	**11,20**	**34,33**
Level of alcohol use						
no use (ref)	1			1		
occasional	**4,25**	**3,08**	**5,88**	**3,50**	**2,53**	**4,83**
regular	**9,30**	**4,79**	**18,06**	**6,70**	**3,25**	**13,80**
Employed (no)	1,19	0,85	1,66	1,18	0,82	1,68
Negative life events						
None (ref)	1			1		
1	1,17	0,93	1,47	1,09	0,86	1,39
2	**1,58**	**1,18**	**2,11**	**1,54**	**1,13**	**2,11**
>2	**2,02**	**1,34**	**3,04**	**1,83**	**1,16**	**2,90**
At least one postulation	1,16	0,88	1,53	1,15	0,86	1,54
Educational/work drawback	1,00	0,72	1,39	1,00	0,71	1,40
Changing school/work	1,10	0,84	1,45	1,11	0,82	1,49
Low grades	1,21	0,97	1,49	1,10	0,87	1,38
Psycosomatic symptoms	1,23	0,97	1,55	1,21	0,94	1,56
Faith in future	**0,77**	**0,63**	**0,94**	0,84	0,67	1,04
Very satisfied with training	0,92	0,74	1,14	0,96	0,76	1,22
Social support	0,87	0,54	1,40	0,90	0,53	1,50
Self-esteem	1,11	0,87	1,41	1,07	0,82	1,39
Positive affectivity	0,95	0,78	1,17	0,97	0,78	1,21
Negative affectivity	1,15	0,95	1,39	1,18	0,97	1,43
Perseverance in training	1,02	0,80	1,30	1,00	0,77	1,30

(Note: significant values are in bold type)

When cannabis use is added to the equation (model 6b), both its occasional (OR: 8.27) and regular (OR: 19.61) use become significant as do occasional (OR: 3.50) and regular (OR: 6.70) alcohol use. Having

been in an extended requirements (OR: 1.34) or basic requirements (OR: 1.49) academic track in compulsory school, having lived two (OR: 1.54) or more (OR: 1.83) negative life events, being foreign-born (OR: 1.78), and belonging to a wealthier family (OR: 1.17) are also predictive factors. Both having been in an other class in compulsory school (OR: 1.57; p=0.066) and being an apprentice (OR: 1.29; p=0.056) show a clear although not significant trend. Finally, living in the Italian part of the country is a protective factor (Table 11).

Tobacco smokers, cannabis users, or both (model 7)

Occasional (OR: 4.38) and regular (OR: 10.99) alcohol use, having lived two (OR: 1.66) or more (OR: 2.06) negative life events, having low academic grades (OR: 1.25), having low faith in the future (OR: 0.75), being foreign-born (OR: 1.71) or belonging to a wealthier family (OR: 1.25) were predictive of the use of cannabis, tobacco or both substances (Table 12).

Table 12. Variables predicting belonging to the cannabis users, tobacco smokers or both substances group.

	Cannabis users, tobacco smokers or both (model 7)		
	OR	**95%CI**	
Region			
German (ref)	1		
French	0,84	0,67	1,05
Italian	0,75	0,56	1,03
Compulsory school			
Pre-gymnasium (ref)	1		
Extended requirements	1,25	0,98	1,60
Basic requirements	1,11	0,80	1,54
Other	1,20	0,73	1,97
Gender (male)	1,07	0,86	1,32
Country of birth (other)	**1,71**	**1,14**	**2,56**
Age	0,99	0,98	1,01
Family wealth	**1,25**	**1,10**	**1,41**
Socioeconomic status			
Student (ref)	1		
Apprentice	1,19	0,91	1,54
Worker	1,26	0,82	1,94
Nothing	1,21	0,45	3,29
Level of alcohol use			
no use (ref)	1		
occasional	**4,38**	**3,19**	**6,00**
regular	**10,99**	**5,46**	**22,12**
Employed (no)	1,12	0,80	1,56
Negative life events			
None (ref)	1		
1	1,24	0,98	1,57
2	**1,66**	**1,24**	**2,21**
>2	**2,06**	**1,36**	**3,14**
At least one postulation	1,21	0,92	1,59
Educational/work drawback	1,04	0,75	1,46
Changing school/work	1,07	0,81	1,41
Low grades	**1,25**	**1,01**	**1,55**
Psycosomatic symptoms	1,22	0,97	1,54
Faith in future	**0,75**	**0,61**	**0,91**
Very satisfied with training	0,86	0,69	1,07
Social support	0,73	0,45	1,19
Self-esteem	1,11	0,87	1,41
Positive affectivity	0,96	0,78	1,19
Negative affectivity	1,09	0,89	1,33
Perseverance in training	1,02	0,80	1,30

(Note: significant values are in bold type)

Becoming an abstinent (model 8)

Subjects who become abstinent show lower odds for being occasional (OR: 0.33) or regular (OR: 0.23) alcohol users and to be in an extended requirements academic track in compulsory school (OR: 0.57). Additionally, they are also older (OR: 1.03) (Table 13).

Becoming a consumer (model 9)

Subjects who will start using cannabis and/or tobacco show higher odds to be occasional (OR: 3.62) or regular (OR: 7.88) alcohol users and less faith in their future (OR: 0.72) (Table 13).

Table 13. Variables predicting becoming an abstinent or becoming a user.

	Becoming an abstinent (model 8)			**Becoming a consumer (model 9)**		
	OR	**95%CI**		**OR**	**95%CI**	
Region						
German (ref)	1			1		
French	0,88	0,57	1,38	0,81	0,58	1,14
Italian	1,35	0,59	3,09	0,97	0,66	1,44
Compulsory school						
Pre-gymnasium (ref)	1			1		
Extended requirements	**0,57**	**0,36**	**0,92**	1,31	0,95	1,81
Basic requirements	0,66	0,36	1,21	0,93	0,60	1,45
Other	0,89	0,39	2,03	1,60	0,84	3,04
Gender (male)	0,66	0,42	1,05	1,07	0,82	1,39
Country of birth (other)	0,60	0,28	1,29	1,50	0,93	2,43
Age	**1,03**	**1,01**	**1,06**	0,99	0,97	1,01
Family wealth	1,08	0,81	1,44	1,13	0,95	1,36
Socioeconomic status						
Student (ref)	1			1		
Apprentice	0,78	0,50	1,23	1,07	0,75	1,53
Worker	0,58	0,29	1,20	1,24	0,76	2,01
Nothing	0,34	0,07	1,75	1,23	0,46	3,30
Level of alcohol use						
no use (ref)	1			1		
occasional	**0,33**	**0,19**	**0,57**	**3,62**	**2,37**	**5,53**
regular	**0,23**	**0,09**	**0,56**	**7,88**	**3,12**	**19,91**
Employed (no)	1,35	0,84	2,19	0,99	0,69	1,44
Negative life events						
None (ref)	1			1		
1	1,05	0,68	1,64	1,30	0,97	1,73
2	1,15	0,68	1,94	1,27	0,85	1,90
>2	1,20	0,62	2,32	1,11	0,62	1,99
At least one postulation	0,82	0,44	1,54	1,46	0,93	2,30
Educational/work drawback	1,08	0,52	2,22	1,05	0,65	1,70
Changing school/work	0,91	0,45	1,85	0,96	0,63	1,46
Low grades	1,03	0,65	1,63	1,17	0,85	1,61
Psycosomatic symptoms	0,95	0,58	1,55	1,08	0,79	1,48
Faith in future	1,03	0,73	1,45	**0,72**	**0,56**	**0,92**
Very satisfied with training	0,99	0,66	1,49	0,92	0,69	1,23
Social support	1,39	0,58	3,31	0,77	0,48	1,25
Self-esteem	1,12	0,73	1,73	0,98	0,76	1,27
Positive affectivity	1,02	0,74	1,41	1,00	0,80	1,25
Negative affectivity	0,95	0,70	1,29	1,12	0,90	1,39
Perseverance in training	1,17	0,71	1,94	1,01	0,72	1,43

(Note: significant values are in bold type)

Changes in substance use

One of the main points that we wanted to research was whether a change in the use of one the substances also implies changes among the other ones. For this purpose we have created 4 possibilities between each wave based on the changes between the 3 basic categories (no / occasional / regular use): none (meaning no use of the substance in both waves); stable (meaning no level change between waves); increase (meaning an increase in the level of substance use between waves); and decrease (meaning a decrease in the level of substance use between waves).

Changes in cannabis use

Independently of the type of tobacco consumption, cannabis remains mainly stable over time although with different patterns. When there is no tobacco smoking or this is stable, there is no cannabis use in over 90% of the cases. When smoking increases, cannabis remains stable in about 70% of the cases and increases in 10-15% of subjects. When tobacco decreases, no cannabis use increases overtime from 60 to 80% and in 10-20% of the cases it diminishes (Figures 1 to 4).

Figure 1. Effect on cannabis use of no tobacco smoking

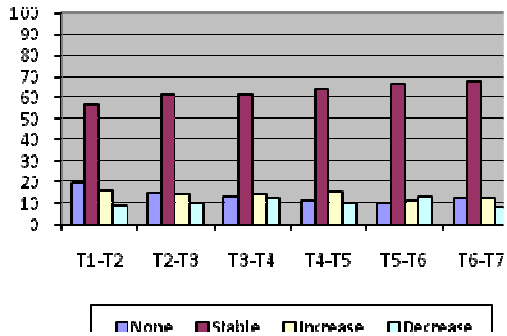


Figure 2. Effect on cannabis use of stable tobacco smoking

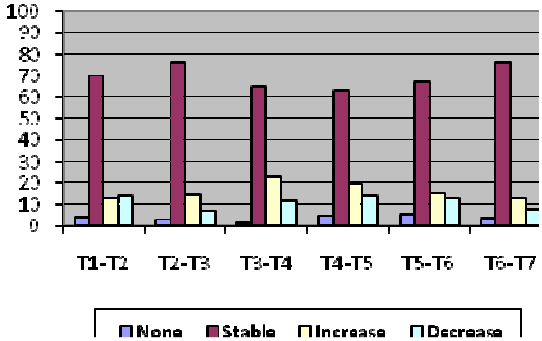


Figure 3. Effect on cannabis use of increased tobacco smoking

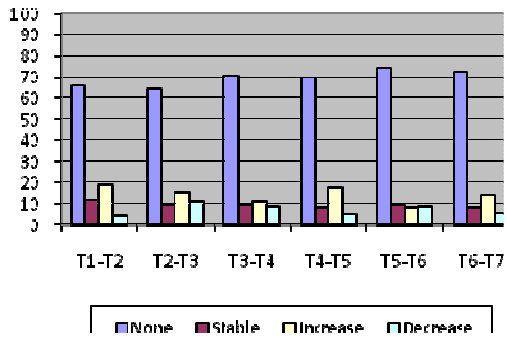
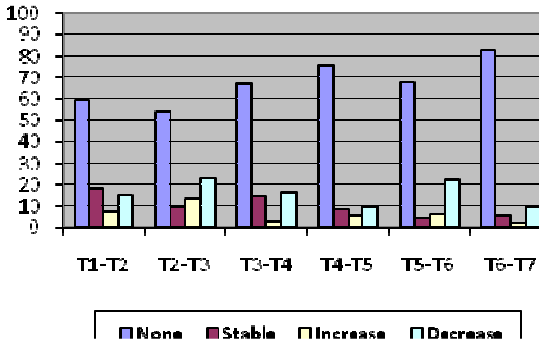


Figure 4. Effect on cannabis use of decreased tobacco smoking



When there is no alcohol use there is no cannabis use either in around 90% of the cases (Figure 5). When alcohol use is stable, there is mainly no cannabis use and the proportion increases from 60% at T1-T2 to 80% at T6-T7 (Figure 6). When alcohol use increases, there is still mainly no cannabis use (around 70%), or it increases slightly (10-15%) (Figure 7). When alcohol use decreases, there is no cannabis use in 60-80% of the cases but it diminishes in small percentages. (Figure 8)

Figure 5. Effect on cannabis use of no alcohol use

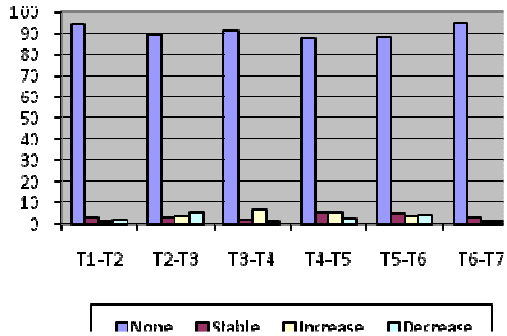


Figure 6. Effect on cannabis use of stable alcohol use

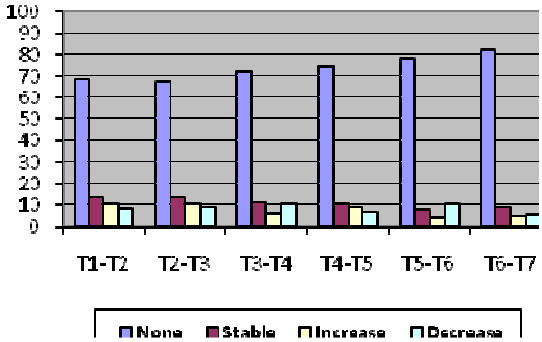


Figure 7. Effect on cannabis use of increased alcohol use

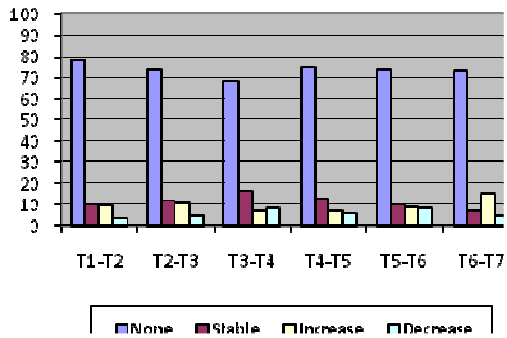
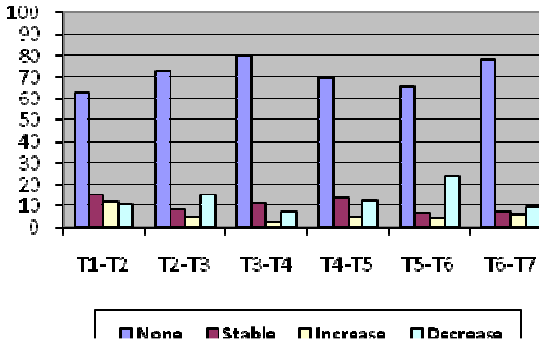


Figure 8. Effect on cannabis use of decreased alcohol use



Variables predicting increase in cannabis use

Although any level of tobacco change is a significant predictor of increase in cannabis use, when tobacco smoking increases the probability for cannabis use to increase shows the highest odds ratio (7.19). For alcohol, the only change that is significant is an increase in its use (OR: 2.71). Being male (OR: 1.56) and having less faith in the future (OR: 0.76) also predict this increase. (Table 14)

Table 14. Variables predicting changes in cannabis use.

