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Early Determinants of Alcohol Consumption Trajectories from Adolescence to Adulthood: Analysis of the TEMPO Cohort, 1991-2018

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Early Determinants of Alcohol Consumption Trajectories from Adolescence to Adulthood: Analysis of the TEMPO Cohort, 1991-2018

Abstract

Background: Despite decreasing since the 1960s, alcohol consumption still ranks among the top three risk factors for mortality and disability in France. There are no studies assessing distinct longitudinal patterns of alcohol use in the French population. This study aims to identify alcohol consumption groups from adolescence to early adulthood and to explore factors associated with these groups.

Methods: Using data from the TEMPO ("Trajectoires EpidéMiologiques en Population") cohort 1991 to 2018, we modeled developmental trajectories of alcohol consumption frequency via Group-Based Trajectory Modeling from age 12 to 44 (n=2,278). Multinomial logistic regression was applied to identify individual and parental factors (derived from the GAZEL ("GAZ et ELectricité") cohort) linked to the trajectory groups.

Results: Five trajectories were identified: non-drinkers (5.0%), occasional (61.6%), late onset (6.0%), volatile (7.6%) and frequent drinkers (19.9%). Using occasional drinkers as the reference, males had a lower likelihood to be non-drinkers (OR 0.48, 95%CI 0.30-0.77) and a higher likelihood to be volatile (2.13, 1.52-2.98) and frequent (2.70, 2.14-3.40) drinkers. The odds of late onset (0.38, 0.26-0.57), volatile (0.70, 0.49-0.99) and frequent (0.31, 0.24-0.40) drinking were lower for subjects with an education lower or equal to Baccalauréat+2 level. Grade repetition and having left the parental home before age 18 were further associated with non-drinking. Experimentation with cannabis before age 17 was associated with volatile drinking (3.47, 2.17-5.56). Regular smoking and the experimentation with other psychoactive drugs were related to both volatile and frequent drinking. Suicidal ideation and parental smoking were linked to late onset drinking; parental former smoking and heavy drinking were associated with frequent drinking.

Conclusion: Alcohol consumption follows various multifactorial patterns over time. A combination of a population-wide strategy and individual-based approach is necessary to tackle the complex and culturally entrenched nature of the different alcohol consumption patterns in the French population.

Keywords: alcohol, Group-Based-Trajectory Modeling, France, adolescence

Determinants précoces des trajectoires de consommation d'alcool de l'adolescence à l'âge adulte : analyse de la cohorte TEMPO, 1991-2018

Résumé

Contexte : Malgré une diminution constante depuis les années 1960, la consommation d'alcool demeure l'un des trois principaux facteurs de risque de mortalité et de morbidité en France. Il n'y a actuellement aucune étude évaluant les tendances longitudinales de la consommation d'alcool dans la population française. Cette étude vise à identifier les groupes de consommation d'alcool de l'adolescence au début de l'âge adulte, et à explorer les facteurs associés à ces groupes.

Méthodes : A partir des données de la cohorte TEMPO («Trajectoires EpidéMiologiques en Population») de 1991 à 2018, nous avons modélisé des trajectoires de la fréquence de la consommation d'alcool entre 12 et 44 ans (n = 2 278) avec la méthode Group-Based Trajectory Modeling. Une régression logistique multinomiale a été appliquée pour identifier les facteurs individuels et parentaux (données issues de la cohorte GAZEL («GAZ et ELectricité») liés à l'appartenance à un groupe de trajectoire.

Résultats : Cinq trajectoires ont été identifiées : non-consommateurs (5,0%), les consommateurs occasionnels (61,6%), avec début tardif (6,0%), volatils (7,6%) et réguliers (19,9%). En utilisant les consommateurs occasionnels comme référence, les hommes étaient moins susceptibles que les femmes d'être non-consommateurs (OR 0.48, $IC_{95\%}$ 0.30-0.77) et plus susceptibles d'être des consommateurs volatils (2.13, 1.52-2.98) et réguliers (2.70, 2.14-3.40). Les probabilités d'appartenir aux trajectoires de consommation tardive (0.38, 0.26-0.57), volatile (0.70, 0.49-0.99) et régulière (0.31, 0.24-0.40) étaient plus faibles chez les sujets dont le niveau d'éducation était inférieur ou égal au Baccalauréat+2. Le redoublement et le fait d'avoir quitté le domicile parental avant l'âge de 18 ans étaient également associés au profil non-consommateur. L'expérimentation du cannabis avant l'âge de 17 ans était associée au profil de consommateur volatil (3.47, 2.17-5.56). Le tabagisme régulier et l'expérimentation d'autres substances psychoactives étaient liés à des profils de consommation d'alcool volatil et régulier. Les idées suicidaires et le tabagisme parental étaient aussi associés à une trajectoire de consommation tardive. Avoir des parents ex-fumeurs ou consommateurs excessifs d'alcool étaient associés à une trajectoire de consommation réguliere d'alcool.

Conclusions : Les profils de consommation d'alcool au fil du temps sont multiples et multifactoriels. Des campagnes de prévention devraient utiliser des approches à l'échelle de la population et de l'individu pour lutter contre la nature complexe et culturellement ancrée de ces divers profils de consommation d'alcool dans la population française.

Mots-clés: alcool, Group-Based-Trajectory Modeling, France, adolescence

Table of Contents

List of Figures

(figures in the appendix)

List of Tables

(tables in the appendix)

List of Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
AUDIT	Alcohol Use Disorders Identification Test
AvePP	Average posterior probability
BIC	Bayesian Information Criterion
Bac	Highschool diploma, *Baccalauréat,*
CBCL	Child Behavior Checklist
CCTIRS	Advisory Committee on the Treatment of Information for Health Research
CI	confidence intervals
CNIL	National Commission for Data Processing and Liberties
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
EDF-GDF	Électricité de France-Gaz de France
ESCAPAD	Survey on Health and Consumption on Call-up and Preparation for Defense Day
ESPAD	European School Survey Project on Alcohol and Other Drugs
FD	Frequent drinker
GAZEL	GAZ et ELectricité
GBTM	Group-Based Trajectory Modeling
HBSC	Health Behaviour in School-aged Children
HED	heavy episodic drinking
ICD-10	International Statistical Classification of Diseases and Related Health Problems
Inserm	French National Institute of Health and Medical Research
LOD	Late onset drinker
MAR	missing at random
MILDECA	Interministerial Mission for Combating Drugs and Addictive Behaviours
MINI	Mini International Neuropsychiatric Interview
ND	Non-drinker
OCC	odds of correct classification
OD	Occasional drinker
OECD	Organisation for Economic Co-operation and Development
OFDT	French Observatory of Drugs and Drug Addiction
OR	odds ratio
TEMPO	Trajectoires EpidéMiologiques en Population
US	United States
VD	Volatile drinker
WHO	World Health Organization
ZIP	zero-inflated Poisson

1. Introduction

1.1. Consequences of alcohol consumption globally

Evidence shows that the brewing of alcohol was already introduced in Neolithic society around 10 thousand years ago with the onset of agriculture.[1] In the meantime, as the most commonly used psychoactive substance, alcohol has turned into the seventh leading cause of both death and disability on a global scale as of 2016.[2] Now accounting for more deaths worldwide than tuberculosis, violence and the Acquired Immunodeficiency Syndrome (AIDS) altogether, this translates into 3 million deaths yearly.[3] More precisely, globally alcohol use accounted for 2.2% of female and 6.8% of male deaths in 2016. In the age group of 15-to-49-year-olds alcohol use was even responsible for the majority of deaths. Whereas controversial in the past, according to the Global Burden of Disease Study 2016 by the Lancet, alcohol is detrimental to health, even in small amounts.[2] However, it is undeniable that alcohol forms an essential part of sociocultural behavior for both men and women throughout human evolution.[4] Therefore, a highly accepted and widespread substance, the damage it causes is perpetually underestimated. As a consequence, alcohol has turned into one of the most dangerous psychoactive drugs in terms of physical, social and addictive harm.[5]

Despite being responsible for over 5.1% of the global disease burden measured in disability-adjusted life years,[3] considerable geographical variation and new trends of alcohol consumption can be observed. In contrast to northern Europe and emerging economies, countries in the south and center of Europe have experienced a decrease in alcohol consumption over the last two decades.[1] However, growing tendencies towards risky drinking behaviors, a reduction in the age of alcohol initiation and a convergence of drinking levels between girls and boys pose new challenges to public health authorities. Even though alcohol dependence is the most common among all substance use disorders, with approximately 100.4 million cases in 2016, other outcomes of alcohol use contribute more to the disease burden.[6] In fact, harmful alcohol use is causally linked to a spectrum of mental and behavioral conditions, both non-communicable and infectious diseases, and injuries, amounting to more than 200 adverse health outcomes.[3,7] In this context, along with dependence, the World Health Organization (WHO) names intoxication and toxic effects as the principal direct mechanisms of harm on human health caused by the intake of alcohol.[8] Apart from directly attacking the liver as a detoxifying organ, alcohol targets the entire immune system. Liver disorders like alcohol cirrhosis and Korsakoff's syndrome, a neurological disease, are direct causes of alcohol use. Furthermore, it is associated with certain forms of cancers, cardiovascular diseases and affects cognition.[7,9] Not just those engaging in drinking, but third parties may be harmed as a consequence of accidents, violence and drinking during pregnancy (fetal alcohol syndrome).[3,1] Besides being a risk factor for human health, alcohol consumption affects the economy and society as a whole.[6]

1.2. Adolescence – A critical period for lifetime drinking behavior

Commonly referred to as the "Gateway Theory", as a legal substance, alcohol use is also hypothesized to serve as a risk factor for an increasing abuse of illicit drugs. This so-called "sequential pattern" of substance abuse has been observed in various contexts and tested for many decades.[10,11] Notably, early exposure in adolescence is positively associated with continuous substance-related problems later in life.[11,12] The interim period between child- and adulthood is marked by multiple changes of psychosocial and physical nature. Individuals are more likely to experiment with substances in a more carefree and risk-taking way in this stage of life. At the same time, the brain is still in development and thus even more vulnerable at this age.[13,14] Of particular harm to the central nervous system is the episodically heavy drinking behavior in adolescence that essentially transitions to a less excessive but more continuous use of alcohol in adulthood. As a consequence, young drinkers are at higher risk of developing alcohol dependence in adulthood and thus have a greater propensity to adverse mental and neurodevelopmental outcomes in the short- and long-term.[13,15]

Various behavioral and social models aim to conceptualize the initiation and causes of substance use.[8,16] The similarity of these models consists in attributing alcohol use to risk factors on different levels of the environment each individual is embedded in and the acknowledgment of their interdependencies. One such framework discriminates between factors on an individual and societal level as illustrated by Figure 1.[17,8]