	Increase in cannabis use			Decrease in cannabis use		
	OR	95%CI		OR	95%CI	
Region						
German (ref)	1			1		
French	0,92	0,65	1,30	0,75	0,53	1,05
Italian	1,03	0,65	1,64	0,71	0,46	1,11
Compulsory school						
Pre-gymnasium (ref)	1			1		
Extended requirements	0,99	0,70	1,40	0,91	0,65	1,28
Basic requirements	0,95	0,60	1,51	1,15	0,72	1,84
Other	0,66	0,37	1,16	0,81	0,45	1,47
Gender (male)	**1,56**	**1,16**	**2,10**	1,18	0,87	1,59
Country of birth (other)	0,79	0,48	1,29	0,85	0,52	1,37
Age	0,99	0,96	1,01	0,99	0,97	1,01
Family wealth	1,03	0,85	1,25	1,00	0,81	1,23
Socioeconomic status						
Student (ref)	1			1		
Apprentice	0,79	0,55	1,13	0,67	0,45	1,02
Worker	0,80	0,42	1,56	0,70	0,42	1,17
Nothing	0,43	0,14	1,37	0,40	0,11	1,44
Evolution of tobacco smoking						
no use (ref)	1			1		
stable	**5,94**	**4,01**	**8,79**	**5,90**	**3,80**	**9,17**
augmentation	**7,19**	**4,80**	**10,76**	**3,15**	**1,80**	**5,50**
diminution	**3,30**	**1,74**	**6,26**	**8,15**	**5,07**	**13,10**
Evolution of alcohol use						
no use (ref)	1			1		
stable	2,23	0,90	5,53	**2,60**	**1,25**	**5,38**
augmentation	**2,71**	**1,06**	**6,89**	1,67	0,71	3,94
diminution	1,80	0,63	5,20	**3,33**	**1,52**	**7,31**
Employed (no)	1,01	0,61	1,66	0,98	0,70	1,39
Negative life events						
None (ref)	1			1		
1	1,30	0,86	1,94	1,29	0,93	1,77
2	0,99	0,65	1,51	1,03	0,63	1,66
>2	1,04	0,61	1,78	1,45	0,90	2,35
At least one postulation	1,16	0,67	2,03	1,23	0,70	2,14
Educational/work drawback	1,19	0,68	2,06	0,97	0,56	1,68
Changing school/work	1,20	0,73	1,97	0,99	0,61	1,63
Low grades	1,26	0,87	1,81	1,13	0,79	1,63
Psycosomatic symptoms	1,32	0,93	1,85	1,14	0,82	1,58
Faith in future	**0,76**	**0,59**	**0,98**	0,84	0,64	1,09
Very satisfied with training	0,96	0,67	1,37	0,81	0,58	1,13
Social support	0,72	0,33	1,61	1,24	0,63	2,43
Self-esteem	0,94	0,69	1,26	1,12	0,81	1,54
Positive affectivity	0,96	0,75	1,24	0,98	0,76	1,26
Negative affectivity	0,86	0,68	1,08	1,05	0,83	1,34
Perseverance in training	1,01	0,69	1,48	0,96	0,68	1,37

(Note: significant values are in bold type)

Variables predicting decrease in cannabis use

The only variables predicting a decrease in cannabis use is the use of the other two substances. Although all levels of tobacco smoking are significantly associated to it, a decrease in tobacco smoking shows the highest odds (OR: 8.15). A stable level of alcohol use is also associated (OR: 2.6), but the highest odds are when alcohol also decreases (OR: 3.35). Although not significant, being an apprentice reveals an inverse trend (OR: 0.67; p=.061) towards a decrease in cannabis use. (Table 14)

Changes in tobacco use

The vast majority of youths not using cannabis overtime do not use tobacco either, although the percentage diminished from 60% at T1-T2 to 50% at T6-T7. This decrease is compensated by an increase in the percentage of stable tobacco users (Figure 9).

When cannabis use is stable overtime, tobacco smoking is also mainly stable (around 70%) (Figure 10).

Figure 9. Effect on tobacco smoking of no cannabis use

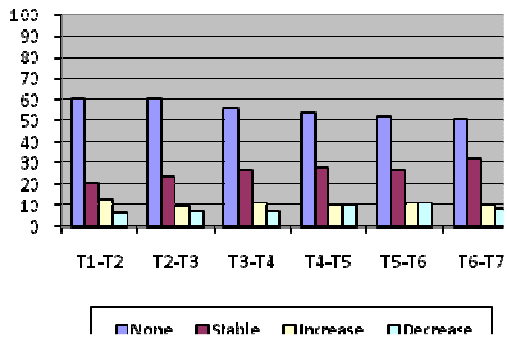
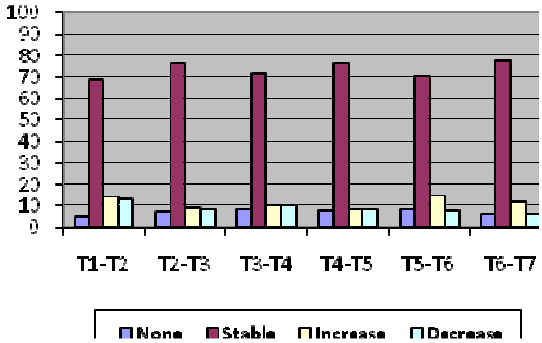


Figure 10. Effect on tobacco smoking of stable cannabis use



When cannabis use increases or diminishes overtime, tobacco smoking also remains stable although with lower percentages (50-60%). The main difference is that when cannabis increases tobacco also increases in 20-30% of the cases, while when cannabis diminishes so does tobacco in around 20% of the cases (Figures 11 & 12).

Figure 11. Effect on tobacco smoking of increased cannabis use

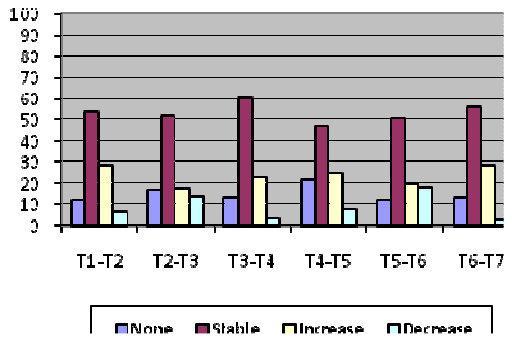
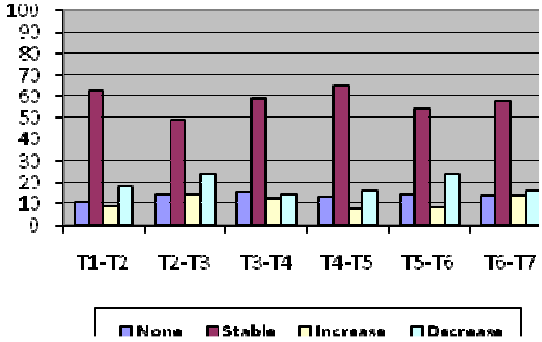


Figure 12. Effect on tobacco smoking of decreased cannabis use



When there is no alcohol use, there is no tobacco smoking either in most cases, although the proportion decreases from over 80% at T1-T2 to 60% at T6-T7. This decrease is compensated by an increase of stable tobacco smoking (from below 10% to over 20%) (Figure 13).

When alcohol use is stable, tobacco smoking is almost equally distributed (around 40%) among those not smoking and those with stable tobacco smoking (Figure 14). When alcohol use increases, the percentage of those not smoking decreases overtime from 50 to 40%, stable smokers remain around 30% overtime and those increasing tobacco smoking rise from 10 to 20% across waves (Figure 15). However, when alcohol use decreases, the same percentages (around 40%) of non smokers or stable smokers are found. In around 10% of the cases tobacco smoking will also decrease. (Figure 16)

Figure 13. Effect on tobacco smoking of no alcohol use

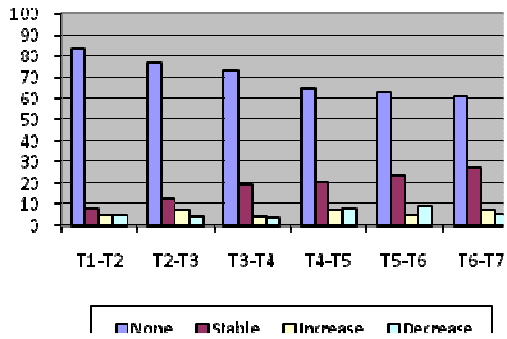


Figure 14. Effect on tobacco smoking of stable alcohol use

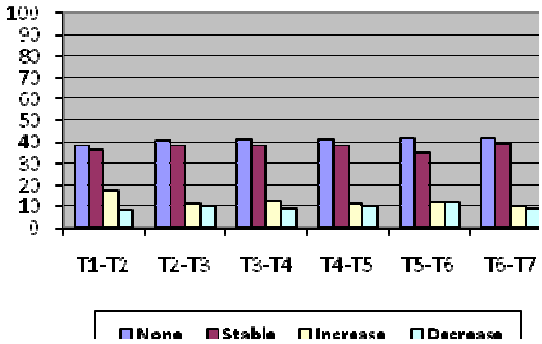


Figure 15. Effect on tobacco smoking of increased alcohol use

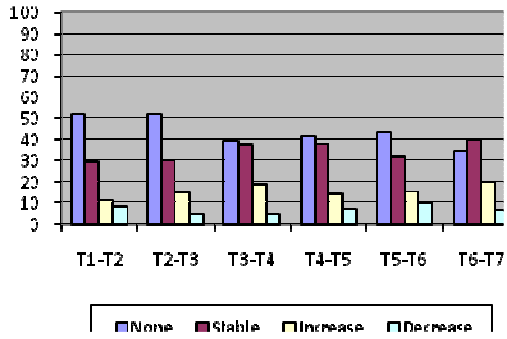
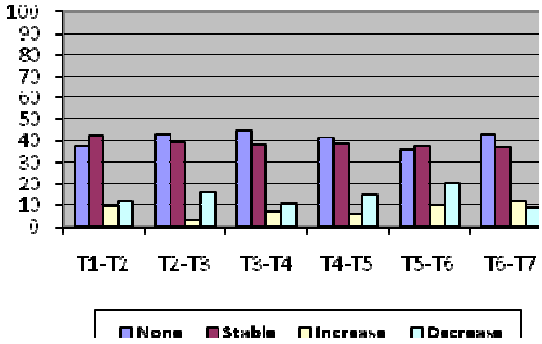


Figure 16. Effect on tobacco smoking of decreased alcohol use



Variables predicting increase in tobacco smoking

Both an increase in cannabis use (OR: 2.59) or in alcohol use (OR: 3.12) predict an increase in smoking, although so does a stable alcohol use level (OR: 2.93). Being in an other class in compulsory school (OR: 1.68) and being foreign born (OR: 1.50) are also predictors. (Table 15)

Variables predicting decrease in tobacco smoking

Both a decrease in cannabis (OR: 2.94) or alcohol use (OR: 3.44) predict a decrease in the smoking level. However, a stable level of alcohol use is also a predictor (OR: 2.18). Being a worker (compared to a student) reveals lower odds to decrease smoking (OR: 0.50) (Table 15).

Table 15. Variables predicting changes in tobacco smoking.

	Increase in tobacco smoking			Decrease in tobacco smoking		
	OR	95%CI		OR	95%CI	
Region						
German (ref)	1			1		
French	0,83	0,62	1,09	1,04	0,76	1,43
Italian	0,85	0,59	1,22	0,92	0,58	1,47
Compulsory school						
Pre-gymnasium (ref)	1			1		
Extended requirements	1,22	0,93	1,59	1,19	0,88	1,62
Basic requirements	1,03	0,71	1,50	0,89	0,59	1,34
Other	**1,68**	**1,03**	**2,76**	1,04	0,62	1,75
Gender (male)	1,00	0,79	1,27	0,80	0,61	1,05
Country of birth (other)	**1,50**	**1,00**	**2,24**	0,94	0,58	1,52
Age	0,99	0,97	1,01	1,01	1,00	1,03
Family wealth	1,09	0,93	1,28	1,12	0,94	1,34
Socioeconomic status						
Student (ref)	1			1		
Apprentice	0,95	0,70	1,28	0,87	0,62	1,21
Worker	0,93	0,59	1,45	**0,50**	**0,31**	**0,80**
Nothing	0,95	0,37	2,47	0,56	0,21	1,49
Evolution of cannabis use						
no use (ref)	1			1		
stable	0,97	0,60	1,57	1,31	0,77	2,22
augmentation	**2,59**	**1,78**	**3,76**	1,20	0,68	2,10
diminution	1,09	0,63	1,86	**2,94**	**2,08**	**4,16**
Evolution of alcohol use						
no use (ref)	1			1		
stable	**2,93**	**1,73**	**4,94**	**2,18**	**1,28**	**3,69**
augmentation	**3,12**	**1,75**	**5,58**	1,62	0,84	3,12
diminution	1,32	0,65	2,65	**3,44**	**1,84**	**6,45**
Employed (no)	1,01	0,74	1,40	1,37	0,97	1,92
Negative life events						
None (ref)	1			1		
1	1,18	0,91	1,54	0,90	0,68	1,20
2	1,09	0,78	1,53	1,27	0,85	1,88
>2	0,92	0,59	1,43	1,18	0,74	1,87
At least one postulation	1,21	0,75	1,93	0,75	0,43	1,30
Educational/work drawback	0,86	0,55	1,33	1,03	0,62	1,69
Changing school/work	1,04	0,70	1,54	1,49	0,88	2,53
Low grades	1,06	0,81	1,40	0,94	0,70	1,27
Psycosomatic symptoms	0,95	0,72	1,27	1,00	0,74	1,35
Faith in future	0,92	0,74	1,15	0,87	0,69	1,10
Very satisfied with training	0,98	0,76	1,28	1,16	0,86	1,56
Social support	0,87	0,54	1,39	1,26	0,71	2,24
Self-esteem	0,98	0,78	1,22	1,02	0,75	1,37
Positive affectivity	1,01	0,79	1,30	1,01	0,82	1,25
Negative affectivity	1,09	0,91	1,30	0,97	0,79	1,19
Perseverance in training	1,03	0,77	1,36	0,91	0,67	1,24

(Note: significant values are in bold type)

Changes in alcohol use

Whatever the use of cannabis (none, stable, increasing or decreasing), alcohol use remains mainly stable, with percentages around 70% (except for no cannabis use, where the percentages are slightly lower). However, when cannabis increases, alcohol also increases, especially at T6-T7, when there is an increase in almost 40% of the cases. Similarly, when cannabis use decreases, alcohol seems to also decrease, although with lower percentages (10-20%) (Figures 17 to 20).

Figure 17. Effect on alcohol use of no cannabis use

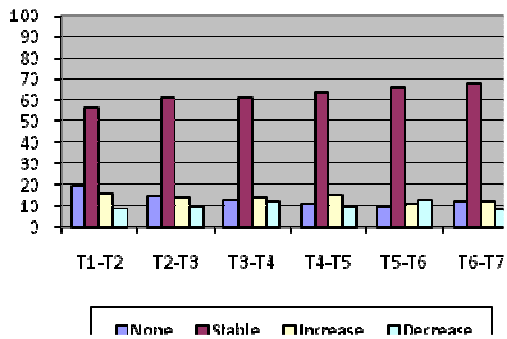


Figure 18. Effect on alcohol use of stable cannabis use

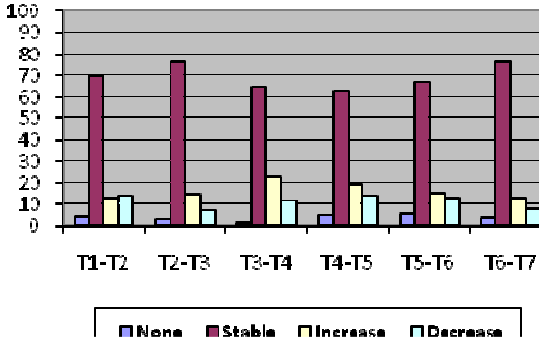


Figure 19. Effect on alcohol use of increased cannabis use

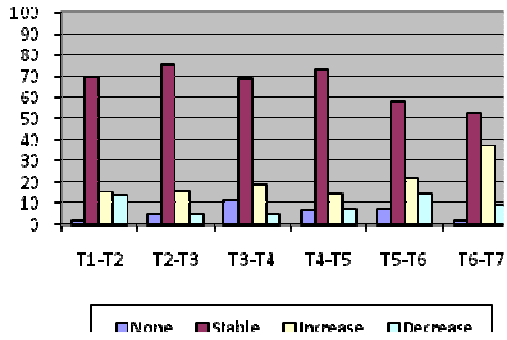
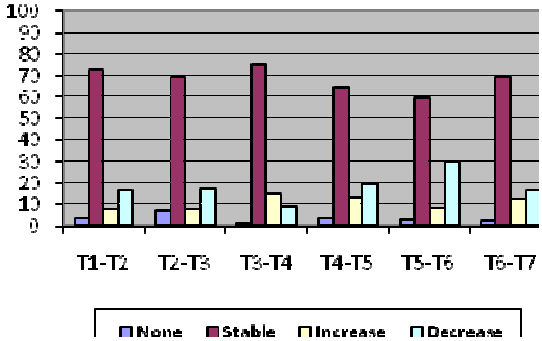


Figure 20. Effect on alcohol use of decreased cannabis use



Among those not smoking tobacco, alcohol is mainly stable although increasing from half of the group at T1-T2 to two-thirds at T6-T7. This difference is mainly due to a decrease in alcohol non-users.

When tobacco smoking is stable, so is mainly alcohol use (around 70%). When tobacco smoking increases, so does alcohol use (from 10% of the cases at T1-T2 to almost one quarter of the cases at T6-T7), although most cases remain stable. On the contrary, when tobacco smoking decreases, so does alcohol use in 10-15% of the cases (and remains stable in 60-70%) (Figures 21 to 24).

Figure 21. Effect on alcohol use of no tobacco smoking

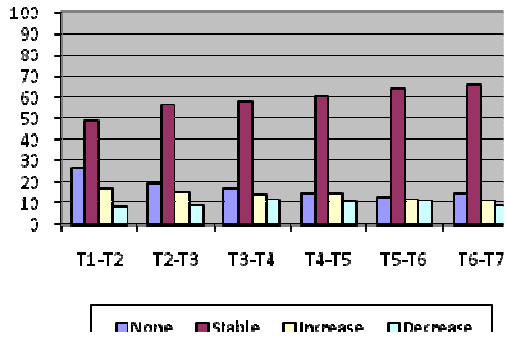


Figure 22. Effect on alcohol use of stable tobacco smoking

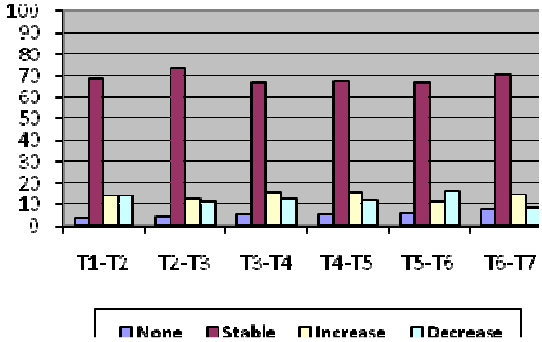


Figure 23. Effect on alcohol use of increased tobacco smoking

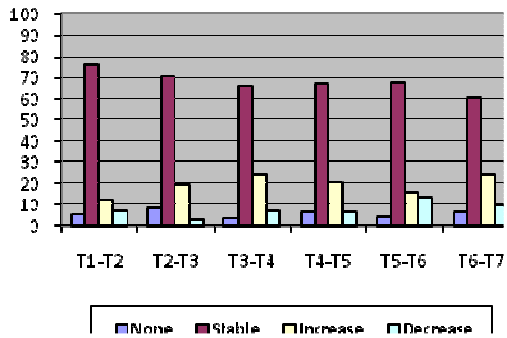
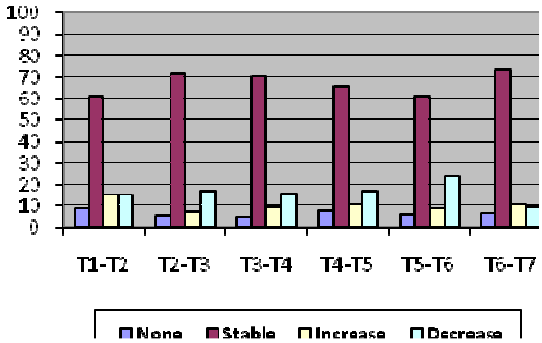


Figure 24. Effect on alcohol use of decreased tobacco smoking



Variables predicting increase in alcohol use

Only being male (OR: 1.27) and working (OR: 1.67) have an influence on an increase in alcohol use. However, living in the Italian part of the country (OR: 1.34; p=.069) and being in the basic requirements academic track in compulsory school (OR: 1.36; p=.066) show a trend towards an increase in alcohol use. Contrarily, a decrease in tobacco use shows a trend to be inversely associated (OR: 0.63; p=.061) to it. (Table 16)

Variables predicting decrease in alcohol use

A decrease in tobacco smoking is associated with a decrease in alcohol consumption (OR: 1.67) while an increase in tobacco smoking is inversely associated (OR: 0.57). Those being in the basic requirements academic track are also more likely to decrease alcohol use (OR: 1.49). (Table 16)

Table 16. Variables predicting changes in alcohol use.

	Increase in alcohol use			Decrease in alcohol use		
	OR	95%CI		OR	95%CI	
Region						
German (ref)	1			1		
French	0,95	0,73	1,24	1,20	0,91	1,59
Italian	1,34	0,98	1,84	1,33	0,93	1,89
Compulsory school						
Pre-gymnasium (ref)	1			1		
Extended requirements	1,12	0,88	1,42	1,13	0,86	1,49
Basic requirements	1,36	0,98	1,88	**1,49**	**1,05**	**2,11**
Other	0,75	0,48	1,17	1,28	0,82	2,00
Gender (male)	**1,26**	**1,02**	**1,56**	1,08	0,84	1,38
Country of birth (other)	1,03	0,73	1,45	0,97	0,64	1,46
Age	0,99	0,97	1,01	1,01	1,00	1,03
Family wealth	0,96	0,85	1,09	1,04	0,91	1,20
Socioeconomic status						
Student (ref)	1			1		
Apprentice	0,81	0,61	1,07	1,07	0,80	1,43
Worker	**1,67**	**1,13**	**2,46**	0,93	0,61	1,41
Nothing	0,80	0,21	3,03	1,00	0,40	2,50
Evolution of cannabis use						
no use (ref)	1			1		
stable	1,36	0,89	2,09	0,80	0,44	1,44
augmentation	1,34	0,88	2,04	0,80	0,47	1,36
diminution	0,68	0,38	1,20	1,26	0,83	1,91
Evolution of tobacco smoking						
no use (ref)	1			1		
stable	0,79	0,59	1,05	1,10	0,81	1,50
augmentation	1,22	0,88	1,69	**0,57**	**0,37**	**0,89**
diminution	0,63	0,39	1,02	**1,67**	**1,15**	**2,43**
Employed (no)	1,30	0,97	1,74	1,06	0,77	1,47
Negative life events						
None (ref)	1			1		
1	1,13	0,89	1,45	1,24	0,93	1,65
2	1,26	0,92	1,73	1,16	0,81	1,66
>2	1,28	0,86	1,91	1,20	0,77	1,86
At least one postulation	0,73	0,48	1,09	0,84	0,51	1,38
Educational/work drawback	1,04	0,71	1,53	1,17	0,76	1,80
Changing school/work	0,93	0,64	1,37	0,85	0,55	1,32
Low grades	1,12	0,86	1,46	1,15	0,88	1,51
Psycosomatic symptoms	1,18	0,91	1,52	1,01	0,77	1,32
Faith in future	0,95	0,79	1,15	1,09	0,84	1,42
Very satisfied with training	1,00	0,79	1,26	0,85	0,65	1,11
Social support	0,98	0,60	1,62	0,97	0,60	1,55
Self-esteem	0,98	0,77	1,25	1,09	0,83	1,44
Positive affectivity	1,15	0,94	1,40	0,85	0,66	1,07
Negative affectivity	0,96	0,82	1,14	1,02	0,83	1,25
Perseverance in training	0,86	0,64	1,14	1,02	0,76	1,38

(Note: significant values are in bold type)

KEY FINDINGS

Overall

- ☐ Overall, whatever the substance used (or non used) at age 16, there are high chances to continue to be using the same substance(s) at age 22, especially when tobacco is involved. The same holds true for abstinence.
- ☐ Among those using tobacco and/or cannabis, the main changes (whether increasing or decreasing) happen mainly between waves 5 and 6, which correspond to 20-21 years of age.
- ☐ Most abstainers will continue to be so, and those who do not will become mainly tobacco smokers.
- ☐ For both tobacco and cannabis, the trajectories of occasional and regular users seem quite different. While the former are more likely to become abstinent, the latter are more likely to be regular users of any or both substances.
- ☐ Although it remains mainly stable, there is a trend indicating that when one substance increases the other one(s) does the same and that when it decreases so does the other(s).

Cannabis

- ☐ Globally, cannabis use decreases overtime.
- ☐ The majority of cannabis users are occasional users.
- ☐ Males are more likely to be using cannabis than females. This difference appears mainly among regular cannabis users.
- ☐ There are few individuals using cannabis only and they diminish overtime. Half of them are abstinent by age 22, although sizeable percentages will become tobacco smokers (28%) or tobacco and cannabis users (16%).
- ☐ The vast majority of cannabis only users that become abstinent were occasional users and probably just experimenters. Those shifting to tobacco only or to tobacco and cannabis were mainly regular users.
- ☐ However, cannabis only users have higher odds than abstainers to become occasional or regular cannabis users or regular smokers overtime.