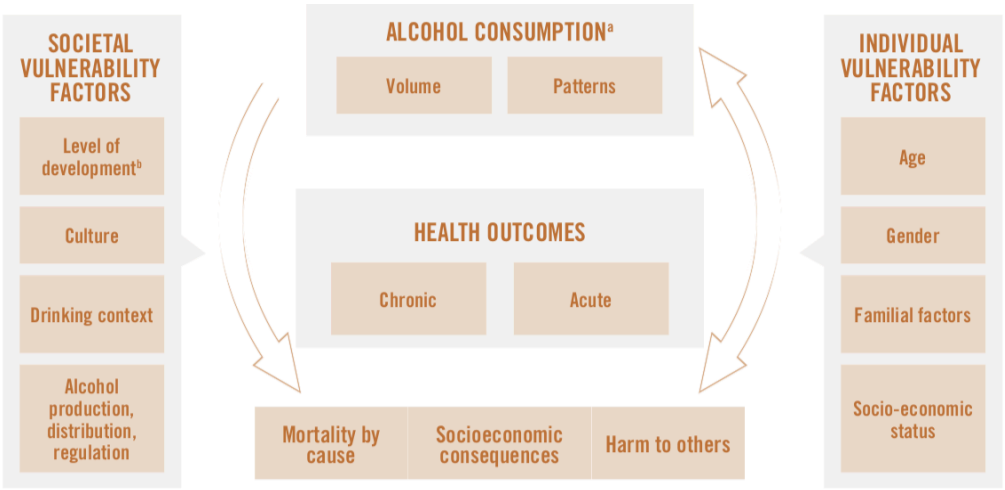

Figure 1: Conceptual framework of causes and harm caused by alcohol consumption[8]; a=Quality of the alcohol consumed can also be a factor; b=Development of health and welfare system, and economy as a whole

Accordingly, alcohol consumption is shaped by both the unique combination of individual factors and by societal influences that are shared among individuals because they belong to the same community. Though no particular factor can be held solely responsible, previous research suggests that the likeliness of developing an alcohol problem is inherently correlated with the amount of vulnerability factors one is affected by.[17,8] Various studies also classify risk factors by environmental (e.g. parental and peer influences, educational level) and genetic

influences and the interaction between the two.[18,19] While initially environmental factors predominantly influence the use of alcohol, genetic factors become more relevant in the course of life.[19] Considering that alcohol drinking patterns, defined by both volume and frequency, can fluctuate throughout life, longitudinal studies are necessary to not only determine the onset but also to assess continuity of alcohol use.[18] In addition, there is a growing trend to identify different types of alcohol consumption patterns over time and to link risk factors associated to these trajectories.[18,20,21] Beyond a merely variable-centered approach, these methods enable to capture and thus address the more complex nature of drinking patterns in terms of trajectory groups, facilitating effective decision-making for governmental bodies.[18,20,22,23]

1.3. Alcohol consumption estimates in the French population

Traditionally a country with a prominent drinking culture, France has experienced a constant decrease in alcohol consumption, which has halved since the 1960s.[7,24] Despite control measures undertaken since the 1980s, alcohol-related mortality in France remains constant and above the global average with estimates of 7% or 41,000 deaths for adults aged 15 and older in 2015.[25] Thus, in conjunction with tobacco and dietary risks, alcohol use persists in being among the top risk factors for mortality and disability.[26] Its social cost was estimated at 118 billion euros in 2010, slightly below that for tobacco. This accounts for the expenses for prevention and treatment and the economic costs due to years of life lost or disability.[27] At 10% prevalence, a significant fraction of the adult population (15% among males and 5% among females) continue having an alcohol problem in terms of dependence or harmful use.[7] Another survey from 2017 further confirms the heterogeneity in drinking patterns among males and females and additionally by age. Accordingly, daily alcohol consumption was primarily observed for 65-to-75-year-olds (26%), whereas regular drunkenness (drunk at least 10 times in the last 12 months) mainly concerned 18-to-24-year-olds (19.4%).[28]

The French Observatory of Drugs and Drug Addiction (OFDT) is the main informative body in the field of drugs and addictions.[29] In collaboration with various institutes, the OFDT synthesizes and assesses information published on addiction. Current data on alcohol consumption mostly comes from cross-sectional surveys, some of which are repeated over time. The Health Barometer *(Baromètre Santé)* is one such survey that focuses on the adult population aged 18 to 75 years.[30] To specifically monitor psychoactive substance abuse among adolescents in France, the OFDT supports the coordination of three main surveys since the 1990s: the Health Behavior in School-aged Children (HBSC) of middle to high-school children aged 11, 13 and 15 years; the European School Survey Project on Alcohol and Other Drugs (ESPAD) of adolescents aged 15 to 16 years and the national Survey on Health and Consumption on Call-up and Preparation for Defense Day (ESCAPAD) of 17-year-olds.[15,29]

According to the latest ESCAPAD survey, since the 2000s, an ongoing increase in the number of 17-year-olds that abstain from alcohol has been recorded, totaling 14.3% in 2017

(versus 5.4% in 2000). Regular alcohol use, consisting of a minimum of 10 occasions in the month preceding the survey, has dropped to 8.4% among this population, but has shown a more volatile trend over the past surveys.[31] Even a decline in heavy episodic drinking (HED), a phenomenon on the rise in previous years and defined as a minimum of five units of alcohol on one occasion, has been observed.[7,32] However, with 44% of 17-year-olds having experienced at least one of these episodes in the month prior to the survey, it still remains high.[31] The same downward trends were observed in the latest HBSC and ESPAD surveys from 2014 and 2015.[33] In contrast, for those aged 18 to 25 years old, both regular use and HED has continued to rise. Apart from these trends, gender-related drinking discrepancies are gradually diminishing with girls approaching boys in terms of drinking patterns.[34,35] Excessive alcohol use tends to be more present in adolescents from the vocational school system in comparison to their counterparts with a general school path.[33] However, the role of socioeconomic status in alcohol use remains controversial. Even though vulnerable adolescents in terms of socioeconomic status are thought to suffer more often from problem use,[34] a longitudinal study from 2014 found a positive association between consistently high socioeconomic trajectories and alcohol use.[36]

Despite these developments, most minors who reported drinking alcohol in the month prior to the survey had no difficulty in purchasing alcoholic beverages. This questions the effectiveness of the Hospital, Patients, Health and Territories Act *(Loi portant réforme de l'hôpital et relative aux patients, à la santé et aux territoires)* that was changed in 2009 to include the prohibition of alcohol and tobacco sales to underaged consumers.[28,31,34] Apart from this Act, an entire spectrum of alcohol control measures has been implemented since the 1960s: the abolishment of “happy hours” unless also applied to alcohol-free drinks; the reduction in allowable blood alcohol concentration for drivers; and the Évin Law *(Loi Évin)* on advertisement restrictions for alcohol.[37,38] Nevertheless, the latter has been under constant criticism for not effectively protecting young people from alcohol-related publicity. Ever since its implementation in 1991, perpetual modifications have essentially weakened its impact on alcohol producers and retailers.[37] Even though in the meantime various studies have proven that deregulation of advertising is effective, lobbyists achieved another amendment in 2015 in favor of the alcohol industry.[9,38]

In the face of this development, Public Health France *(Santé publique France)* has recently redefined benchmarks for the weekly and daily intake of alcohol and developed an online platform to raise awareness on the risk factors of alcohol use.[39] Additionally, the second action plan on addiction 2018-2022 has been launched by the Interministerial Mission for Combating Drugs and Addictive Behaviours *(Mission interministérielle de lutte contre les drogues et les conduites addictives,,* MILDECA) with a focus on the totality of psychoactive substances and further addictive behaviors.[40] MILDECA is the main governmental body in

charge of combatting the use of drugs and addiction, spanning all the actions from prevention over monitoring and training to treatment.[40,41]

1.4. Limitations of previous research and study rationale

Despite the current surveys in place that measure drinking levels, the public authorities are acknowledging that, especially among adolescents, knowledge about risk factors for alcohol consumption in France remains scarce. In an attempt to close the gap on qualitative information, the OFDT recently conducted a study of 200 minors on the contexts, patterns and motivations associated with alcohol use.[42] The study concluded that alcohol forms an essential part in sociability, is omnipresent in the environment of the adolescents, is accessible and is generally associated with positive feelings like joy, conviviality and relaxation amongst others. The findings depict well the denial of risks linked to alcohol among study participants and call for a greater necessity to investigate and clarify the risk factors associated with alcohol use.[42,43]

Generally, most studies focus on alcohol consumption as a risk factor for health conditions rather than exploring the determinants of this behavior.[6,44] To this date, mainly cross-sectional studies have addressed the issue in the French context.[45–49] Whereas longitudinal clustering methods have been applied to illicit substance[50] and tobacco use,[51] alcohol trajectories have not been studied, and least of all among young people. Group-Based Trajectory Modeling is one such method to identify distinct developmental trajectories of alcohol consumption (see Chapter 2.2).[52,53] The few studies applying trajectory analysis in the context of alcohol consumption from an early age onwards have been mainly conducted in the United States (US).[18,23,54,55] However, the trajectories vary substantially across studies and different factors are found to be associated with these developmental courses of alcohol consumption.[18,21,55,56] The heterogeneity of these study results acknowledges the imperative to carry out a context-specific analysis of alcohol trajectories in the French population.

1.5. Aim and objectives

Given that no previous study has explored alcohol consumption trajectory groups in France, this study proposes a first exploratory analysis. Using longitudinal data from two cohorts in France, our study aims to address the following questions about alcohol consumption groups in the French population: which subgroups can represent different patterns of alcohol consumption from adolescence to adulthood in our study population? By which factors can these alcohol trajectory groups be characterized?

The specific objectives for this exploratory analysis are as follows:

1.) To identify alcohol consumption trajectory groups of the subjects participating in the TEMPO (“Trajectoires EpidéMiologiques en Population”) cohort via Group-Based Trajectory Modeling.

2.) To analyze factors associated with the distinct alcohol consumption trajectories, including parental factors coming from the GAZEL ("GAZ et ELectricité") study.

2. Materials and Methods

2.1. Study design and population

2.1.1 The TEMPO and GAZEL cohorts

Administered by the French National Institute of Health and Medical Research (*Institut national de la santé et de la recherche médicale,* Inserm), the TEMPO and GAZEL cohorts are two large French longitudinal observational cohort studies that collect quantitative and qualitative data on health-related, lifestyle and socioeconomic factors.

The study participants of the TEMPO cohort are the offspring of the GAZEL cohort. The GAZEL cohort is a closed occupational cohort that started in 1989. It consisted of 20,624 voluntary employees of the French national gas and electricity company *Électricité de France-Gaz de France* (EDF-GDF) at its inception. The cohort was designed to analyze different scientific questions related to human health. Besides holding a wide range of occupations, EDF-GDF employs workers across the entire country and has its own social security system facilitating health surveillance of its employees. The study participants, initially aged 35 to 50 years old, received postal questionnaires annually on socio-demographic, economic, occupational characteristics and health behaviors.[57] With its large size, diverse population, richness in both self-reported and extracted data, long duration and high average response rates of around 75% with minimal lost to follow-up, the GAZEL cohort has been used for many research questions.[58]

The TEMPO cohort was created in 2009, using the same participants as the "Children of GAZEL" cohort that were first surveyed in 1991 and also in 1999. In 1991, of the 4,766 randomly selected families stratified by socioeconomic status and family size, one child aged 4 to 16 years old was chosen at random to be included.[59] A total of 2,708 of the respective parents then responded to questions in a self-administered questionnaire about behavioral and psychosocial aspects of their children, especially concerning their social and schooling environment. The follow-up survey in 1999 consisted of two separate questionnaires for the children (n=1,148) and their parents (n=1,268) on the development and additionally psychoactive substance abuse of the study subjects, specifically on alcohol and tobacco.