Tobacco

- ☐ Tobacco smoking increases overtime. Most of this increase is due to regular smokers. Again, males outnumber females.
- ☐ Tobacco only smokers have higher odds than abstainers to continue to smoke overtime and most of them will continue to be smokers. However, they do not have higher chances to become cannabis users.
- ☐ Only one fifth of tobacco only smokers will become abstinent overtime, and most of them were occasional smokers. On the contrary, the majority of those who continue to smoke or who shift to tobacco and cannabis were regular smokers.

Tobacco & cannabis

- ☐ The combination of tobacco & cannabis use also decreases overtime
- ☐ About the same percentage (40%) of those using both substances continue to use both or only tobacco overtime. However, those who continue to use both substances were mainly already regular

users of both substances while those switching to tobacco only were more likely to be regular smokers but occasional cannabis users.

Alcohol

- ☐ The vast majority of adolescents and young adults drink alcohol and its use increases with time. As is the case for the other substances studied, males outnumber females.
- ☐ There is a clear gender difference: females are more likely to be occasional drinkers, while males are more likely to be regular drinkers. Moreover, males outnumber females in two-three-fold among regular drinkers.
- ☐ Interestingly, the percentage of regular drinkers doubles (in both gender) between T3 and T4. This corresponds to ages 18-19 when youth are allowed to consume any kind of alcohol.

Risk factors

- ☐ Alcohol use is a risk factor for the use of any of the other two substances, and its effect appears in all models. The fact that abstinent youths show lower odds seems to confirm this point.
- ☐ Being foreign born also shows a clear association with any form of tobacco use, and the same is true for belonging to a wealthier family.
- ☐ Having little faith in their future is a risk factor for any kind of cannabis use except cannabis only, for tobacco smoking (independently of the use of cannabis), and for any combination of both substances.
- ☐ Being in an academic track other than pre-gymnasial in compulsory school is globally a risk factor for tobacco use.

- ☐ Having lived two or more negative life events also influence starting smoking tobacco (whether or not with cannabis use) or starting any substance use.
- ☐ Low academic performance is mainly associated to using both substances.
- ☐ Being a student (compared to an apprentice) is a risk factor to engage in cannabis use, especially when tobacco is also used.
- ☐ Gender has little influence, except that being male is associated to being a cannabis only user or a cannabis user independently of using or not other substances.
- ☐ The same applies to age: younger age is a risk factor solely for tobacco only smokers.

Protective factors

- ☐ Being in a high-school/pre-gymnasial academic track in compulsory school is associated both to being an abstinent and to becoming one.
- ☐ Living in the Italian part of the country is a protective factor for tobacco and for tobacco & cannabis use, and to remain abstinent.
- ☐ Being older predicts becoming an abstinent.

MAIN CONCLUSIONS

- The data indicate that the type of substance(s) used at age 22 is already present at age 16. This finding reinforces the need to start prevention of substance use early, as at age 16 it seems to be well established among them.

- Nevertheless, an important difference can be observed depending on the level of substance consumption: occasional users are very likely to abandon the use of the substance overtime while regular users remain. This can be seen among those using both substances: if their use of cannabis is occasional, they will become mainly tobacco smokers overtime, while if they use both substances regularly they have higher odds to continue to use both.

- For any of the three substances analyzed, males outnumber females. This difference is much more accentuated among regular users. From this point of view, prevention programs should be targeted by gender.

- The use of cannabis (whether alone or combined with tobacco) decreases overtime. The main change towards a decreasing trend (both among occasional and regular users) seems to occur between T5 and T6 which corresponds to ages 20-21 years. The fact that this age corresponds for many youths to the end of the education and entering the working force may play a role.

- The use of both legal substances (tobacco and alcohol) increases overtime. However, while regular tobacco use increases steadily, regular alcohol use shows an important increase at ages 18-19 years, coinciding with attaining the legal age to drink any kind of alcohol.

- As described in the literature, cannabis users have high chances to become tobacco users. However, the reverse is not true: a tobacco only smoker at age 16 very rarely will become a cannabis user.

- As reported in the literature, alcohol is the most widely used substance among youth at any age, and its use increases overtime.

- Alcohol use is a risk factor for the use of the other two substances, whether alone or combined. This finding links Kandel's gateway theory with those who consider the reverse effect between cannabis and tobacco. As described by Kandel, alcohol continues to be a previous step for cannabis use, but, as described in the reverse gateway theory, cannabis use leads to tobacco use, especially among regular cannabis users.

- Having faith in the future is an important factor influencing the use of cannabis and/or tobacco. Having a life goal and being convinced that the goal can be achieved would be an important protective factor, while having little faith on what the future can bring seems to be a risk factor for substance use. Assuring a future for youth (be it academically or, more importantly, professionally) is an crucial way to prevent substance misuse or abuse.

- Interestingly, cannabis only use seems to be more related to being a student while tobacco only smoking to being an apprentice. One the one side we know that most cannabis only users will become abstinent overtime or, in the worse of cases, tobacco smokers. On the other, we also know that by age 20-21 cannabis use decreases significantly and this coincides with entering the professional world or higher education. From this point of view, cannabis use, particularly occasional use, seems to suit the students' trajectory. On the contrary, the earlier exposition to the adult world that face apprentices probably causes their higher implication in tobacco smoking.

- Nevertheless, and it has been widely described in the literature, a low academic performance is a risk factor for the combined use of cannabis and tobacco. This finding indicates that low achievers should be an important target population for prevention.

- One of our hypothesis was that a decrease in the use of tobacco or cannabis would be followed by an increase of the other. However, our results seem to indicate that, even though in small percentages, when one substance increases so does the other and when one decreases the other one follows the same trend. In fact, in most cases the use of the other substance remains stable. Nevertheless, this could be due to the way the data were collected. Actually, our data allow us to determine the frequency of use but not the quantity used. From this perspective it could well be, for example, that when cannabis use decreases tobacco smoking remains stable but that, in reality, the frequency does not change (for example, they continue to smoke daily) but the quantity (more cigarettes per day) does. Future research should assess this hypothesis.
- Our results also confirm the important association between cannabis and tobacco use and reinforce the need to tackle both substances in any cannabis cessation program.

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Annex 1: Review of the literature

Adolescence is no longer described exclusively as an inevitable period of storm and stress(1). Even so, substance use and its related disorders are significant problems appearing mostly during adolescence and young adulthood(2). Being a public health issue of great concern, substance use is also one of the major social and legal challenges of our modern world(3). The possible adverse consequences related to the use or abuse of any drug are global and touch individuals physically, socially and psychologically(3). Because key determinants of later adult health develop during teenage years, substance use is therefore a subject of utmost importance during this period(4).

As adolescents continue to use illicit and legal substances at alarming rates(4;5), the investigation of the recent changes in the prevalence of their use continues to be necessary. Thus, several surveys keep tracking those trends internationally(6;7). Switzerland, in regard to substance use, seems to exhibit a particular status. In fact, despite the recent reduction seen in the use of several substances, Swiss adolescents remain among the highest cannabis users in Europe. This observation is however not valid regarding all drugs as rates of other substances usually initiated during adolescence, such as tobacco and alcohol, are positioned near international average.

Differing by their singular psychoactive effects and by their health consequences, some significant relations have however been found between many substances used during adolescence. Indeed, substances such as tobacco and cannabis seem intrinsically linked on many aspects. The fact that both substances are smoked(8), their pattern of use across adolescence(2) and their level of dependence being influenced when concomitantly used(9) are only some examples of those significant connections. In addition, consumption of both tobacco and cannabis are associated with alcohol and ecstasy use and to other drugs as well(10). As concurrent use of multiple drugs is now becoming relatively common(11), growing attention is oriented to predict the course over time of their use and possible interactions. Common risk and protective factors for substance use are also being closely examined to better understand which adolescents are at risk for adverse health outcomes.

As prevention and early intervention programs continue to be the most cost-effective solutions regarding substance use and its related problems(5), research examining the epidemiology of legal and illegal drug use, and the complex associations existing between them, remains of main interest. As not every adolescent having used substances still uses them at an older age, understanding substance use trajectories and factors influencing their courses are imperative to plan adequate interventions and, consequently, improve adolescent health.

In this review of the literature, the epidemiology of tobacco, cannabis and other drugs used during adolescence in Switzerland will be addressed. Current prevalence rates and trends of these substances in Switzerland will be examined. Additionally, Swiss data will be compared with European data. Besides, the relationships existing between substances will be examined with a special attention to the particular links connecting tobacco with cannabis. Specifying the common relevant trajectories of substance use, we will also enumerate the different risk and protective factors of substance use during adolescence.

Tobacco use

Tobacco is still the leading cause of preventable death in the world. Causes of mortality such as cardiovascular diseases, chronic pulmonary diseases and lung cancer are highly associated with chronic tobacco use. Extremely rare during adolescence, those complications however result from chronic lifetime consumption and intense use having started at younger age. Consequently, tobacco initiation during adolescence is considered as worrisome(7).

Current prevalence rates

Data from the 2006 *Health Behavior of School-aged Children* (HBSC) survey demonstrate that initial tobacco use among Swiss students occurs at an early age. For teens aged 15 who had tried tobacco at least once (61% of males and 56% of females), first cigarette use took place on average at age 12 for males and at age 13 for females(12). Even if not all adolescents become regular smokers after that initial cigarette, a fair proportion of them however do. Current prevalence rates for 15 year-old weekly smokers are 15%, for both males and females and one out of ten youth smoke daily at this age(7).

Data from the 2007 Swiss Health Survey (SHS) display a similar situation. In fact, in a population of adolescents and young adults ranging from 15 to 24 years-old, the proportion of current smokers was 36.6% for males and 30.5% for females(13). Previously, in 2002, the SHS further analyzed the difference of smoking status according to age in Switzerland. A net progression of use was seen with age: at age 15, 16% reported to smoke tobacco, a maximum of 48% was seen at age 18 and then stabilized near 42% between 19 and 24 years(14). Additionally, in 2007, the *European school survey project on alcohol and other drugs* (ESPAD) study also observed the same pattern as 12.5% of adolescents aged 13, 18.6% aged 14, 29.4% at 15 and 31.5% at 16 reported having smoked tobacco in the month preceding the survey(12).

Tobacco use among adolescents reporting different academic tracks has been assessed for the last time in Switzerland with the Swiss Multicenter Adolescent Survey on Health (SMASH) in 2002. This survey was based on a nationally representative sample of Swiss adolescents in post mandatory school aged 16 to 20 years. The rate of regular smoking among apprentice females ranged from 29% at age 16 to a maximum 41.3% at 20. This maximum was only surpassed by apprentice males who reported at age 16, 25.1% of regular smoking in comparison to 45.2% at 20. For male and female students, regular smoking at age 20 was quite lower: 22.4% among females and 34.3% among males(15).

Trends

Tobacco smoking prevalence rates among adolescents in Switzerland have declined in the last years. However, peaks of use were seen in 1998 and 2002. Tobacco use has decreased for 15 year-olds from a high 24% for both gender in 1998 to a low 15% in 2006 for weekly smoking. These rates are the lowest ever observed. For daily smoking, after peaking at 16-17% in 1998 and 2002, prevalence rates in 2006 (10-11%) are mostly the same as they were in 1994, the lowest ever and barely the same for both gender(16) (Figure 1).

As seen in Figure 2, trends from the SMASH surveys(17) show that regular tobacco use has also increased between1993 and 2002 (both for males and females). However, this raise was significant among apprentices but not among students. In 1993, 27% of female apprentices aged 16-20 smoked regularly compared to 37% in 2002. In the same way, regular smoking of same age male apprentices rose from 30% to 38%. Among students, regular smoking increased a little from 17.4% in 1993 to 19.2% in 2002 in girls and stayed stable from 20.4% to 21.0% for boys(17). In conformity with data from younger adolescents, daily tobacco use among adolescents aged 20 in Switzerland had also increased from 32.2% to 41.5% for males and from 23.2% to 30.5% for females between 1993 and 2002(18).