It was not until 2009 that the TEMPO cohort was formally established with the purpose of understanding the health development and needs specifically of young adults in France. The questionnaire intends to grasp even more profoundly the psychosocial and family situation of the participants in order to comprehend social disparities. As a response to attrition, the TEMPO cohort was expanded in 2011. Because lost-to-follow-up not only resulted in fewer study participants but in an increase in average age, an additional 688 subjects, younger in

age, were recruited. This amounted to 1,214 respondents aged 18 to 37 years old.[60–62] The last collection phase took place in 2018. Figure A1 (Appendix A) represents a flowchart of the study participants in successive survey waves with their respective age range.

The TEMPO and GAZEL studies have been ethically approved by both responsible regulatory bodies in France, the Advisory Committee on the Treatment of Information for Health Research (*Comité consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé,* CCTIRS) and the National Commission for Data Processing and Liberties (*Commission Nationale Informatique et Liberté,* CNIL).[61,63]

2.1.2 Inclusion and exclusion criteria

From 1991 to 2018, the TEMPO cohort counts a total of 3,396 participants. Subjects that only participated in 1991 (n=1,085) were excluded since no information on the children's alcohol status was collected. An additional 33 subjects were exempted since each study subject is required to have responded at least once to alcohol consumption in order to perform Group-Based Trajectory Modeling.[64] Therefore, our final study population consisted of 2,278 individuals that participated in at least one of the five waves of 1999, 2009, 2011, 2015 or 2018.

2.2. Group-Based Trajectory Modeling

Group-Based Trajectory Modeling was used to estimate the developmental trajectories that best describe the study population. This method was developed by Daniel Nagin and is especially useful when modeling longitudinal data to identify behavioral patterns specific to groups of individuals.[53]

2.2.1 Principles of GBTM

Also called Latent Class Growth Analysis, Group-Based Trajectory Modeling (GBTM) is a semiparametric probabilistic method that hypothesizes the existence of distinct developmental trajectories over time within one population.[64] Particularly applied in social sciences, it defines a finite number of latent trajectories that are not directly observable, modeled from a series of data collected over time. Individuals are not required to have the same amount of data points, nor the collection to have occurred at the same time or age. Since the model is probabilistic, imputation of missing data is not necessary and theoretically individuals can already be included with a single data point.[53,64–66] However, this requires the model to be appropriately validated a posteriori.

Apart from the assumption of homogeneity of individuals within the discrete groups, GBTM ascertains, given group membership, the individuals' outcomes from different periods to be independent. This conditional independence from time only applies at the latent group and not population level.[64,67] To select the model that corresponds best to the dataset, the maximum likelihood estimation is used.[68] GBTM therefore uses a likelihood function adjusted

to different data types. This allows the modeling of binary (using a Bernoulli distribution), count (using a zero-inflated Poisson distribution (ZIP)) and censored data from psychometric scales or with a normal distribution (using a censored normal distribution). Considering that we have count data with a high proportion of abstainers or moderate drinkers (see Chapter 2.3.1), ZIP fits the data best. Alcohol consumption is commonly found to be modeled with Poisson due to its skewed distribution.[54,55,69] If we assume our outcome is the number of glasses of alcohol consumed per day, the probability y_{it} of observing a drinking rate of 0, 1, 2,… glasses on a given day t for an individual i depends on the mean count λ observed in a given group j for that particular day:

$$p(y_{it}) = \frac{\lambda_{jt}^{y_{it}} e^{-\lambda_{jit}}}{y_{it}!} (for\ y_{it} = 0,1,2, \dots)$$

Creating a linkage between our outcome and age via a polynomial relationship, the Poisson model is specified as follows for a trajectory group of a polynomial order of three:[64,67]

$$log(\lambda_{it}^{j}) = \beta_0^j + \beta_1^j Age_{it} + \beta_2^j Age_{it}^2 + \beta_3^j Age_{it}^3$$

2.2.2 Model selection and specifications

There are no stringent rules on how to infer the correct trajectory model. However, the Bayesian Information Criterion (BIC) is widely used for this purpose.[53] It is defined according to the following equation: $BIC = log(L) - 0.5k\ log(N)$

The BIC takes the likelihood of the estimated model L and adjusts for both the sample size N and the number of model parameters k. The model with the highest BIC is considered to best fit the data by maximizing the probability of the outcome. Since its values are negative, this is the one closest to zero.

The model is defined by two components: the expected trajectory for each group and the group membership probabilities. Each predicted trajectory is the result of a polynomial function of age or time. Our main interest laid in modeling trajectories over the course of life and therefore based on age. Individuals that have responded more than once to alcohol consumption were therefore captured at various age points in the model. The number of parameters a trajectory model is composed of depends on both the number of trajectories and the polynomial order used to model the trajectory groups. The higher the polynomial order used to describe a trajectory shape, the more parameters have to be added to the model. A trajectory of a polynomial order equal to zero has a slope of zero (constant). A monotonous increasing or decreasing trajectory is determined by a polynomial order equal to one (linear). A trajectory of a polynomial order equal to two enables to model a change in the direction of the evolution of the outcome (quadratic). And finally, a trajectory of order three can account for two changes occurring throughout time (cubic). In favor of parsimony, the BIC penalizes the addition of parameters.[53,64]

In order to choose between two models, Jones, Nagin and Roeder suggest the use of the BIC log Bayes factor based on Jeffrey's scale of evidence for Bayes factors[70] and consistent with Kass and Raftery.[71] Accordingly, the more complex model is then significantly different from the simpler model if two times the difference between the BICs is superior to 10 ($2\Delta BIC>10$) (Appendix B, Table B1).[67,72]

The choice of the model is realized in two steps. First, the number of trajectories is determined using the statistical criterion described above and through rational reasoning. The latter consists of a visual inspection to verify the model's capacity to discriminate well between consumer groups in terms of dispersion of data points around the modeled trajectories, the differences in the course and the number of subjects represented in each group. To identify the number of trajectory groups, a stepwise approach is applied by adding trajectory groups and comparing the more complex model with the simpler, previous model. The polynomial order is hereby arbitrarily set to quadratic. Once the number of trajectory groups is determined, the same procedure is applied to identify the best combinations of polynomial orders out of all possible combinations.

2.2.3 Evaluation of model adequacy

The models with the highest BICs that have significant parameters and are not significantly different ($2\Delta BIC\leq10$) from the reference model (the one with the highest BIC) are then compared under further validation criteria. These serve to evaluate the quality of the models' fit with the underlying data, essentially aiming at maximizing each individual's likelihood of belonging to one of the trajectory groups. They include: a comparison of the difference between the estimated probability of group membership (π) and the observed proportion assigned to each group (P), the average posterior probability (AvePP), the odds of correct classification (OCC) and the confidence intervals for both the group membership probabilities π and the predicted trajectories.

Based on an individual's pattern of behavior over the collection period, posterior probabilities belonging to each trajectory group are calculated per individual. The group membership probability is therefore the estimated proportion of the population in each trajectory group j, computed as an average of all individuals' i posterior probabilities, with θ_j being the model estimates of each predicted trajectory:

$$\pi_j = \frac{e^{\theta_j}}{\sum_{j=1}^{j} e^{\theta_j}}$$

A group membership probability of at least 5% for each trajectory is commonly used as a rule of thumb but can be adjusted to the sample size.[73] The individuals are then assigned to a trajectory group according to their maximum posterior probability. Ideally, the proportion of individuals observed in each group from the entire population ($P = \frac{N_j}{N}$) corresponds closely to

the average group membership probability. The AvePP for each trajectory is then computed as an average of the maximum posterior probabilities of particularly those individuals attributed to that group:

$$AvePP_j = \frac{\left(\sum P_{ij} \mid individual\ i\ in\ group\ j\right)}{N_j}$$

At its best, the AvePP is close to one if the probability of each individual belonging to his trajectory group is equal to one. However, to validate the trajectory model, an AvePP of at least 0.7 is recommended. This translates into an average chance of 70% of each individual to effectively belong to this group. Subsequently, P and π are then equal if all individuals are assigned to a group with 100% of certainty. The OCC is an odds ratio with the odds of the AvePP in the nominator and the odds of π in the denominator:

$$OCC_j = \frac{AvePP_j/(1 - AvePP_j)}{\pi_j/(1 - \pi_j)}$$

The larger the OCC, the more accurately individuals are assigned to a trajectory group. An OCC superior to five is considered to have high assignment accuracy. Narrow confidence intervals around the predicted trajectories serve as an additional diagnostic to assess the performance of the model.[53,64,74,75]

The trajectory analysis was performed on SAS® 9.4 software using the PROC TRAJ procedure. The validation criteria were calculated separately, and the trajectories were redrawn on Excel 2013.

2.3. Measures

2.3.1 Outcome variable

The computation of alcohol trajectories requires a common alcohol indicator across all waves. Alcohol consumption frequency was selected as the outcome for this research study. Study subjects were asked about their frequency of alcohol consumption in the 12 months prior to the questionnaire. In 1999 the question contained seven response categories, whereas from 2009 through 2018, the question was retrieved from the Alcohol Use Disorders Identification Test questionnaire (AUDIT) and only comprised five answer options labeled with alcohol frequency ranges. To allow for comparability across all waves, the variables were homogenized and recoded uniformly, which required variables to be collapsed. Prior to this concatenation, the original categories were recoded using the midpoint between the two values of each category, which can be applied to ordinal variables that are ranges of count data.[76] Taking into account the distribution of subjects per initial category, we then computed a weighted average to assign a value to each newly created category of the variable. This resulted in four categories representing subjects that on average never consumed alcohol, consumed alcohol once, three times and at least 11 times a month. Instead of using the

category value, subjects were assigned the actual average alcohol consumption frequencies as this allowed for more discrimination[77] later in the trajectory model (see description of trajectory model in Chapter 3.1).

The following potential outcomes were excluded: frequency of drunkenness per year, the number of glasses consumed per occasion, frequency of heavy episodic drinking per month ("binge drinking" as of now), and alcohol consumption assessed via the AUDIT score. These alcohol indicators were ruled out after a thorough assessment of the number of waves the variable was available for, the response rates per wave, if categorical, the number of respondents to each category of the variable, best practices according to literature and finally the quality of the trajectory model produced by each variable (see Appendix C, Tables C1-C6, Figures C1-C4 for the thorough comparison).

2.3.2 Determinants

Because this is an exploratory analysis, we did not distinguish between exposures and covariates. A variety of potential determinants were selected based on literature and data availability. Besides studying the influence of individual factors on alcohol consumption trajectories, we included parental factors as part of the individual's environment. We prioritized information that was collected prior to or at the initiation of the alcohol consumption trajectories in order to assess the impact of factors during childhood and early adolescence on the alcohol consumption course later in life. Since only the parents of the TEMPO subjects received a questionnaire in 1991 and most questions of interest were addressed as early as 1999, the majority of the variables were based on both years. If our subjects' and their parents' responses were available in 1999, we prioritized the former and only used the latter to fill in missing data. However, to not exclude those individuals from our study population that joined the study in 2011 (30.2%), information from that year was used specifically for these subjects. Unless otherwise specified, parental factors were mainly derived from the GAZEL data using the year 1991 since this marks the initiation of the study. Most of our variables are time-variant, or time-related because of the linkage of certain participant characteristics to their age and required a more complex coding mechanism (Appendix D, Table D1).

2.3.2.1 Individual factors

Sex: The only time-invariant covariate used was sex, which is one of the few measures consistently controlled for in studies centered on alcohol consumption.