Figure 1. Trends in tobacco smoking among Swiss 15-year-olds Swiss by gender (HBSC data)

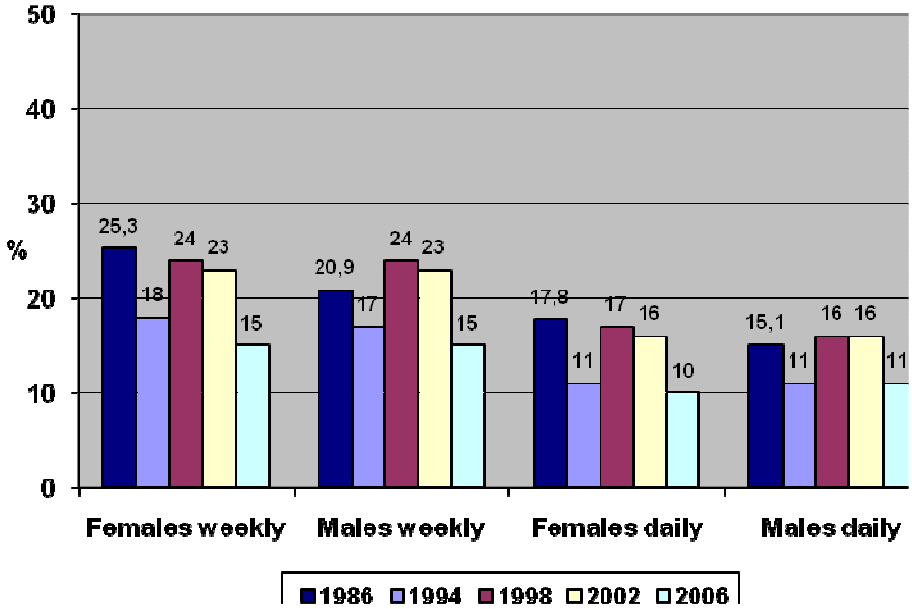
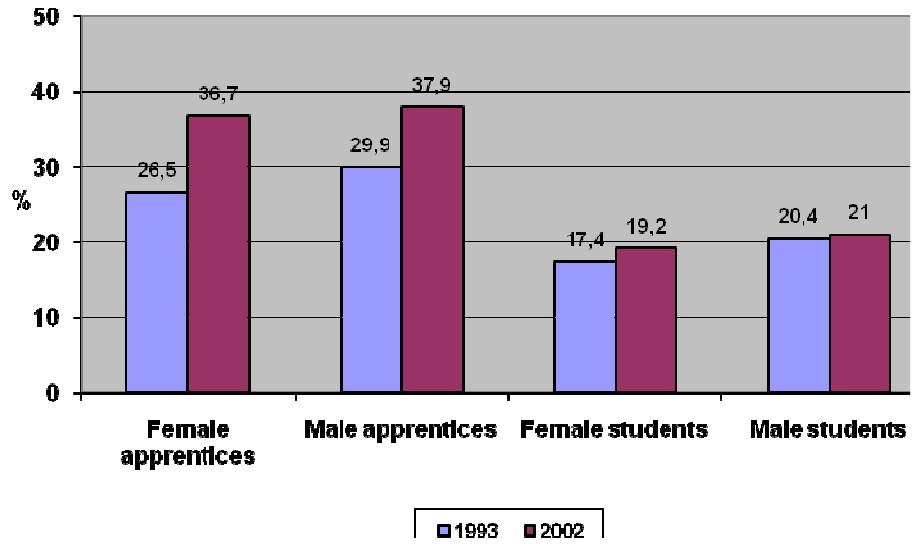
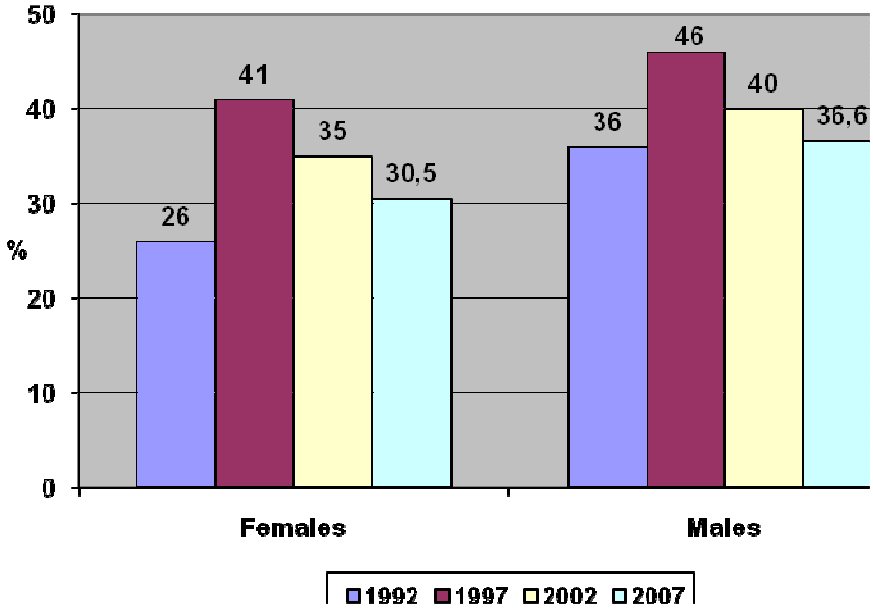


Figure 2. Trends in daily tobacco smoking among Swiss 16-20 year-olds by academic track and gender (SMASH data)



The Swiss Health Survey shows trends for youth aged 15-24 years between 1992 and 2007 (13;14). This data show that although tobacco smoking seems to be more prevalent among males in this age group, both gender show a similar curve with a peak in 1997 and a decrease afterwards. However, rates in 2007 are still somewhat higher than they were in 1992 for females although not for males (Figure 3)

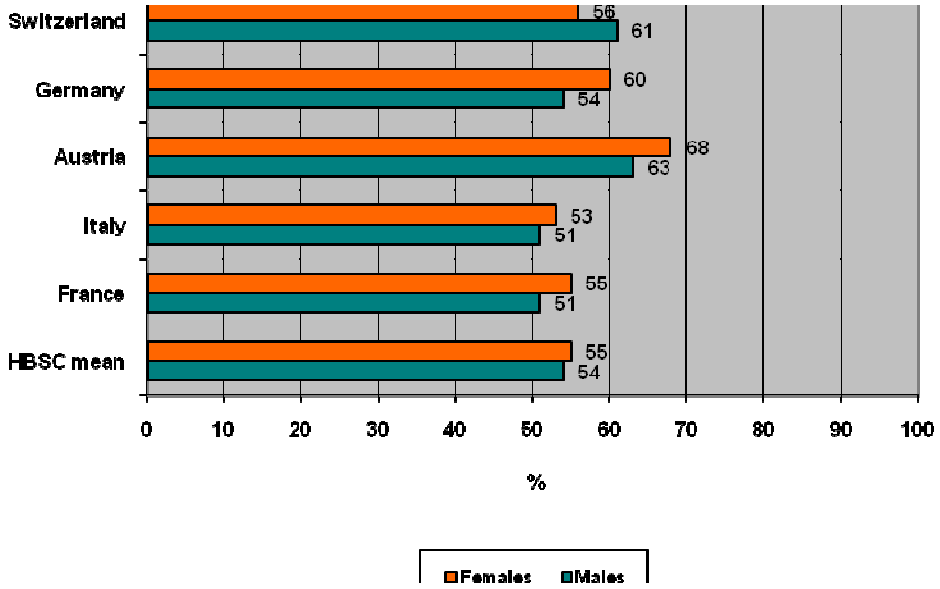
Figure 3. Trends in regular tobacco smoking among Swiss 15-24 year-olds by gender (SHS data)



International comparison

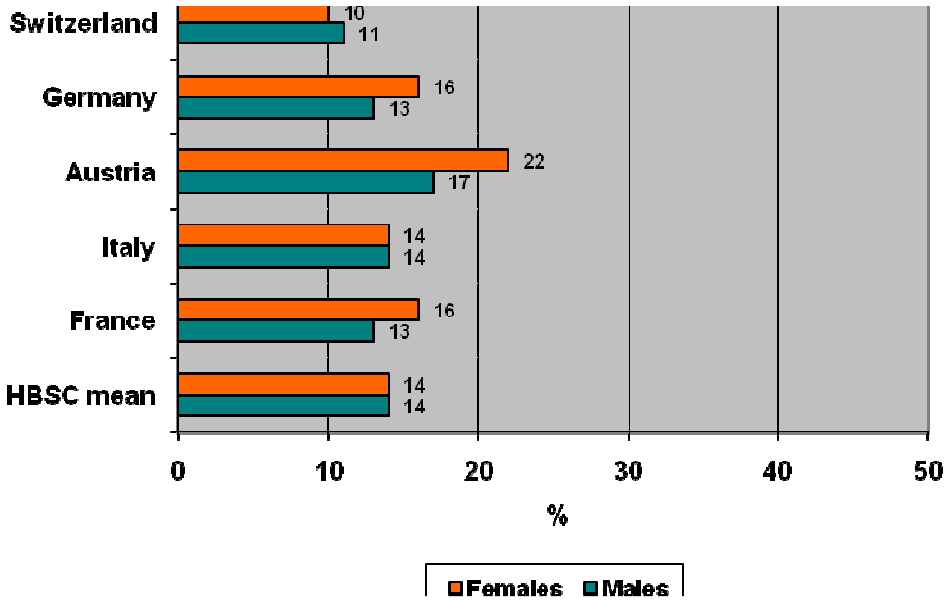
In many European countries, data from 2006 indicated that a majority of their teenagers aged 15 had smoked a least once in their lifetime, ranging from 77% (Lithuania) to 36% (The Former Yugoslav Republic of Macedonia). With the exception of Austria, Switzerland shows the highest rates of ever smoking among its neighboring countries, with rates slightly above the mean for all the HBSC participating countries. Compared to its neighboring countries, Switzerland is the only one where males report higher smoking rates than females(7) (Figure 4).

Figure 4. Rates of ever smoking among adolescents aged 15 by gender in selected European countries in 2006 (HBSC data).



Nevertheless, at age 15, one tenth of Swiss adolescents are daily smokers. These proportions are lower than those reported in its close neighbors and below the HBSC mean. Again, Switzerland is the only one of these countries where daily smoking rates are higher in males than in females, although the difference is minimal(7) (Figure 5).

Figure 5. Rates of daily smoking among adolescents aged 15 by gender in selected European countries in 2006 (HBSC data).



A higher proportion of young girls than boys are now smoking regularly in many European countries. However, when rates of weekly smoking among boys and girls at ages 13 and 15 in the countries having participated in HBSC in 2006 are cumulated, they tend to be similar. Therefore, where significant differences do exist, they favor boys and girls in roughly equal proportions(7).

Cannabis use

Cannabis is a generic term used to denote the several psychoactive preparations of the marijuana plant including marijuana leaf (in street jargon: grass, pot, dope, weed) or hashish (derived from the resin of the flowering heads of the plant), and hashish oil(19). In western countries, cannabis is the third most used substance after alcohol and tobacco(20). The vast majority of European students who reported having tried an illicit drug in their lifetime, have in fact used marijuana or hashish(6). Even if divergence still exists on the harmful somatic health consequences of its use(21-23), cannabis consumption may lead to dependence and to other adverse mental health consequences, like psychotic disorders(24) and depression(25). With prevalence rates highest among young people, cannabis use during that period remains worrisome as it has frequently been associated with poorer psychosocial outcomes in adult life(26).

Current prevalence rates

The most recent HBSC data (2006) indicate that among 15 year-old Swiss teenagers, 34.2% of males and 26.8% of females have ever tried cannabis. Having reported using cannabis at least once, those Swiss adolescents had their first experience with the substance, on average, by age 13 for both genders and generally after first tobacco use(27). At the same time, reports of cannabis use in the previous year for Swiss teens in 2006 were roughly of one fourth of males and one fifth of females aged 15(16). Even if less prevalent, regular cannabis use is not uncommon in that particular population. In fact, increasing among older adolescents, cannabis use in the last 30 days currently ranges from 5.6% among students aged 13 to 18% of those aged 16(27). Globally, 11.5% of Swiss males and 5.1% of females aged 15 to 24 reported active cannabis use in 2007(13).

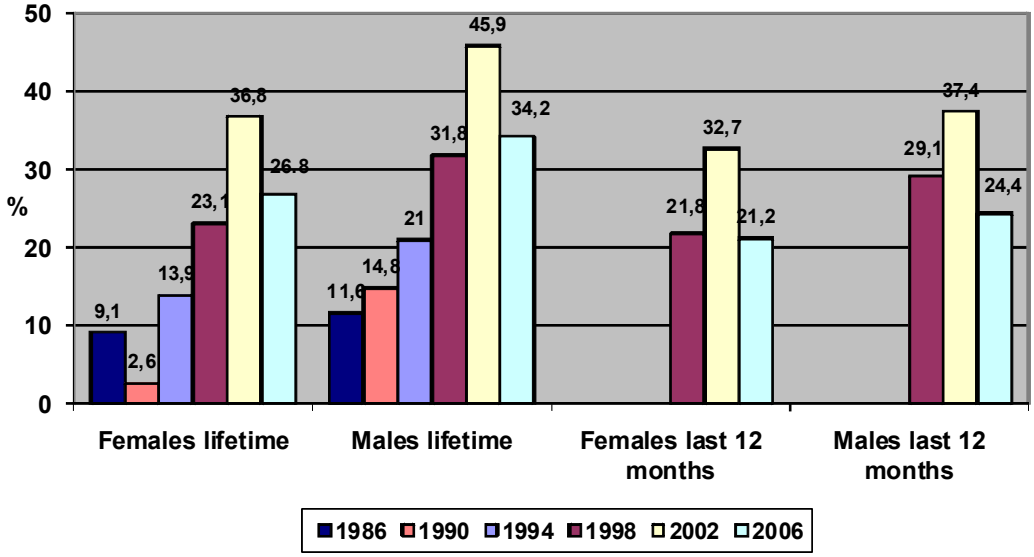
It is worth noting however that a fair proportion of adolescents stop using cannabis in the years following first use or just never start using it regularly after a first experimentation. In 2006, 5.7% of females and 9.8% of males aged 15 having formerly used cannabis reported not having used that substance in the year preceding the survey(27).

Discrepancy in cannabis use status differs between younger and older adolescents but also according to different academic tracks among Swiss adolescents. The last SMASH survey of 2002 showed small but significant differences between students and apprentices, where students (males: 27%; females: 12%) reported a slightly lower prevalence of last month cannabis use than apprentices (males: 29%; females: 15%)(15).

Trends

During the 90's, the proportion of adolescents who were cannabis users in Switzerland grew considerably. From experimentation to regular use, all type of cannabis use increased and peaked in 2002. At that time, it was almost half of boys and one-third of girls aged 15 having tried cannabis at least once in their life(27). In fact, from 1986 to 2002, the rate of 15 year-olds having ever tried cannabis showed a four-fold increase: from 9% to 37% for females and from 12% to 46% for males. However, prevalence rates have declined in 2006, although they remain higher than they were in 1998(28). When looking at users in the previous 12 months, after peaking in 2002, rates have also decreased in 2006 for both genders: among girls they are at the same level than they were in 1998 while among boys they are even lower(16) (Figure 6).

Figure 6. Trends in cannabis use among Swiss 15 year-olds by gender (HBSC data)



An increase in current (last 30 days) cannabis use has also been observed among youth in post-mandatory education, although with some gender and academic track differences. Among 16-20 year-olds, males report rates that are twice those reported by females, and apprentices report higher rates than students, although the difference tends to diminish, specially among boys(15;17) (Figure 7).

Nevertheless, daily cannabis use has doubled among 20 year-old Swiss males between 1993 (6.7%) and 2003 (14.6%) and has been multiplied by a four-fold ratio among females during the same period (from 1.2% to 5.2%)(18).

More broadly, among Swiss youths aged 15-24, males reported the highest prevalence (37.2%) of lifetime use since 1992, while the rate for females, although twice as high than in 1992, had slightly decreased compared to 2002. This can probably be explained because the 15 year-olds with a very high prevalence in 2002 are now part of this age group. Nevertheless, current cannabis use in this age group has decreased in 2007 to levels close to those observed in 1992(13;14) (Figure 8).

Figure 7. Trends in current cannabis use (last 30 days) among Swiss 16-20 year-olds by academic track and gender (SMASH data)

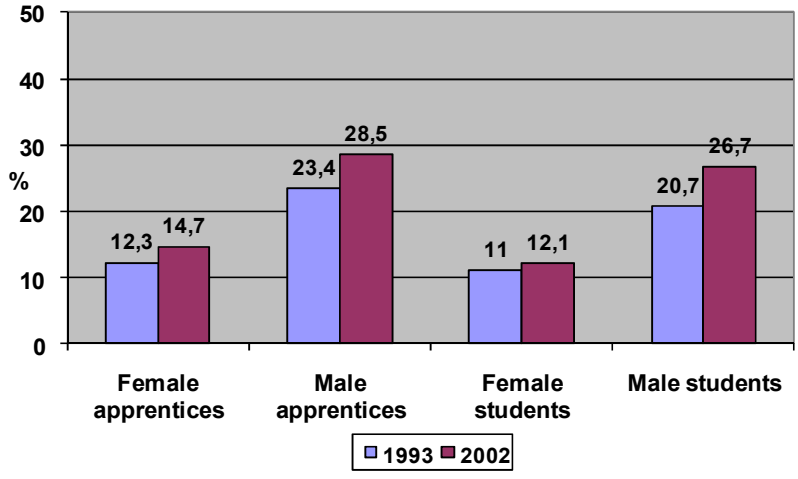
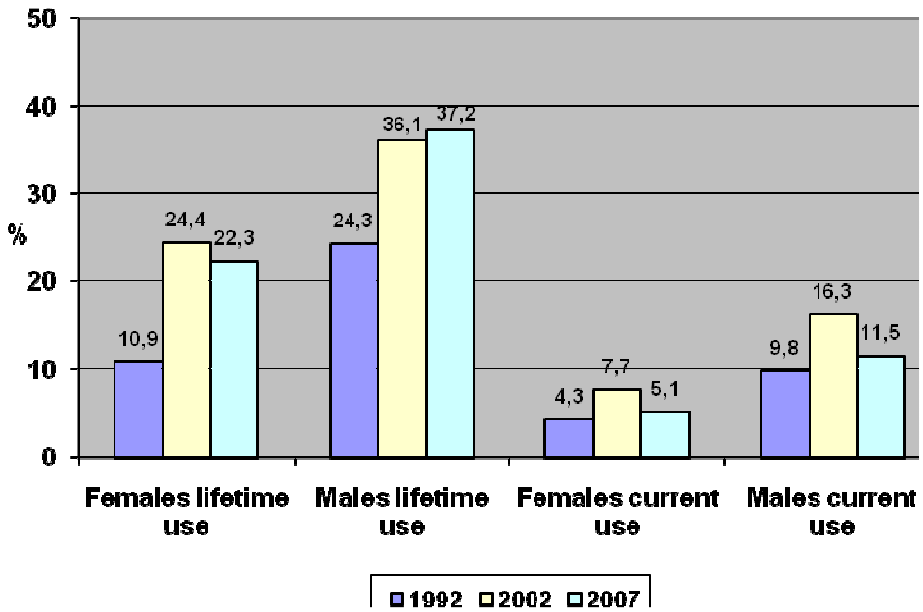


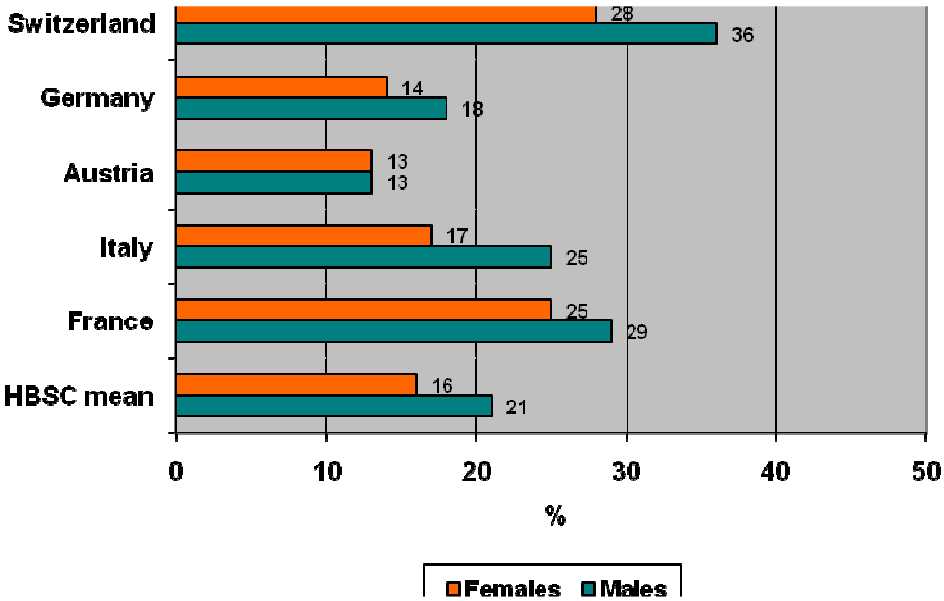
Figure 8. Trends in cannabis use among Swiss 15-24 year-olds by gender (SHS data)



International comparison

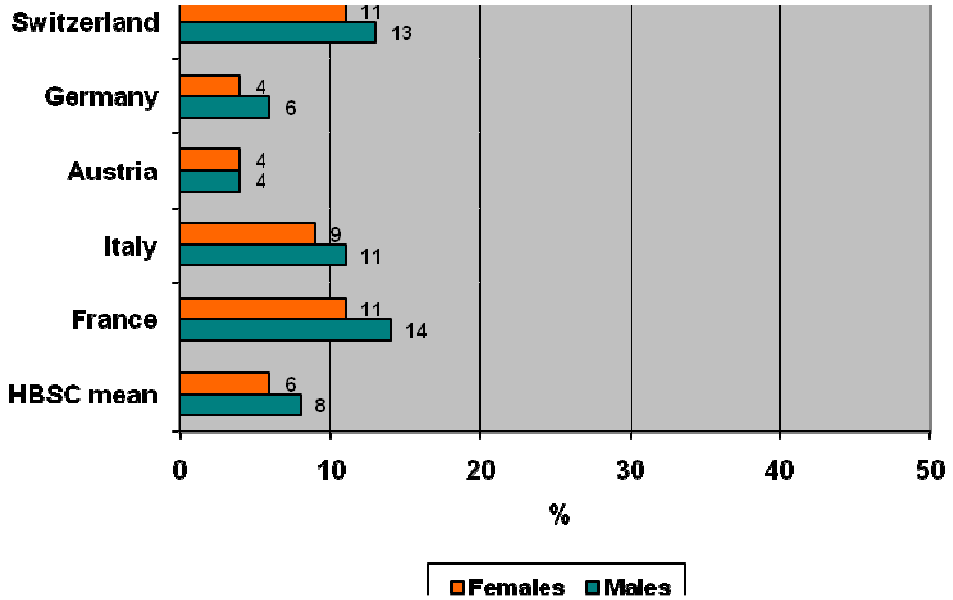
International data from the 2006 HBSC survey indicate that at age 15, Swiss teens continue to show the highest rates in Europe for lifetime use for males (36%). Additionally, female rates are higher than those reported in its neighboring countries. For both gender, rates are much higher than the observed mean prevalence of the HBSC participating countries(7) (Figure 9).

Figure 9. Lifetime cannabis use among 15 year-olds by gender in selected countries in 2006 (HBSC data).



For current cannabis use (last 30 days), the rate among 15 year-old Swiss adolescents is similar to the ones observed in France and Italy, but well above the HBSC mean. As described previously, in this case males also outnumber females(7) (Figure 10).

Figure 10. Current cannabis use (last 30 days) among 15 year-olds by gender in selected countries in 2006 (HBSC data).



One should however discern, in examining those rates, that national and international statistics are probably an underestimation of actual prevalence, as adolescents not included in school surveys, such as school drop-outs and teens in correctional facilities, usually report higher substance use rates(11;29;30). Scarce, surveys inquiring those adolescents have rarely been done in Switzerland. Yet, Swiss data from 1993 reported drop-outs having tried at least once cannabis to be as twice prevalent than peers in regular academic tracks at age 16-20(30).

Other substances

Among other substances predominantly used during adolescence, alcohol and a group of drugs described as "club drugs" have captured the interest of researchers because of their relative prevalence and the adverse health outcomes of their misuse. As initiation to alcohol usually occurs before adulthood, misuse of this substance is not rare among adolescents. Being an important risk factor for mortality and to the disease burden worldwide(31), age-specific prevention and education programs regarding alcohol misuse are now aiming especially at teenagers. Due to the relative recent apparition of various "club drugs", mostly ecstasy, and their consumption on particular occasions(32), limited literature has defined their long-term use and possible health consequences.

Alcohol

Research demonstrates that nearly all school students in developed countries report some experience with alcohol before the completion of mandatory school(33). Representing one of the desired privileges of adulthood by many adolescents(34), alcohol use can however result in adverse health outcomes mostly by injuries which are unfortunately common among young people. Many alcohol-related deaths occur in fact relatively early in life(35).

Having first met, for most, alcohol in the familial setting, Swiss adolescents' regular alcohol use has declined in comparison to 2002 as for proportion of its misuse(36). Actually, data from HBSC 2006 reveal that one out of four Swiss males aged 15 and one out of six Swiss females of the same age drink alcohol weekly. Those rates, although not the highest in Europe, contrast with the illegality to sell and give alcohol to teens less than 16 years-old in Switzerland(36). Moreover, the rate of 15 year-olds reporting at least two episodes of drunkenness in their life was 28% for males and 19% for females in 2006. Although they represented a decrease regarding the 2002 data (32% and 23%, respectively, for males and females), they are still much higher than those reported in 1986 (17% and 12%)(28) (Figure 11).

Data derived from the SMASH surveys show an increase in the number of youth aged 16-20 with at least one drunkenness episode in the previous 30 days between 1993 and 2002: from 15% to 30% for females and from 34% to 51% for males(15).

When adolescents and young adults are examined together, proportions of males and females aged 15-24 who drink alcohol on a daily basis are, respectively, 2.8% and 0.7%. This rates represent a slight decrease since 2002 for males (3.2%) and no change for females(13). Moreover, data from the 2002 Swiss Health Survey(37) indicate that 30% of males and 10% of females aged 15-24 years have a problematic alcohol use. This rates are the highest of all age groups.

Swiss males aged 15 years show rates of drunkenness episodes similar to those observed in France and Germany (29-31%) and lower than the ones in Austria (41%) or the mean for HBSC-participating countries (37%). Swiss females report rates similar to France and Italy (18% in all cases) and much lower than the HBSC mean (30%) or the one from Austria that is twice as high (36%). As was the case for other substances, in all cases males outnumber females(7) (Figure 12).