Educational indicators: The academic background was assessed with two measures, whether subjects had repeated a grade before and with the highest educational level attained. This information was obtained using all surveys containing this information. Since most of the students with a high school degree (*Baccalauréat,* Bac*)* go on to higher education courses,[78] we hypothesized that subjects completing more than two years of studies post Bac are

associated differently with the drinking trajectories than those with a degree lower or equal to Bac+2 level.

Mental health indicators: Different mental health indicators were examined. Both, externalizing and internalizing symptoms in childhood have been found to be linked to alcohol consumption.[54,56,79,80] However, since the nature of the association varies among studies,[81] they were examined separately. Scales that are centered on the identification of behavioral and emotional difficulties were used for this purpose. The questionnaires in 1991 and 1999 included around 60 items of the Child Behavior Checklist (CBCL) that parents of the TEMPO subjects responded to in both years and the subjects themselves in 1999 via the Youth Self-Report, another version of the CBCL. The CBCL is composed of various scales that enable the assessment of both externalizing (aggressive and oppositional behavior, thinking, and attention problems) and internalizing symptoms (anxiety, depressive and somatic symptoms). Instead of the CBCL, the survey of 2011 included the Mini International Neuropsychiatric Interview (MINI) that enables psychiatric disorders to be diagnosed based on the 4th Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the 10th revision of the international classification of diseases (ICD-10).[82] Because the MINI had retrospectively asked TEMPO subjects about externalizing symptoms before the age of 15, we combined the CBCL and MINI to create a dichotomized variable to assess if children who had suffered from behavioral problems by the age of 14 were associated differently with the drinking trajectories than the remaining subjects. Similarly, to evaluate the presence of internalizing symptoms, we used a variable that combined the sections of the MINI focusing on anxiety and depression with the equivalent section of the CBCL. Subjects that had scored ≥ 85th percentile on either of the scales of the CBCL or affirmed a certain combination of questions of the MINI were considered to have suffered from psychological difficulties.[83] As another proxy for emotional distress, we included suicidal ideation and therefore complemented questions of the CBCL and MINI with further questions on suicidal thoughts in order to minimize the amount of missing responses.

Substance use indicators: As alcohol is a substance often consumed in conjunction with tobacco,[36] we included a variable classifying subjects into smokers and non-smokers, defining regular smoking by at least one cigarette a day. Apart from tobacco and alcohol consumption, cannabis is the most common illicit drug consumed in the world, with France in particular having the highest rate of cannabis use in Europe.[84,85] Various studies have disclosed the age of initiation in substance involvement to play a crucial role in the future trajectory of substance abuse.[34,86,87] Because subjects were retrospectively asked about their first age of cannabis use, we were interested in analyzing the association between those who had experimented with cannabis for the first time by the age of 16 versus those who were older or never consumed cannabis with the drinking trajectories. Additionally, we examined whether subjects

who had experimented with other psychoactive substances[a] were more likely to be linked to trajectory groups consisting of regular alcohol consumers.

2.3.2.2 Parental factors

A multitude of variables can be used to assess the impact of familial context on drinking trajectories. Apart from the living arrangement, the family structure, relationship with family members and socioeconomic background have been found to be associated with alcohol consumption.[45,46,48,88]

Leaving home before 18: The majority of French adolescents live with their parents for at least the completion of high school.[89] We were interested in exploring whether subjects that had left their parental home for the first time by the age of 17, and therefore most likely prior to receiving their Bac, differed from others in terms of their alcohol consumption trajectory.

Stressors in the family environment: We separately explored the association between parental divorce or separation by the age of 16 and parental depression by the age of 16 of our subjects with their drinking trajectories. Both factors could serve as stressors and affect the well-being of children, especially of certain age groups.[88,90]

Parental profession: In 1989, the subjects of GAZEL were asked about their profession and that of their partner. As a proxy for socioeconomic status, we therefore created a dichotomous variable of blue-collar and white-collar workers, using the higher occupational status of the parents. This was based on the *Professions et categories socioprofessionnelles en France*, the official classification system in France. White-collar workers included managers, technicians and administrative associates, whereas parents who were clerks or manual workers were classified as blue-collar workers.[b]

Parental substance use indicators: As studies have revealed a relationship between parents and children's substance behavior, we examined parental substance abuse.[45,91] Therefore, we studied parental tobacco (smoker/ ex-smoker/ non-smoker) and alcohol consumption (heavy drinker/ drinker/ abstainer).[c] We combined parents self-report in 1991 with the TEMPO subject's answers on parental smoking and alcohol problem from 2011. Assuming that substance use behavior of adults remains largely constant throughout adulthood,[92] we prioritized the response that indicated higher alcohol and tobacco use.

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[a]Other drugs include hallucinogens, amphetamines, ecstasy, cocaine, barbiturates, tranquilizers, heroin, narcotics

[b] White-collar workers*: artisans, commerçants et chefs d'entreprises, cadres et agriculteurs, et professions intermédiaires*. Blue-collar workers: *employés et ouvriers*

[c] Heavy drinkers defined as alcohol problem or at least 28 glasses for males and 21 glasses for females per week; drinkers defined as 1 to 27 glasses for males and 1 to 20 glasses for females per week

2.4. Statistical and sensitivity analyses

To test the assumption that the alcohol consumption trajectories are characterized by different factors, statistical analysis was performed. First, univariate analysis to describe the study population and characteristics of each trajectory group separately was carried out. We then assessed the relationships with bivariate and multivariate analyses. Using chi-squared tests or Fisher's exact test when required, variables that were significantly associated with our outcome at a 0.2 alpha level were included in the multivariate model. This threshold is commonly used for variable selection, since an alpha level of 0.05 has been argued to be too stringent, often excluding variables that might not be associated with the outcome in bivariate but become significant in the multivariate analysis.[93] Independent of significance, we incorporated parental alcohol consumption for conceptual reasons. Because our dependent variable consists of more than two unordered categories, we applied a multinomial (polytomous) logistic regression model. Unlike linear regression, no normality, linearity or homoscedasticity is required.[94] In multinomial regression, the log odds of the different outcomes are modeled separately as linear combinations of the studied factors.[95] Specifically, this is the natural log odds of the probability of any of the outcomes occurring π_j versus the probability of the baseline outcome π_J:

$$\ln\left(\frac{\pi_j}{\pi_J}\right) = \beta_{0,j} + \beta_{1,j}x_1 + \cdots + \beta_{K,j}x_K \; (j = categories;\; k = independent\; variables)$$

The probability π_j of any of the outcomes to occur is then described by the following equation:

$$\pi_j = \frac{e^{\beta_{0,j}+\beta_{1,j}x_1+\cdots+\beta_{K,j}x_K}}{1 + \sum_{j=1}^{J-1} e^{\beta_{0,j}+\beta_{1,j}x_1+\cdots+\beta_{K,j}x_K}}$$

where the sum of all probabilities of the outcome has to be one:

$$\pi_K = 1 - \sum_{j=1}^{J-1} \pi_k$$

Adjusted odds ratios (OR) and 95% confidence intervals (CI) were estimated comparing each of the additional trajectory groups to the baseline group. The variables were considered to be significantly associated with the outcome with a p-value≤0.05. Sensitivity analysis was performed to test the robustness of our trajectory model. Because of attrition, at 42%, a high proportion of subjects contributed only one data point to our trajectory model (Appendix E, Table E1). We therefore carried out GBTM with subjects that have at least two data points (n=1,331). All analyses were conducted on SAS® 9.4 software.

2.5. Multiple imputation for missing data

Multiple imputation for missing observations among covariates was carried out. The proportion of missing data varied between 1.4% and 15.8% per determinant (Appendix F, Table F1). However, in a complete case analysis 32.4% (n=737) of the observations would have been

excluded. Considering that our outcome variable consists of various categories, in terms of statistical power, it is crucial to maintain a large sample size. After identifying an arbitrarily missing data pattern and assuming our observations are missing at random (MAR), we decided to use multiple imputation by chained equations (also called fully conditional specification). This imputation method allows to specify any type of variable and requires fewer iterations than the Markov Chain Monte–Carlo method.[96,97] Missing observations were imputed on the determinants only and not the outcome. We included all our variables in the imputation procedure, regardless of whether they had missing observations or whether they were significantly associated with our outcome in the bivariate analysis. Adding auxiliary variables allowed for a more accurate estimation of our determinant factors. Using the PROC MI procedure in SAS, we specified a logistic regression method for the ordinal variables and a discriminant function method for the nominal variables.[98] Additional imputation diagnostics were used to continuously assess the quality of the imputation and adjust the number of imputations. Finally, 20 imputed datasets were created with 100 iterations between the variables in order to determine the missing values. Each imputed dataset was analyzed separately and then combined under the PROC MIANALYZE procedure. After having adjusted the imputation procedure properly, the relative increase in variance and fraction of missing information were sufficiently small with high relative efficiencies of above 99%.[99]

3. Results

After the exclusion of 1,118 individuals, our total study population consisted of 2,278 (67.1%) participants. A subsequent comparison (Appendix G, Table G1) showed that, except for parental depression, participants excluded were statistically different from our participants included. However, according to the Phi Coefficients ($-0.19 \leq r \leq +0.19$) these associations were very weak and therefore negligible.[100] The difference in gender can be explained by more withdrawal from the study among males than females post 1991. The variation in birth year is due to the intentional inclusion of younger study participants in 2011 that decreased the average birth year for the population included. Because our excluded observations are related to observed data, we assume MAR.

On average, our study population was aged 18.6 years old in 1999, the first year used to model our alcohol consumption trajectories and consisted of more female than male participants. Half of the participants had a degree higher than Bac+2 level and 6% of the parents were classified as blue-collar workers. Regarding substance use, the majority of parents were moderate drinkers and about one quarter of both our subjects and their parents had reported smoking regularly.

3.1. Description of the trajectory model

When selecting the number of trajectory groups for alcohol consumption frequency, the BIC consistently improved with an increasing number of groups (Appendix H, Table H1). However, we decided to retain a model consisting of five trajectories in the face of coherence issues with each additional trajectory group. The latter models did not provide any additional information and merely divided existing trajectory groups into further ones assigning few individuals to these newly established groups.

The estimation of the best polynomial order for the curves of the trajectories led us to choose a model with four cubic trajectories and one linear trajectory (model with polynomial order of 33133). Of the 1024 possible models (4^5 combinations of polynomial orders), this trajectory model was the first with significant parameters among the models with the highest BICs. Thus, it is considered our reference model. The models with $2\Delta BIC \leq 10$ to our reference model were then compared among each other. Visually, no fundamental differences could be detected between the two remaining trajectory models. Table 1 compares the trajectory models with their respective groups on the basis of the criteria used to assess model adequacy.

Table 1: Comparison of trajectory models with alcohol consumption frequency per month

Model		**33133**	**33033**
BIC		**-11469.32**	**-11469.34**
2ΔBIC		Ref	0.05
Proportion P and group membership probability π with 95% CI and absolute difference between P and π	Non-drinker		
	P (%)	4.96	5.14
	π (%)	8.16 (5.51-10.81)	8.40 (5.73-11.07)
	Occasional drinker		
	P (%)	61.55	61.41
	π (%)	44.91 (41.13-48.69)	44.61 (40.79-48.43)
	Late onset drinker		
	P (%)	6.01	6.01
	π (%)	13.37 (10.84-15.90)	13.45 (10.92-15.98)
	Volatile drinker		
	P (%)	7.59	7.55
	π (%)	11.19 (9.29-13.09)	11.16 (9.26-13.06)
	Frequent drinker		
	P (%)	19.89	19.89
	π (%)	22.37 (19.47-25.27)	22.39 (20.14-24.64)
	Δ total (%)	33.28	33.61
AvePP (%)	Non-drinker	75.34	74.97
	Occasional drinker	70.67	70.32
	Late onset drinker	85.97	85.98
	Volatile drinker	83.81	83.95
	Frequent drinker	89.18	89.16
OCC	Non-drinker	34.39	32.66
	Occasional drinker	2.96*	2.94*
	Late onset drinker	39.70	39.46
	Volatile drinker	41.08	41.64
	Frequent drinker	28.60	28.51

The models performed similarly, which is additionally reflected in the BICs that differed by 0.05 units (using 2ΔBIC). Both models had a group membership probability π of above 5% and the total difference between the latter and the proportion P oscillated between 33.28% and 33.61%. None of the two models had an AvePP below the suggested threshold of 70%. Across both models, the trajectory group of occasional drinkers had an OCC lower than five*. The confidence intervals of the group membership probabilities had approximately the same width in both models. Even though very similar, because the reference model overall outperformed slightly the remaining model in all assessment criteria, we chose to retain this model.

Figure 2 displays the different trajectory groups with the average alcohol consumption frequency observed at each age, the predicted trajectory produced by GBTM and their respective 95% confidence intervals.

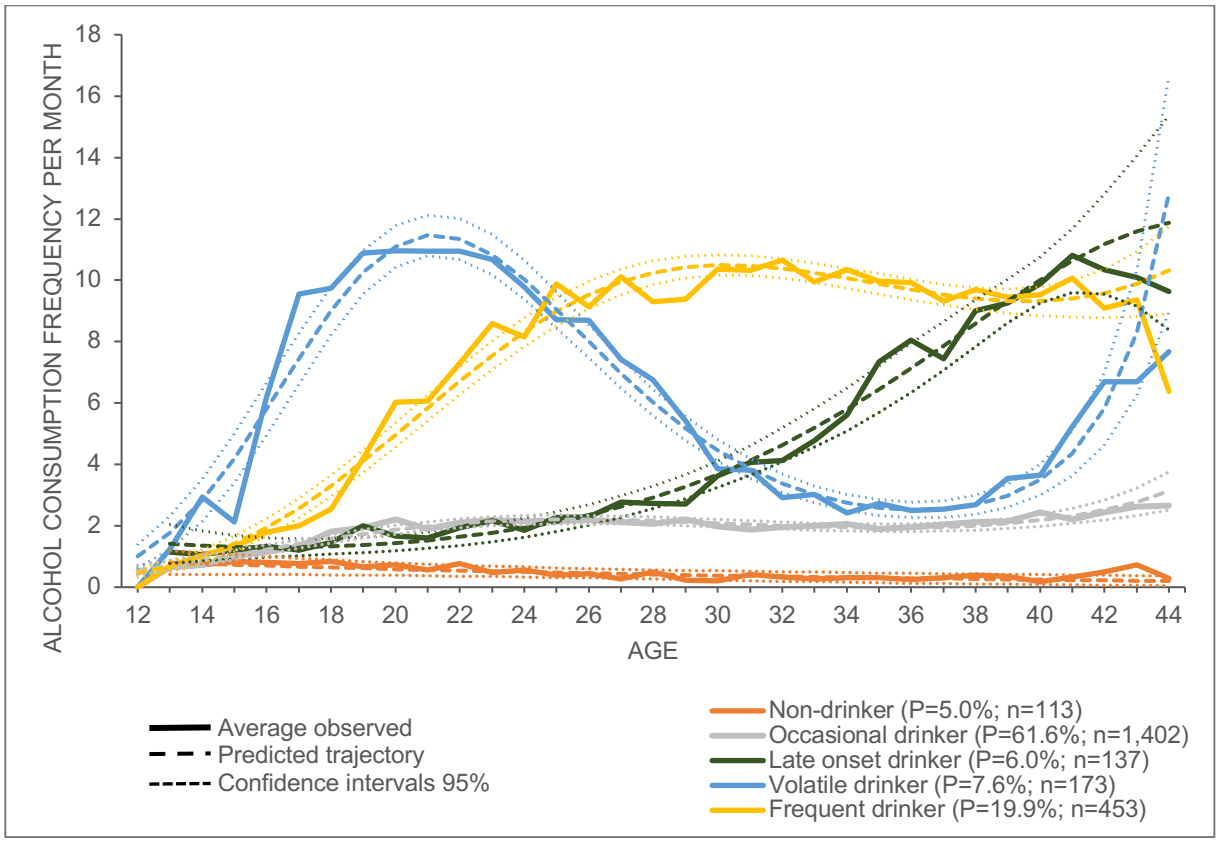

Figure 2: Alcohol consumption trajectories with alcohol consumption frequency per month

All groups uniformly initiated their alcohol consumption trajectory as abstainers or low alcohol users at around the age of 12 or 13. Spanning 32 years, 44 was the maximum age captured in our trajectory model. The first trajectory group can be described as non-drinkers and made up 5.0% of the study population. Despite minor fluctuations, this trajectory group persistently abstained from alcohol for the most part of their adolescence and early adulthood (min, 0.2, max 0.8, med 0.4).[d] Those individuals that consumed alcohol approximately twice

[d] min=minimum; max=maximum; med=median

per month could be considered occasional drinkers and formed the largest trajectory group with 61.6% (min 0, max 2.7, med 2.1). Confidence intervals for the predicted trajectories of these groups remained fairly narrow indicating a high level of precision and homogeneity within the groups. Another group of subjects that started out with a similar trajectory to the occasional drinkers but persistently increased their alcohol intake, leading to a diverging development at around the age of 26, were considered late onset drinkers. These made up 6.0% of the population (min 1.1, max 10.8, med 2.8). Further, there were individuals that could be considered volatile drinkers. This group consumed alcohol frequently in their adolescence around the age of 21, lowered their consumption in the meantime and increased their intake again later in adulthood at approximately the age of 37 (min 0, max 11, med 5.4). Lastly, our second largest group, consisting of 19.9% of the population, were subjects who frequently consumed alcohol throughout their early adulthood (min 0, max 10.7, med 9.3). They had a less steep increase in alcohol consumption frequency in their adolescence than the volatile drinkers, but after the age of 25 their consumption remained fairly constant fluctuating between nine and 10 occasions of alcohol consumption per month. Overall, except for those aged 41 to 44, within-group variations are minimal for these trajectory groups.

Regarding the sensitivity analysis, neither visually, nor based on the inter-rater reliability method with Cohen's Kappa, major differences between our trajectory model and the model with subjects of at least two data points were detected (Appendix I, Table I1, Figure I1). According to the unweighted coefficient of 0.95 (95% CI, 0.940-0.968), very strong and an almost perfect level of agreement existed. We therefore decided to retain our trajectory model.

3.2. Descriptive statistics of the trajectory groups

Compared to all other trajectory groups, the non-drinkers had a significantly higher representation of females (77.9%). Additionally, this group is characterized by a higher proportion of subjects that repeated a grade (66.7%), fewer regular smokers (19.4%) and as having left their parental home more frequently by the age of 16 (8.9%) than the total population. In terms of parental factors, above average, 11.5% of this group's parents reported to be blue-collar workers and more than a quarter to have suffered from depression by the time their children turned 17 (see Appendix J, Tables J1-J2 for characteristics & crude ORs).

As the majority of the study participants belong to the trajectory group of occasional drinkers, they resembled the total study population in most characteristics. Unlike the occasional drinkers, the late onset drinkers had a more distinct profile as compared to the average participant. In particular, the latter group consisted of a greater proportion of subjects with a degree higher to the Bac+2 level (65.7%) and of individuals that repeated a grade (67.7%). Also, relatively more individuals reported to have had suicidal thoughts (18.3%) and to have experienced externalizing symptoms by the age of 14 (19.3%). In addition, relatively

more parents of these subjects were smokers (29.2%) and ex-smokers (27.7%), and fewer had divorced or separated by the time their children were 16 years old (6.6%).

Despite variations, similar features could be observed for volatile and frequent drinkers. Accordingly, a higher proportion of subjects were found to be males (55.5% and 58.1%, respectively), regular smokers (39.2% and 34.85%, respectively) and to have experimented with psychoactive drugs other than alcohol, tobacco and cannabis (17.0% and 13.9%, respectively) in comparison to the total population. Whereas a higher proportion of frequent drinkers received a degree higher than the Bac+2 level (65.3%), volatile drinkers experimented three times more with cannabis than the average participant (32.7%) and had reported more often to have had externalizing symptoms in childhood. With respect to parental substance abuse, a higher proportion of the frequent drinker's parents were classified as heavy drinkers (14.6%). Whereas parents smoking rate was similar among the two consumer types, relatively more parents were non-smokers in the group of the volatile as compared to the frequent drinkers (60.7% and 49.3%, respectively).

Except for anxio-depressive symptoms (p-value=0.261), parental divorce or separation by the age of 16 (p-value=0.565) and parental depression by the age of 16 (p-value=0.551), all remaining factors were included in the multivariate regression.

3.3. Regression analysis with the trajectory groups

As the occasional drinkers constituted the largest group, we used this trajectory group as our reference for the regression analysis. The fully adjusted multivariate regression models yielded nearly the same results for complete cases (Appendix K, Table K1) as for all subjects post imputation of missing data. This reassures our assumption that observations are at least MAR and at most related to variables included in the analysis. Crude ORs can be found in Table K2 of Appendix K.

Overall, except for having experienced externalizing symptoms by the age of 14 and the profession of the subject's parents, all variables were significantly associated with our trajectory groups.

With respect to non-drinkers, the odds of abstaining from alcohol was lower for males as compared to females (OR=0.48, 95% CI=0.30-0.77). Additionally, subjects that had repeated a grade or left their parental home for the first time before the age of 18, were 1.76 (1.11-2.79) and 2.67 (1.29-5.51) times more likely to be a non-drinker.

A degree lower or equal to the Bac+2 level was negatively associated with late onset drinking (0.38, 0.26-0.57), while suicidal ideation and parental tobacco consumption were positively related to late onset drinking (1.66, 1.00-2.73 and 1.58, 1.02-2.45, respectively) (Table 2).