Figure 11. Trends in alcohol misuse (at least two drunkenness episodes in their life) among Swiss 15-year-olds by gender (HBSC data)

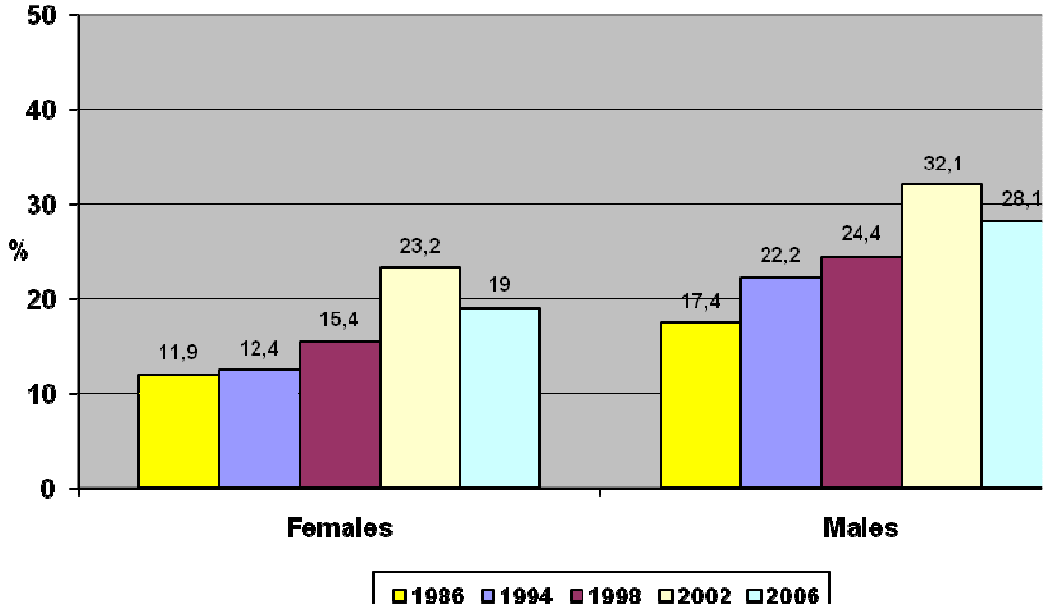
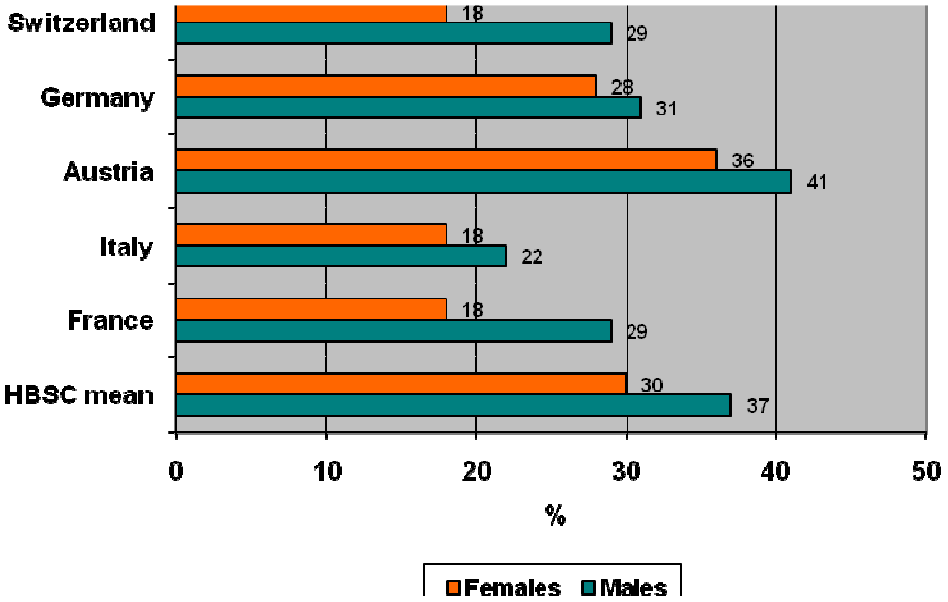


Figure 12. Alcohol misuse (at least two drunkenness episodes in their life) among 15 year-olds by gender in selected countries in 2006 (HBSC data)



Club drugs

Regarding other drugs, ecstasy has become the second most commonly consumed illegal substance, after cannabis in the European Union(10). In Switzerland, for 2006, ecstasy lifetime use however ranked after amphetamine/speed, hallucinogenic mushrooms and cocaine with prevalence rates all below 5% among teens aged 15(38). For lifetime use of ecstasy, the recent declining trend seen for tobacco, cannabis and alcohol is not present. In fact, among Swiss adolescents and young adults aged 15-24, lifetime use of

ecstasy has remained stable at 3.1% between 2002 and 2007 among males and at 1.4% among females. In addition, SMASH data for 2002 reported lifetime use of ecstasy, in addition to speed, to be of 5.5% among girls aged 16-20 and 10.5% among boys. For last month use, prevalence rates among the same population were respectively of 1.7% and 3.9%(15).

Relationship between substances

Several associations have been found between substances of possible abuse. In particular, there is a significant relationship linking cannabis and tobacco(21;39-47). In addition, associations between those two substances and the use of other substances during adolescence has been proven as well(10;48;49).

Association between tobacco and cannabis

Cannabis and tobacco usually share the same route of administration(50) and, as a result, the gestures related to their consumption are similar(8;41;51). In a recent study by Agrawal and Lynskey, the association between cannabis and tobacco use has been found to be only significant when tobacco was smoked in comparison to smokeless tobacco use(52), adding to the notion that part of the relationship between those two substances comes from the act of smoking. Yet, tobacco and cannabis smoking have distinct smoking topography as marijuana smoking involves deeper inhalation and longer breath holding(53).

The association between tobacco and cannabis is also observed when, even among non-tobacco smokers, some tobacco is usually used to prepare cannabis cigarettes(8), a process called mulling (54), to ensure a smooth combustion of the preparation(55). This method has been proven to increase the amount of Tetrahidrocannabinol (THC) inhaled per gram of cannabis used by as much as 45% under certain conditions(56). This act of mixing cannabis and tobacco therefore increases the psychoactive effects of cannabis and is also, for some adolescents, a first exposition to tobacco(55).

Manifesting very different effects, active ingredients in tobacco and cannabis, respectively nicotine and THC, have been shown to have common neurological results, mostly via the dopaminergic system(55;57). Never been proven to our knowledge, cross-sensitization between nicotine and THC stays however plausible in light of former animal studies(57). As the adolescent brain continues to evolve with age until adulthood(58), the use of one substance during that critical period could then predispose to the consumption of other drugs due to prior sensitization(57).

Craving symptoms and even cessation attempts, when both substances are used simultaneously, seem also to display the firm link existing between tobacco and cannabis. Using tobacco in combination with cannabis contributes to cannabis dependence symptoms(9). Moreover, withdrawal symptoms during simultaneous cessation of both substances are more severe than for each substance separately(59). In the same way, treatment of cannabis dependence may be more effective if it addresses the issue of concurrent tobacco use(9).

It is noteworthy that cannabis use is almost systematically accompanied by tobacco use at some point during adolescence. French data indicate that the co-consumption of tobacco and cannabis is even on the rise(60). A recent Swiss report indicates that 4 out of every five current cannabis users are also cigarettes smokers(61). As tobacco use usually precedes the onset of cannabis use, research has mainly looked at tobacco as a risk factor for cannabis use(50). In fact, Kandel's gateway theory(62;63) postulates that both tobacco and alcohol use are the previous necessary steps to cannabis use, and then to other illegal drugs such as cocaine and heroin. This hypothesis implies 3 interrelated propositions(64): (1) sequencing implies that there is a common fixed sequence of substance initiation; (2) association of initiation implies that the use of one substance increases the likelihood of initiation of the other, and (3) causation, that the first substance causes the use of the second. Causation, a controversial proposition, has never been unequivocally proven. Consequently, the gateway theory stays for many authors a controversial hypothesis(57). However, drug policies in many countries are partly based on that assumption(65).

In contrast, recent research also indicates that cannabis use may precede(10;55) or be simultaneous(66) to tobacco use and that, in fact, its use may reinforce cigarette smoking(41;51) or lead to nicotine addiction independently of smoking status(50;55). This is defined as the reverse gateway theory(55). An Australian study(55) found that among non-smoking teens, at least one report of weekly cannabis use in adolescence predicted a more than eightfold increase in the odds of later initiation of tobacco use and that for 21-year-

old smokers not yet nicotine-dependent, daily cannabis use raised the odds of nicotine dependence at the age of 24 years more than threefold after controlling for possible confounders. These data evidence that cannabis use during adolescence and young adulthood is associated with higher risk of tobacco initiation. Moreover, data from young adult American females (aged 18-29 years) show that women with a prior history of cannabis use are significantly more likely to transition from initiation to regular smoking, and from regular smoking to nicotine dependence(50). For some adolescents smoking cannabis has literally been described as having been either an introduction to smoking cigarettes, a reinforcement of their cigarette use or a barrier to quit tobacco(41). Most importantly, evidence now indicates that nicotine dependence and persistent cigarette smoking may be the main public health consequences of cannabis use(50). While US data report that only 7% of young adult females had used cannabis before tobacco(50), Swiss data among adolescents aged 16-20 years indicate that among current cannabis users 21% declare never having smoked a cigarette(61).

Association of tobacco and cannabis use with other substances

The associations found among substances used during adolescence are not limited to the relation between tobacco and cannabis. In fact, alcohol use is predominant among adolescents smoking those substances. The majority of adolescent tobacco smokers also consume alcohol. In 2006, 25% of all adolescents aged 15 in a German sample reported recent concurrent use of both substances. Compared to consumers of alcohol only, those adolescents using both substance during the same period had significantly higher levels of consumption, more excessive use of alcohol, started to drink at an earlier age and showed a higher dependence score to nicotine(67). In addition, adolescent smokers are also known to have a 4.5-fold higher odds of alcohol use disorders than never smokers(68). Problematic drinking among adolescents is also associated with cannabis use(69;70). American longitudinal data even reported that use of cigarettes and marijuana at age 18 predicted heavy drinking at age 35(70).

Ecstasy has become a well known drug among teenagers. In 2005 a prospective-longitudinal study done in Germany demonstrated that cannabis use during adolescence is a powerful risk factor for ecstasy consumption owing a six-fold increase risk for subsequent onset of ecstasy use(10). As seen among the majority of cannabis users having used tobacco previously, nearly all ecstasy users in that same German study had also used cannabis at least once before age 24(10). The use of illicit drugs other than cannabis has also been described, in a French population of adults and adolescents, to range from 0.4% among cannabis abstainers to 25% in cannabis regular users(60).

Trajectories in substance use

Substance use along lifetime is not static. Some pathways of use are well known to exist for specific substances and recent studies continue to add knowledge on the influence that substances have on their trajectories when used concurrently. For instance, 95% of tobacco and cannabis users started to use the substance before the age of 20 years and their use seems to peak at age 19-21 to decrease afterwards(2;26). In addition, timing of initiation of one substance seems not only to influence its own use but the use of other substances too. As cannabis onset before late-adolescence predisposes to cannabis dependence (71), early cannabis use predicts other substance-related problems as well such as nicotine dependence(50;55). Similarly, early tobacco use is associated to the use of both alcohol(67;72) and illegal drugs such as ecstasy, cocaine or amphetamines at an older age(2). As timing of initiation of one drug influences diverse courses of substance use, intensity of use also seems to have a major importance on further consumption.

Being initiated on diverse moments and used at various intensities, substances used during adolescence and young adulthood may be examined within diverse pathways which can predict further type of use as outcomes. For instance, cannabis use initiated during early adolescence is associated to heavy cannabis use afterwards(2;73). When examined more closely, considerable heterogeneity exists in the developmental trajectories of substance use. Ellickson et al. reported that, using a sample of 5883 adolescents aged 13 who were followed until young adulthood (age 23), 4 trajectory groups were identified for cannabis use, after removal of abstainers: early high users, stable light users, steady increasers and occasional light users. Among those, abstainers consistently had the most favorable behavioral, socioeconomic and health outcome by age 29, whereas early high users, the least(26).

When several drugs are used at the same time, trajectories of use seem to become intrinsically joint. A recent examination of the co-occurrence of at least weekly cannabis use among low risk teenage alcohol users in an Australian cohort predicted a sevenfold higher rate of daily cannabis use in young adults and a twofold increase in high-risk alcohol use(48). Identification of those specific jointed trajectories, with substances sequencing of initiation and intensity of use turns out to be a complex task but also has some benefits. A study carried out in the United States, has evidenced that having maintained smoking cessation more than 12 months during adolescence was associated with significantly lower rates of future alcohol use disorders in young adults(49). Thus, the introduction of a change in the use of one substance may therefore be associated with a significant evolution on the consumption of concurrent substances. Additionally, the study of those concurrent consumptions is more than theoretical given the evidence that interventions such as policies affecting the use of one substance may affect the use of another substance (for example, the effect of pricing and age of legal use of alcohol reduces its consumption and influences cannabis use in the same direction) (74).

Trajectories of substance use are also influenced by crucial events happening during adolescence and young adulthood. In this sense, data from the US-based project *Monitoring The Future* show that life events such as being married, becoming a parent, being employed or attaining higher education are associated to lower rates of cannabis use in young adulthood(75). The same can be said for cigarette smoking and heavy drinking(76;77). A Norwegian study(78) also found that, among adolescent and young adult women, life events such as childbirth, abortion or living with the father of the child have an influence on subsequent substance use.

It is also worth noting that adolescents using substances are at higher risk to become substance dependent as adults(76;79;80). Consequently, substance use also affects educational attainment and professional development. Smokers have lower academic aspirations than non-smokers(81) and young adults not enrolled in school are more likely to smoke(82). Cannabis use seems to decrease educational achievement in young people(83), and early marijuana users are more likely to have problems that limit the acquisition of skills necessary for employment(45). Early tobacco use(84) and the use of cannabis(85) or illegal drugs(86) have also been related to higher rates of school drop-out. Actually, school dropouts and

unemployed adolescents are more likely to be using substances(87;88). Substance users are also more likely to skip classes(89). In fact, reducing substance use is associated with increased likelihoods of school attendance(90). Overall, adolescent substance use disorder is associated with less education and recent unemployment at age 30(80). Accordingly, cannabis abstainers from early adolescence through adulthood have the most favorable outcomes on behavioral, socioeconomic and health outcomes whereas early high users consistently have the least favorable outcomes(26). However, not all studies regarding adolescents and young adults who use substances confirm that substance use is solely associated with adverse outcomes. In fact, Suris et al. reported that cannabis-only users, compared with abstainers, among a nationally representative sample of Swiss adolescents aged 16-20 years-old, reported similar academic performances(61) and were more socially driven(61;91). However, other results refute the idea that adolescents who abstain from substance use are socially maladjusted, and suggest instead that they function better than cannabis experimenters later in life(91).