Table 2: Multivariate logistic regression results with adjusted ORs

	Non-drinker (ref=OD)	p-value	Late onset drinker (ref=OD)	p-value	Volatile drinker (ref=OD)	p-value	Frequent drinker (ref=OD)	p-value
	OR (95% CI)		**OR** (95% CI)		**OR** (95% CI)		**OR** (95% CI)	
Individual factors								
Sex								
Males vs. Females	0.48 (0.30-0.77)	0.002**	1.10 (0.75-1.60)	0.630	2.13 (1.52-2.98)	<.0001***	2.70 (2.14-3.40)	<.0001***
Education ≤Bac+2†								
Yes vs. No	0.69 (0.46-1.05)	0.083	0.38 (0.26-0.57)	<.0001***	0.70 (0.49-0.99)	0.044*	0.31 (0.24-0.40)	<.0001***
Grade repetition†								
Yes vs. No	1.76 (1.11-2.79)	0.016*	1.57 (0.94-2.61)	0.082	0.83 (0.58-1.19)	0.312	1.27 (0.94-1.72)	0.121
Externalizing symptoms ≤14 years								
Yes vs. No	1.30 (0.75-2.26)	0.341	1.45 (0.91-2.33)	0.120	1.28 (0.83-1.96)	0.261	1.13 (0.82-1.56)	0.443
Suicidal ideation†								
Yes vs. No	1.51 (0.83-2.73)	0.176	1.66 (1.00-2.73)	0.048*	0.80 (0.44-1.47)	0.470	0.86 (0.58-1.28)	0.458
Regular smoker†								
Yes vs. No	0.92 (0.53-1.58)	0.751	0.88 (0.54-1.42)	0.594	1.58 (1.06-2.36)	0.026*	1.89 (1.39-2.55)	<.0001***
Age at first experimentation with cannabis ≤16								
Yes vs. No	0.90 (0.41-1.95)	0.782	1.13 (0.57-2.22)	0.725	3.47 (2.17-5.56)	<.0001***	1.14 (0.76-1.72)	0.528
Experimentation with other psychoactive drugs†								
Yes vs. No	0.54 (0.19-1.56)	0.256	1.66 (0.89-3.10)	0.113	2.07 (1.24-3.46)	0.005**	2.03 (1.36-3.02)	0.001***
Parental factors								
Age left home ≤17 years								
Yes vs. No	2.67 (1.29-5.51)	0.008**	1.56 (0.71-3.45)	0.269	1.28 (0.62-2.66)	0.507	1.55 (0.94-2.56)	0.089
Parental profession†								
Blue-collar vs. White-collar worker	1.78 (0.94-3.37)	0.076	0.73 (0.31-1.74)	0.482	0.96 (0.46-2.01)	0.924	0.77 (0.45-1.30)	0.327
Parental alcohol consumption†								
Heavy drinker vs. Drinker	1.36 (0.74-2.51)	0.327	1.06 (0.59-1.92)	0.841	1.02 (0.57-1.82)	0.946	1.46 (1.02-2.07)	0.036*
Abstainer vs. Drinker	1.63 (0.48-5.47)	0.433	0.42 (0.06-3.14)	0.397	0.70 (0.20-2.45)	0.580	0.82 (0.34-1.98)	0.656
Parental tobacco consumption†								
Smoker vs. Non-smoker	0.79 (0.47-1.31)	0.353	1.58 (1.02-2.45)	0.041*	0.93 (0.61-1.42)	0.740	1.07 (0.81-1.43)	0.624
Ex-smoker vs. Non-smoker	0.79 (0.46-1.33)	0.372	1.53 (0.97-2.40)	0.067	0.93 (0.58-1.48)	0.754	1.38 (1.03-1.83)	0.030*

Note: After carrying out multivariate regression with the pooled results of the multiple imputation procedure, only betas and individual p-values were available. ORs were therefore calculated manually. Ref=reference. OD=Occasional drinker. †=in childhood or adolescence of the TEMPO subjects. *p≤0.05, **p≤0.01, ***p≤0.001

Whereas the male sex was negatively related to the trajectory group of non-drinkers, a reversed direction of the association was observed with volatile and frequent drinkers (2.13, 1.52-2.98 and 2.70, 2.14-3.40, respectively). Accordingly, as compared to females, males were 2.13 (1.52-2.98) times more likely to be a volatile drinker and 2.70 (2.14-3.40) times more likely to be a frequent drinker. While a degree lower or equal to the Bac+2 level was negatively related to volatile and frequent drinking (0.70, 0.49-0.99 and 0.31, 0.24-0.40, respectively), regular smoking was associated positively with both groups (1.58, 1.06-2.36 and 1.89, 1.39-2.55, respectively). A similar pattern was observed for subjects that experimented with substances other than alcohol, tobacco and cannabis. As compared to occasional drinkers, these were twice as likely to be volatile or frequent drinkers (2.07, 1.24-3.46 and 2.03, 1.36-3.02, respectively). Whereas the experimentation with cannabis before the age of 17 was significantly associated with volatile drinkers, this relationship was not found for frequent drinkers. Thus, the likelihood of being a volatile drinker was 3.5-fold (2.17-5.56) for subjects having consumed cannabis by the age of 16 compared to those that either completely abstained or consumed cannabis later on in their lives.

Further factors were found to be related to frequent drinking. Subjects of parents engaging in heavy drinking were 1.46 (1.02-2.07) times more likely to be a frequent drinker. Parental tobacco consumption however was only positively related to frequent drinking for subjects whose parents were ex-smokers (1.38, 1.03-1.83).

4. Discussion

4.1. Key findings

Covering a period of 32 years across adolescence into adulthood, five age-based trajectory groups were identified: non-drinkers, occasional drinkers, late onset drinkers, volatile drinkers and frequent drinkers. Our exploratory analysis revealed especially sex and the educational level to be significantly associated with the trajectory groups, indicating that males and subjects with a degree superior to the Bac+2 level were more likely to follow higher drinking trajectories. We further found grade repetition, suicidal ideation, the smoking status, the experimentation with cannabis before the age of 17, the experimentation with other psychoactive drugs, having left the parental home before the age of 18 and parental alcohol and tobacco consumption to be significantly related to our drinking trajectories.

4.2. A comparison of the trajectory model with the literature

Our findings corroborate that alcohol consumption follows various longitudinal patterns. Typically, three to five trajectories, including non-drinkers, were found in previous research.[101,102] This coincides with the number of trajectories we identified in both our main trajectory model and among the different indicators used (Appendix C). However, differences in the study design limit a direct comparison of the trajectory models.

Are trajectory models comparable amongst each other?

There is no communal literary consensus as to which type of alcohol indicator should be used to not only represent drinking behavior, but to additionally enable a discrimination between tolerable and harmful alcohol use.[101,103,104] Even if the same indicator is used between studies, varying scales imply that comparisons of trajectories must be made with caution (e.g. alcohol consumption frequency per month versus per year). Apart from diverging alcohol consumption indicators across different studies, study designs can vary according to the age of onset (e.g. beginning in early or late adolescence) and range studied if time was not used as the intercept, the frequency of follow-up, the size and type of the sample included (e.g. school-based, household samples etc.), the type of analysis applied (GBTM, latent transition analysis, latent growth mixture modeling) and the decision criteria used to determine the number of groups.[103]

The discussion on which indicator to use is imperative, as specifically these redefine the trajectory model and involve different interpretations. For our trajectory model, we found alcohol consumption frequency to be the most suitable. While binge drinking was commonly used in the past to perform trajectory modeling,[21,101,103] according to Sullivan and Cosden more conservative indicators are applied nowadays, for instance alcohol quantity and frequency that are either modeled separately or combined.[104] Colder et al. however, acknowledge that a combined dimension of quantity and frequency could potentially conceal important patterns and render distinct groups indistinguishable in growth trajectory modeling (e.g. low-frequency heavy drinking and frequent moderate drinking).[23] In fact, both indicators are informative, as alcohol is usually consumed more heavily during adolescence, but more frequently in adulthood. However, compared to quantity, frequency of alcohol consumption was found to be a more specific and sensitive measure among young people.[92] More complex measures are used to identify alcohol use disorders, for example the AUDIT score, and sometimes drunkenness is also studied.[105] Although drunkenness might convey information on the physical response sensed by alcohol consumers, not captured by other indicators, this measure is highly subjective.[106] Essentially, each indicator conveys different information and must be chosen according to the study objective and population.

A general comparison of alcohol consumption trajectories

Despite heterogenous trajectory models, recurring drinking patterns can be observed from the literature that are mostly congruent with our identified trajectories: a group characterized by non-drinkers or low stable drinkers (“low trajectory”), a group of early drinkers that reduce consumption with increasing responsibilities in adulthood (“decreasing trajectory”), a group of late-onset drinkers that gradually increase their consumption (“increasing trajectory”) and a group consisting of persistently high alcohol users (“high trajectory”).[102,104]

Instead of referencing a combined group of non-drinkers and low stable drinkers, various studies modeled these separately, which in our case led to the trajectory groups of the

non-drinkers and occasional drinkers. The moderate drinking group then falls between the low and high trajectories and usually makes up the largest share.[102] Whereas our trajectory model lacks the typical decreasing trajectory, these are partially represented by the volatile drinkers. Sher et al. elucidates that studies beginning early in adolescence often do not identify a trajectory of merely decreasing consumers as they capture the onset of alcohol consumption.[103] In 1997, 87% of male and 85% of female 15-year-olds had consumed alcohol before,[107] so it was important to begin our trajectory models in early adolescence in order to capture as much early consumption as possible. Whereas our late onset drinkers resonate with the increasing trajectory, our frequent drinkers are comparable to the chronic high alcohol consumers. However, the latter are typically characterized by an early onset of drinking,[102] whilst our frequent drinkers experience a less steep increase in alcohol consumption. Apart from the commonly identified trajectories, some studies detect an additional group of so-called "fling drinkers" that are characterized by a heavier drinking pattern throughout adolescence and then decline in late adolescence or in the beginning of adulthood. The volatile drinkers might resemble the classic fling drinkers, with the exception that the former increased their consumption frequency later again in life.

Are our trajectories an accurate reflection of drinking patterns in the French population?

To our knowledge, this is the first study exploring alcohol consumption trajectories in the French population. A comparison of our trajectory groups with drinking estimates of the general population is therefore heavily limited, considering that the latter are average numbers, assessed cross-sectionally at one time point and do not take individual changes into account. Nevertheless, the drinking behavior depicted by our trajectory groups fits the general picture of drinking tendencies among the French population conveyed by available literature.[1,7,35,108,109]

In comparison to other countries, France is rather characterized by a low rate of hazardous[e] and binge drinkers.[1] Accordingly, the upward trend in binge drinking, as described in Chapter 1.3, mainly occurred among the male population. Upon closer inspection of our trajectory model with binge drinking, we can corroborate this observation, as both moderate and episodic binge drinkers comprised a relatively small proportion of the study population. This is also in line with the global status report by the WHO that describes France as a country with a high adult per capita alcohol consumption "driven by more regular but moderate drinking patterns", rather than by a phenomenon such as binge drinking.[109] The trajectory model with the quantity of glasses consumed per occasion also reinforces the assumption that our study population is predominantly composed of moderate drinkers, as 84% of the study population belong to this trajectory group (Appendix C, Figure C2). Irrespective of these tendencies,

[e] Drinking pattern that risks an increase in harmful consequences, ≥140g/week of pure alcohol for women, 210g/week of pure alcohol for men

France continues to have a considerable proportion of the population affected by alcohol use problems,[7] which is reinforced by 7.6% of our study population being classified as moderate risky drinkers in the trajectory model with the AUDIT score (Appendix C, Figure C4). Furthermore, the proportion of lifetime abstainers (6.4%) in the general population is similar to the share of non-drinkers in our trajectory model (5.0%), with the former estimate including individuals who were possibly too young to have initiated the consumption of alcohol.[108] This further adds vital information to the general picture of French drinking patterns.

However, these are rather generic trends of alcohol consumption in the French population. As consistently observed among more extreme drinking trajectories across all models, especially for ages 18 to mid or late twenties, consumption patterns are high. Likewise, Public Health France has compared different age groups and found binge drinking and drunkenness to gradually decrease from 25 years onwards, but daily alcohol consumption to increase.[35] Due to the division of our study population in various trajectory groups, further particularities can be noted, elsewhere not observed. For example, usually early frequent drinking in adolescence was found to be determinant of a consistently high alcohol trajectory throughout life.[102] In contrast, our results indicate a slow but more steady increase for the trajectory of frequent drinkers that makes up one fifth of the study population. This could be explained by alcohol consumption forming such an essential part of the French culture that early consumption is less predictive of heavy drinking later in life. Another striking observation is the previously described upward trend with the volatile drinkers. This is coherent and apparent across the trajectory models for alcohol consumption frequency, drunkenness, binge drinking, and glasses consumed, especially among trajectory groups with a lower proportion of the study population (in the mid and late thirties) (see Appendix C). While the initial downward trend in the early 20s of these trajectories could follow the principle of "maturing out", with the adoption of a more conscientious role in life,[110] the increase in consumption could reflect a change in social roles[111] de novo after a span of approximately 10 years of stability.

4.3. A comparison of the regression results with the literature

Most of our results are consistent with the literature. However, with indicators and drinking habits varying among different study populations, the majority of studies chose the non-drinkers or abstainers as their reference. This has to be kept in mind in the subsequent comparison of our findings with literature.

Is sex the main driver of differences in alcohol consumption trajectories?

Sex is one of the most consistent determinants to be significantly associated with alcohol consumption.[20,48,112] Females were more likely to belong to the group of non-drinkers and males to be a volatile or frequent drinkers, which resonates with the findings of a French study on binge drinking[48] and with results from Jackson and Sher.[101] The physiological and social transformations from adolescence to adulthood have been found to affect boys and girls

differently.[113] Among boys, this manifests itself in higher alcohol tolerance, delayed maturation of structures in the brain that are responsible for more rational decision-making and expectations or beliefs linked to the male gender role. Females usually consider alcohol consumption to be riskier than do males.[114] Consequently, boys tend to engage in heavier drinking than girls. Despite recent studies highlighting the change in gender roles, with drinking patterns converging between boys and girls,[34] this most likely does not apply to our study population, as our participants are now fully-grown adults.

Do socioeconomic factors really matter in the association with alcohol consumption?

Complementing previous research, our findings suggested subjects with an educational level greater than Bac 2+ to be more likely to take on any higher drinking trajectory. According to the Organisation for Economic Co-operation and Development (OECD), French women of a higher education are two times more likely to drink than those with a lower education, whereas men of a higher education are less likely to engage in hazardous drinking.[1] This resembles the findings of Yaogo et al., proposing that participants in an upward, downward or low social trajectory are more likely to abstain from alcohol than those with a stable high social trajectory.[115] However, another study found individuals experiencing social disadvantage temporarily to more excessively consume alcohol when drinking regularly before in their lives, while non-drinkers continued to abstain from alcohol.[116] The role of socioeconomic status therefore remains unclear. It is possible that students of a lower education continue on a professional pathway with less income and simply cannot afford alcohol in the same way as those with a higher academic degree,[48] therefore desisting from long-term drinking patterns beyond occasional drinking. Compatible with these observations, study participants who repeated a grade were more likely to be a member of the non-drinking trajectory. An American study found grade repetition to be linked to material hardship and parental involvement.[117] Therefore, grade repetition could, similar to educational level, serve as a proxy for a lower socioeconomic status. However, as grade repetition occurs more often in France (28% in 2015)[118] than in the US (6.9% in 2016),[119] other factors explaining these results could be involved. Nevertheless, there is limited research assessing the relationship of grade repetition in France and alcohol consumption. Parental profession, on the contrary, was not found to be associated with membership in any of the drinking trajectories. Similar to our results, Melchior et al. did not find a correlation between low parental socioeconomic status and alcohol dependence.[120]

How do psychological difficulties affect alcohol consumption in the long-term?

The presence of externalizing symptoms by the age of 14 was not related to any of the trajectory groups and suicidal ideation was only positively associated with late onset drinking. Contrary to our results, a study in the French context has found adolescent conduct disorder to exacerbate alcohol dependence.[120] Another study found conduct disorder to be related to

alcohol consumption trajectories using different indicators. However, these studies used different time periods in modeling the trajectories or a different study design (e.g. cross-sectional), as well as examined only conduct disorder.[101] Our externalizing symptoms variable includes both conduct disorder symptoms and non-conformist, hyperactive and inattentive behavior, therefore potentially diluting associations with alcohol consumption.[121] In addition, the associations in the literature vary according to the alcohol measure used. The links between conduct disorder and alcohol dependence indicators were found to be far more significant and stronger than those with alcohol quantity-frequency.[101] Likewise, suicidal ideation was found to be significantly associated with alcohol dependence for the chronic and later onset trajectory groups, but to not be related to alcohol quantity-frequency.[101] This implies that psychological difficulties were more likely to be associated with problematic alcohol use measures rather than frequency.

Is early substance use really just a short-term "experimentation phase" in adolescence?

Our results suggest regular smoking and the experimentation with other psychoactive drugs in childhood and adolescence to be associated with volatile and frequent drinking. Similarly, experimentation with cannabis before the age of 17 was found to be a precursor of volatile drinking. This is supported by similar findings comparing occasional and frequent binge drinkers with college students that never binge drank.[48] Alcohol tends to accompany most polydrug use patterns, if various substances are consumed at once.[122] Whereas the experimentation with illicit drugs is more transitory, tobacco and alcohol consumption, as more socially accepted substances, tend to persist into adulthood.[123] Those engaging in polydrug use in childhood and adolescence can be considered greater risk takers and are therefore more likely to continue on a higher drinking course throughout their life.

How do parents come into play in their children's drinking trajectory?

We found leaving the parental home by the age of 17 is positively associated with the non-drinker trajectory. However, no details are available to us as to why 5% of our study participants had left their parental home early. Educational or work-related opportunities and even disrupted family circumstances have been linked to leaving parental home early.[124] Further research is needed to confirm whether these individuals drink less because of a social disadvantage or other reasons.

Nevertheless, non-intact families do not have to negatively affect children, if the parent-child relationship remains stable and children feel supported or parented.[45] In fact, parent-child relationships and parent's capacity to monitor could also influence the intergenerational transmission of substance use behavior.[125] Parents who abuse substances are more likely to neglect their parental responsibilities, therefore facilitating the engagement in similar substance use for their children.[126] Our findings provide evidence of parental heavy drinking to be positively linked to adolescence and early adulthood frequent drinking among their children.

This is corroborated by previous studies assessing the relationship between familial history of alcoholism and child alcohol dependence[120] and generally the association between parental and child drinking behavior.[91] Similar to parental alcohol consumption, we found study participants were more likely to be late onset drinkers if their parents had declared themselves as smokers, and frequent drinkers if their parents had reported to be ex-smokers. As alcohol and tobacco are commonly consumed together and substance use behaviors are often intergenerationally passed on, this is not surprising. Even if parents had quit smoking before their children could perceive it, they could be oblivious in respect to further substance use behaviors, and therefore create a tolerating and favoring environment for alcohol consumption.

4.4. Strengths

To our knowledge, this is the first study to analyze group-based alcohol consumption trajectories of the French population. Growth mixture modeling has been applied to other behavioral patterns in the context of France, for example tobacco consumption, yet not to alcohol consumption. These findings contribute significant information to the literature by enhancing the base knowledge on more person-centered trajectories in relation to alcohol consumption in France. Rather than speculatively defining a number of trajectory groups beforehand, this method allows trajectories to develop solely drawn from the data itself. To describe drinking trends in the entire population with a single average trajectory is oversimplistic and ignorant to the complex developmental patterns that are depicted by the numerous trajectory groups.[65]

The inclusion of the transition period between adolescence and adulthood is another key strength of our study. Despite known recruitment difficulties of young adults for epidemiological studies,[120] we have managed to capture 32 years of age, which is a broad life course spectrum when compared to other studies in the field of trajectory analysis.[21,56,110] This enabled an expansive assessment of the evolution of alcohol consumption behavior, not only in early adulthood, but from adolescence onwards.

The prospective assessment of the study participants at various points in time, allowed us to evaluate the impact of early childhood factors on the subject's respective alcohol consumption trajectory. Our studied factors also cover a wide array of aspects of life, ranging from sociodemographic, over psychological to familial factors. This is important, considering that alcohol consumption is multifaceted and influenced by a variety of determinants. Especially unique to our analysis, is the inclusion of parental characteristics that were directly assessed by the parents, rather than having to fully rely on study participants reporting on their parents.

4.5. Limitations

The findings of this study have to be seen in the light of several limitations.

Selection of study population: The study subjects belong to families in which at least one of the parents participated in the GAZEL study and was therefore employed by a large national company. Adolescents from socially disadvantaged families were less likely to partake, which limits the TEMPO cohort's representativeness and therefore the generalizability of our findings to the French population. Assuming that individuals whose parents did not have a stable job are different from the subjects we included, we could potentially have a selection bias, specifically a "healthy (parent) worker effect". Likewise, our study population has little ethnic and religious diversity.[115] A French study found abstainers to most likely be Muslims.[127] Consequently, our associations could be weaker than they would be in the general population. Nevertheless, our study participants' parents hold a wide range of occupations throughout the entirety of France.[128] Thus, although the cohort is not nationally representative, it accounts for a diverse selection of individuals and experiences.

Attrition of study participants: Cohort studies, in general, are prone to selection bias due to lost-to-follow-up. Our results may be biased if those who withdrew from the study have different drinking patterns. This also accounts for the population we had to exclude due to missing information on their alcohol consumption. Attrition bias is especially likely to have occurred due to a higher proportion of males than females having left the study. Additionally, some of our measures, such as grade repetition and educational level, might be conservative due to participants leaving the study before reporting the repetition of a grade or the attainment of the Bac+2 level. However, at least for individuals who did not report on our outcome in all survey waves, our trajectory model automatically imputed the missing values.

Underreporting in sensitive questions: The OECD has thoroughly explored measurement errors in surveys due to underreporting of alcohol consumption, with larger bias being present among France.[1] Because drinking is socially normalized, an unintentional underreporting of alcohol consumption is probable. This "French paradox" is well-known and more likely to take place among disadvantaged individuals than those of a higher socioeconomic status.[116] Another sensitive question prone to this bias could be whether our study participants had suffered from externalizing symptoms by the age of 14. Nevertheless, interviewer-administered surveys are more likely to be affected by underreporting of counternormative behavior due to "social desirability" than anonymous self-reports.[129]

Inaccurate measurements: Apart from underreporting, inaccuracy in measurement is also likely to have occurred in the assignment of weighted averages for alcohol consumption, biasing our trajectories and the respective associations with our determinants. Furthermore, some characteristics might be susceptible to recall bias as individual questions were asked retrospectively. Whereas the first age of having left parental home might be a more marked event, study participants could have had memory difficulties or lapses in reporting the accurate age of first experimentation with cannabis.

Restriction in data used for analysis: The inclusion of the study subjects in 2011 required us to work with data from different survey waves. Even if the same or a similar question was asked, response options could have differed, so that we grouped categories, leading to a loss of information. Moreover, the gap in data collection between 1999 and 2009 limits the ability to study important factors during that time span of 10 years, which could have been decisive in the association with our alcohol consumption trajectories. In fact, some etiological factors known to be associated with alcohol consumption in previous research, could not be examined, either as a result of not having been measured at all or during a different survey wave. These factors include relationships to family members and peers, other stressful life events such as verbal and physical abuse in childhood, and the age of initial alcohol consumption. The social context has been identified to play a key role in the initiation and progression of alcohol consumption, with complex interaction between social ties. For example, peer pressure to consume alcohol might be counteracted by effective parental monitoring.[113] These factors could potentially confound current associations and give further insight on dominant determinants for alcohol consumption. Likewise, stratification of the analysis by sex would have been ideal, but not possible due to a reduction in statistical power with imprecise results.