Risk and protective factors

Adolescent substance use is embedded in a complex network of personal, familial and social risk factors that may contribute both to substance use and later negative outcomes(39;42-44;81;82;92-94). These multiple factors must be taken into account as they can act both as confounders or explanatory factors (either positively or negatively) on substance use. Personal, family and community-related risk and protective factors are summarized in Table 1.

From an individual point of view, the personal characteristics of adolescents act as important factors in predicting substance use. Impulsivity(5;95), for example, has increasingly been accepted as being a fair predictor of substance use(95). Mental health seems also to be central as an association exists between substance use and depressive symptoms(25;96;97) and this association seems to be bidirectional(98). Both low academic attainment(99) and dropping out of the educational system(88) are associated to negative physical and mental health. Higher numbers of stressful life events experienced by adolescents are also directly related to alcohol use(77;100). Furthermore, having been physically abused or victim of dating violence(5;101;102) are traumatic events that predispose to substance use later in life. However, there are some personal characteristics, such as having a positive self-esteem and some social skills(95;103), which are protective factors from substance use and related disorders.

Family variables, such as family connectedness, play an important role in the motivation and effort to study(104) and therefore have been found to be protective factors against tobacco(42), alcohol(105) and the use of other substances(100). Low family socioeconomic status is associated to substance use problems(106). Young people whose parents are divorced or separated or whose parents have not completed secondary school are more likely to leave school early(94). Students not living in intact families or having a bad relationship with their parents are more likely to use substances(107;108). Additionally, tobacco smoking is associated to a more stressful/problematic environment(81). Finally, adolescent substance use disrupts or delays the conventional developmental transitions to marriage, parenthood and employment(80). In contrast, expectations from parents, mostly academically, were found to be protective against substance use(5).

Research does not support entirely the parental impression that teen socialization is exclusively a risk factor for substance use during adolescence. In fact, close peers are more likely to provide protection against stresses that might lead to substance abuse during adolescence(5). Still, substance introduction by peers in a group is mainly the way adolescents have their first contact with drugs(6) and peer influence is a well know risk factor(109-112). Cannabis use is also associated to educational pathways: high-school students are at higher risk of experimentation while vocational students are at higher risk of continuous use(113). Religiosity has also been found to be protective against drug use. In this respect, it is the fact of being involved in a religious community or in one of its institutions (religiosity, in contrast to spirituality), which seems to provide protection(5).

On account of this list of protective and risk factors to substance use during adolescence, some researchers have examined the eventuality that a common psychosocial syndrome would explain the associations seen among diverse substances. As most of the same psychosocial factors bear protection or predispose to substance use during teenage years, this syndrome, if present, may create a fundamental vulnerability to risky behaviors such as substance use(65;114). Particularly, factors like peer affiliation, novelty seeking and parental illicit drug use may play a predominant role regarding predisposition to cannabis, tobacco and alcohol use as reported by Lynskey et al. in 1998(114). Moreover, evidence continues to grow on the role of genetics in the predisposition for substance abuse and dependence(115;116).

Table 1. Risk and protective factors for substance use

Risk factors	Protective factors
Personal	
Impulsivity and thrill seeking personality (5;95) Depression/Mood Disorder(25; 96-98;102) Antisocial behavior/Violence(95;117) Stress(77;100;102) Physical/Sexual abuse, Victims of dating violence (5;101;102;118) Precocious puberty(119;120) Higher androgen level(5) School absenteeism(121) Low academic grades(4;118;122) Gang involvement(95) Working more than 20 hours a week(5)	High self-esteem(103) Internal locus of control(103) Social skills(95) Good academic grades(103)
Familial	
Low socioeconomic level(102;106) Poor family management(95) Single parent family(107;108;118;123) Authoritarian parenting style(5) Conflictual relation with parents (5;95;107;108;118) Parental / Familial history of drug use (5;95;102) Children assisting the parent in using substances(5)	High socioeconomic level(124) Two-parent family(5) Parent-adolescent connectedness/ Good relation with parents (5;42;100;101;103;1005;121;124) Perceived parental monitoring(5;102) Expectations from parents(5;102;110) Parent-school connectedness(103) Parental availability(5)
Community	
Peer influence(109-112) Low school commitment(95;118) Subjective social norms(111) Substance availability(125) Low neighborhood attachment(95) Media/advertising(5;126)	Feeling connected to school(5) Group of friends(5) School engagement(110) Religiosity(5;95;101;103;124)

In summary

- Fifteen percent of 15 year-olds in Switzerland are weekly smokers and one in ten smokes daily, with no gender differences. These rates are the lowest reported since 1986.
- Among Swiss adolescents in post-mandatory education, apprentices are more likely to be daily smokers than students and males report higher rates than females, although this difference is more marked among apprentices than among students.
- Over one third of males and 30% of females aged 15-24 years are regular smokers. This age group also shows a decreasing prevalence trend and, for males, the rates are back to the level observed in 1992.
- The rate of 15 year-olds having ever smoked in Switzerland is similar to the ones reported by its neighboring countries and slightly above the mean of HBSC-participating countries. However, the rate for daily smoking is below the HBSC mean. For both rates, and contrary to its neighbors, Swiss males report slightly higher prevalence rates than females.
- Rates of lifetime cannabis use have decreased among 15 year-olds but are still higher than they were in 1998. Current use (last 12 months) rates have also diminished and are below those reported in 1998. In both cases, males report higher prevalence rates than females.
- In post-mandatory education, males show higher rates than females and apprentices higher rates than students. Prevalence of current (last 30 days) use have increased between 1993 and 2002, and this increase is more marked among males than among females.
- Cannabis lifetime use among youth aged 15-24 years has increased among males and slightly diminished among females in 2007. Current use has diminished for both gender, although the prevalence is twice as high in males than in females.
- At the international level, Swiss teenagers show the highest rates in Europe for lifetime cannabis use. These rates are higher for males and, for both males an females, above the HBSC mean. For current use, the rates are similar to those observed in France, although they almost double the HBSC mean.
- Alcohol misuse has slightly decreased for 15 year-olds, although the rate is still higher than it was in 1998. Males outnumber females.
- However, alcohol misuse increased between 1993 and 2002 among students and apprentices aged 16-20 years. Males show higher rates than females. Moreover, 15-24 year-old males are three times more likely to report problematic alcohol use than females.
- Alcohol misuse among Swiss 15 year-olds is well below the mean of HBSC-participating countries.
- There is a strong relationship between cannabis and tobacco use. Cannabis use is normally accompanied by tobacco consumption at some point during adolescence. The majority of cannabis users also smoke tobacco.
- Nicotine addiction may be the main consequence of cannabis use.
- Cannabis and tobacco use are also associated to the use of other substances, and specially alcohol.
- Cannabis users are at increased risk of using other illegal substances.
- Timing of initiation and intensity of use of one substance influences the use of other substances. Similarly, changes in the use of one substance may have an effect on the use of other ones.
- Crucial events during adolescence and young adulthood have an influence on substance use trajectories.

- Early substance use initiation increases the risk of becoming substance use dependent in adulthood.

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Annex 2

Multiple imputation

Multiple imputation (MI) was proposed by Rubin (1) as a mean for keeping the diversity of imputed data as large as possible. The principle is to replace the original dataset (*D0*) containing missing data with $m>1$ imputed datasets numbered from *D1* to *Dm* and called *replications.* The values imputed in each replication of the original dataset can be different, so the variability of the data is preserved. Accurate results can be achieved with m as low as 5, but here, in a conservative approach, we chose $m=20$ replications.

In practice, each statistical model is computed independently on the m replications. Results are then aggregated into a final statistics. Let θ be a parameter of interest. From the m replications we obtain m estimations $\hat{\theta}_1$, …, $\hat{\theta}_m$. The multiple imputation estimator is then written

$$\hat{\theta}_{MI} = \frac{\sum_{i=1}^{m} \hat{\theta}_i}{m}$$

The variance of the MI estimator is obtained as a combination of the variance of each $\hat{\theta}_i$ and the variance between the $\hat{\theta}_i$. If we note $\hat{V}_i$ the variance of $\hat{\theta}_i$, then

$$\hat{V}_{MI} = \frac{\sum_{i=1}^{m} \hat{V}_i}{m} + \left(1+\frac{1}{m}\right)\frac{1}{m-1}\sum_{i=1}^{m}\left(\hat{\theta}_i - \hat{\theta}_{MI}\right)^2$$

Nearly any statistical model can be used in a multiple imputation context. Modern statistical softwares can now handle both the computation of the replicated datasets and their use for statistical analyses.

Chained equations

Chained equations is an imputation principle developed among others by Raghunathan, Lepkowski, Van Hoewyk, & Solenberger (2) and Van Buuren, Boshuizen, & Knook (3). Basically, all variables of a dataset can be treated simultaneously by following these steps:

1. Each variable with at least one missing value is explained through a regression model using all other variables of the dataset as explanatory factors, including variables with missing values.
2. Each missing value is first replaced by a random value.
3. Each regression model is then used in turn to impute missing values.
4. The algorithm iterates several times through all regression models, missing values being each time replaced by the value imputed during the preceding iteration.
5. Imputations of the last iteration are retained as final values.

Repeating the whole process m times leads to m different imputed datasets.

This general framework is mainly adapted to datasets with not too many variables and not too many missing values. Since the TREE dataset has many variables and since we wanted to preserve its longitudinal features, we used a modified version of this general framework. First of all, we considered the imputation of only one information at a time (that is in fact generally 7 variables, since most of the variables of interest were observed continuously from wave 1 to wave 7). A regression predictive model was defined for the variable using as predictors the same variable observed the preceding waves as well as

a set of fixed covariates taken from the PISA survey. For practical reasons, the covariates could not have missing data.

No imputation was performed for T1, since there are no previous observations of the same variable to be used as predictor. When two or more than two successive observations were missing, only the first one was imputed (to impute wave *t*, we must have at least the information at *t-1*).

For instance, the variables *t1drug4, t2drug4, ..., t7drug4* represent the level of cannabis consumption from wave 1 to wave 7. The following set of multinomial regression was then defined:

t2drug4 = f*(t1drug4, covariates)*
t3drug4 = f*(t1drug4, t2drug4, covariates)*
t4drug4 = f*(t1drug4, t2drug4, t3drug4, covariates)*
t5drug4 = f*(t1drug4, t2drug4, t3drug4, t4drug4, covariates)*
t6drug4 = f*(t1drug4, t2drug4, t3drug4, t4drug4, t5drug4, covariates)*
t7drug4 = f*(t1drug4, t2drug4, t3drug4, t4drug4, t5drug4, t6drug4, covariates)*

The covariates used as predictors in each regression were

- Sex.
- Age in months at the time of PISA.
- Linguistic region at the time of PISA (German /French /Italian).
- Country of birth (Switzerland / other).
- Family wealth at the time of PISA (scale).
- Secondary school track (pre-gymnasial / extended requirements / basic requirements / no selection).

The following table gives the number of data available per subject for the analysis of substance use (cannabis, tobacco, alcohol) before and after imputation. As we can see, the number of complete sequences available for analysis has more than doubled after imputation (2989 instead of 1131).

Number of observations per subject	Before imputation		After imputation	
	n	%	n	%
0	576	9.08	576	9.08
1	493	7.77	11	0.17
2	651	10.26	494	7.79
3	588	9.27	498	7.85
4	660	10.41	479	7.55
5	753	11.87	626	9.87
6	1491	23.51	670	10.56
7	1131	17.83	2989	47.12
Total	6343	100.00	6343	100.00

Weights

As in many surveys, each respondent in the TREE database does not account for one data point in the analysis. To take into account the survey design and to ensure that, regardless of missing data and attrition, the statistical results stay correct, each respondent is weighted. The weights provided for the TREE database are related to the whole sample, but since, even after imputation, our analyses use only a little less than 50% of these data, we had to transform the initial weights in order to keep the same accuracy in the results. The modified weights were obtained through post-stratification of the original weights by sex and by group of substance users.

The following table shows the repartition of the 4 groups of substance users at T1 using different subsets of data and weights:

Group of substance user	All available data at T1, Original weights		Data available continuously from T1 to T7 after imputation, Original weights		Data available continuously from T1 to T7 after imputation, Modified weights	
	n	%	n	%	n	%
Cannabis only	118.7	**2.32**	50.43	2.58	68.63	**2.32**
Cannabis & Tobacco	941.8	**18.44**	310.86	15.91	544.69	**18.44**
Tobacco only	1352	**26.47**	409.12	20.94	781.87	**26.47**
None	2696	**52.77**	1183.70	60.57	1558.81	**52.77**
Total	5108	**100.00**	1954.12	100.00	2954	**100.00**

At T1 (2001), data on substance use are available for 5108 subjects, regardless of the availability of the same information between T2 and T7. The distribution of the four groups of substance users on these data and with the original weights can be seen as the most accurate distribution available for these four groups. Now, using the same weights on the subset of data continuously available between T1 and T7 after imputation, we obtain the distribution appearing in the center of the table. This distribution clearly differs from the previous one. For instance, the percentage of tobacco only consumers is underestimated (20.94% instead of 26.47%). Moreover, even if the total number of completed sequences is 2989, the sum of weights leads only to a total of 1954.12. Using our modified weights (last column of the table), we are able to find again the correct distribution between the four groups. It must be noted that even after correction of the weights, the grand total is 2954 and not 2989. This difference is due to the fact that a small number of the 2989 imputed sequences had an original weight of zero. Since such weights cannot be transformed, we had to discard these few observations from all subsequent analyses.

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