Assumptions of the Group-Based Trajectory Model: The trajectory model is probabilistic; therefore, we cannot warrant the absence of information bias with respect to the assignment of subjects to the alcohol consumption trajectories if the maximum assignment probability were to be close to another probability of belonging to a different trajectory group. Nevertheless, despite slight differences in allocation, our sensitivity analysis found similar trajectories and high levels of agreement. The assumption of conditional independence of repeated observations from time at the trajectory group level could be unrealistic considering that individuals' patterns of alcohol consumption are probably time-related. It also assumes individuals within a group to be homogenous by fixing the within-group variance to zero. To counteract this loss in information on within-group variability, in comparison to other methods like latent growth curve modeling that takes random effects into account, GBTM favors a higher number of trajectory groups.[65] This, however, makes the model more parsimonious, as fewer parameters are required. Also, in contrast to traditional growth curve models, GBTM allows to model various distributions beyond normality.

5. Conclusion, recommendations and future research

In conclusion, our study provides evidence that alcohol consumption follows various longitudinal patterns. This strongly supports the need to monitor alcohol consumption according to groups of individuals with similar consumption trajectories and to tailor preventive strategies to these subgroups, rather than merely applying a uniform population-wide approach. We have found alcohol consumption to be multifaceted, with a tendency of higher

consumption trajectories being explainable by various factors and not only by a single determinant. Except for the occasional and non-drinkers, trajectories were not simply linear, but indicated changes in consumption frequency throughout the captured life course. This enabled the identification of high-risk groups at different stages in life. Thus, depending on the consumer group, early (e.g. for volatile drinkers) or later (e.g. for late onset drinkers) interventions in life could be more effective in influencing trajectories downwards.

In fact, a combined strategy of an individual-based and population-wide approach is recommendable, as the majority of the study population was still classified as occasional drinkers. Apart from the notion that alcohol consumption is a multidimensional phenomenon, it is imperative to acknowledge that drinking forms an integral part of the French culture in order to develop and implement effective steps. Moderate drinkers are unlikely to seek help in the form of therapeutic interventions, although they equally add to the alcohol-related burden (also known as the "prevention paradox").[130] Therefore, multi-component programs are appropriate to simultaneously tackle the local structures, stakeholders and policies in place that sustain the degree of the drinking culture in France. Recently, doctors have fueled a discussion on a tax rise for alcoholic beverages and on publicity expenses.[131] Affordability as a facilitator in alcohol use also resonates with our findings. Nevertheless, a tax increase might prove difficult as the forces of lobbyism have even accomplished to weaken important regulations, such as Evin's Law, in the past years.[9] To counteract the influence of the industry, community-based awareness campaigns against excess consumption and projects in workplaces, educational institutions and healthcare facilities, to address different target groups, should be reinforced. This could be combined with further unhealthy behaviors, related to for example other substances or nutrition to convey a holistic health portrayal and make efficient use of the scarce resources available in healthcare.

Future research should focus on how to identify the person's potential chance of belonging to a trajectory. Furthermore, we recommend: the study of alcohol consumption trajectories with larger samples; to examine sex-specific trajectories or stratify the regression analysis by sex; to explore if factors could influence the trajectories more strongly at different points in life rather than merely focusing on factors in childhood and adolescence; to study known factors of importance like peer pressure; and to account for interactions between the risk factors. We hope that with the publication of this study we can contribute to raising more awareness on the importance of tackling alcohol consumption, taking different consumer types into account and thus bring more attention on this issue in the political agenda of France.

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Appendices

Appendix A: Study design and population

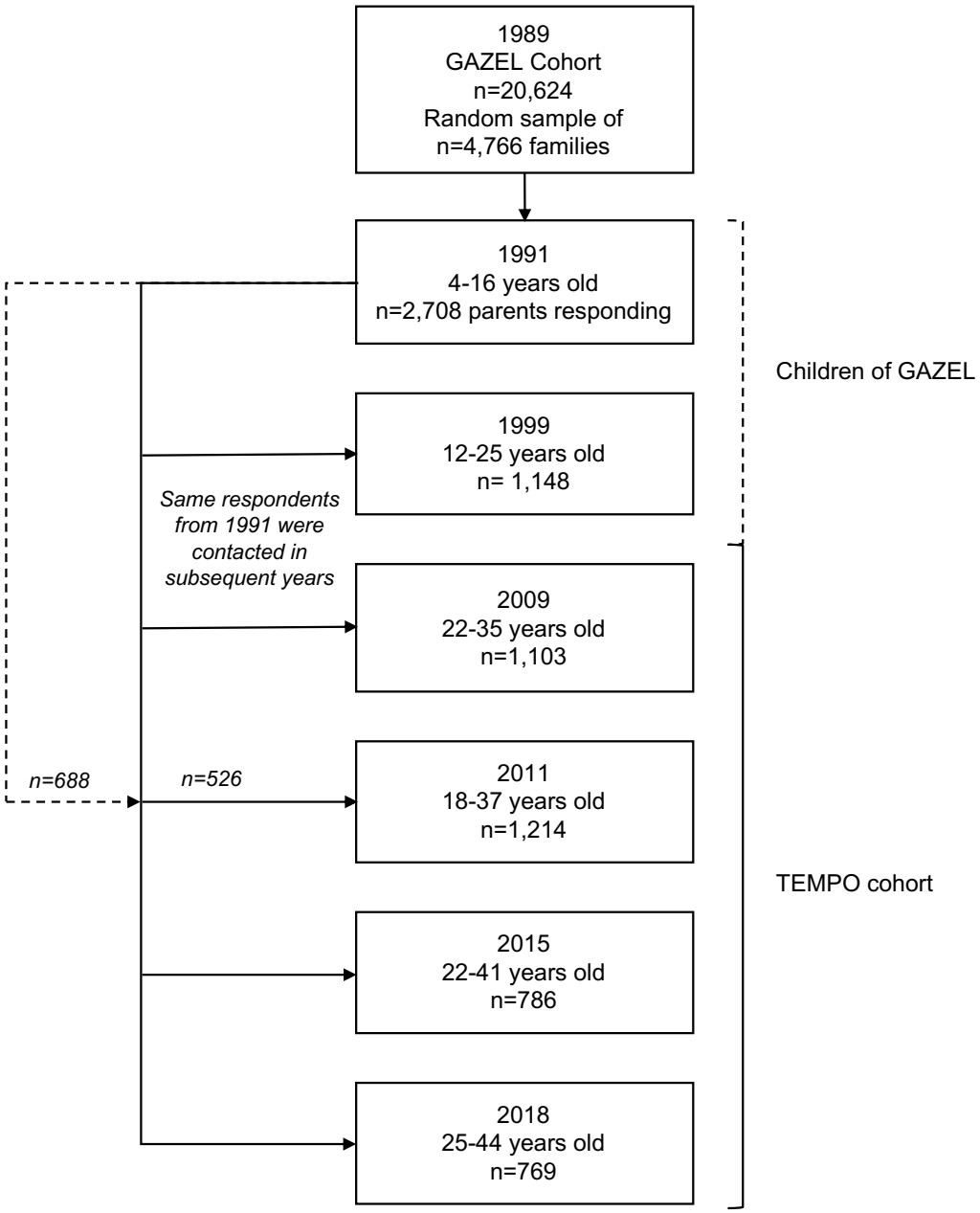

Figure A1: Flowchart of the survey participants of the TEMPO cohort

Appendix B: Model selection

Table B1: Interpretation of the logged Bayes factor

$2\log_e(B_{10}) \approx 2(\Delta BIC)$	B_{10}	Evidence against H_0
0 to 2	1 to 3	weak
2 to 6	3 to 20	positive
6 to 10	20 to 150	strong
> 10	> 150	very strong

Appendix C: Comparison of alcohol consumption indicators

Appendix C displays how the alcohol indicators, we compared, were recoded and illustrates the parameter we took into account for the comparison. Frequency tables additionally enabled to assess how the subjects are distributed over the different categories of each outcome and per wave. Lastly, based on the decision criteria in Chapter 2.2, we selected a trajectory model for each indicator and compared these amongst each other.

The other alcohol indicators were recoded according to the same mechanism as alcohol consumption frequency, resulting in a maximum of four to five categories for all alcohol variables (Table C1). In contrast to the AUDIT[f] score that could not be computed for the year 1999 due to a lack of questions that are required for its compilation, the alcohol consumption frequency was available throughout the entire study period post 1991. With 33 subjects (1.4%), this indicator had the least amount of missing values in comparison to the other indicators ranging from 1.6% to 5.6% of missing data. Because individuals respond differently to alcohol consumption and could have a subjective understanding of drunkenness, we discarded this indicator. Independent of the state of drunkenness, alcohol consumption per se is harmful. As binge drinking was less common than regular drinking, subjects were highly concentrated in few categories. Consequently, in the respective trajectory model[g] consisting of three groups, only 1.5% (n=33) of the population was assigned to the group of episodic binge drinkers, which lies below the suggested 5%-benchmark (Table C5, Figure C3).[73] The visual dispersion of observations within this group additionally indicated a lack of homogeneity and discrimination from other trajectory groups.[133] Except for alcohol consumption frequency and the number of glasses consumed that preferred a model consisting of five and four trajectory groups respectively, three trajectory groups were found to be common (Tables B3-B6 & Figures B1-B4 for comparison of trajectory models).[h] In comparison to glasses consumed, the 95% confidence intervals of the trajectories modeled for alcohol consumption frequency were consistently narrower. Additionally, the smallest group in the trajectory model with glasses per occasion consisted of 3% (n=67) of the population versus 5% (n=113) in the trajectory model of alcohol consumption frequency (Figure C2, Figure 2). On average, a higher AvePP and OCC could be observed for all trajectory groups of alcohol consumption frequency as compared to glasses consumed. We therefore selected alcohol consumption frequency as our final outcome.

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[f] The AUDIT questionnaire is validated by the World Health Organization and enables the identification of heavy drinking and alcohol use disorders.[132]

[g] Considering that our alcohol indicators are count data with a high proportion of abstainers or moderate drinkers, ZIP fits the data best.

[h] Because we discarded various models due to non-significant model parameters, for some indicators there was no model with $2\Delta BIC \leq 10$ to the reference model to allow for a comparison based on this scale. Thus, for the quantity of glasses consumed and the frequency of drunkenness, we carried out a comparison between the reference and the next possible model. In contrast, if a multitude of models were eligible according to Nagin's scale, we only compared a maximum of four models.

Table C1: Comparison of study questions, coding mechanism and missing values

Variable	Original question	Response options		Coding	Missing values
		1999	2009, 2011, 2015, 2018		
Alcohol consumption frequency per month	Frequency of alcohol consumption in the last 12 months.	1=Never	1=Never	0=Never	# of subjects: 2278 (98.6%) # of missing: 33 (1.4%)
		2=1-2 x/ year 3=3-5 x/ year 4=5-9 x/ year	2=Once or less/ month	1=Once/ month	
		5=10-19 x/ year 6=20-39 x/ year	3=2-4 x/ month	2=3 x/ month	
		7=40 x or more/ year	4=2-3 x/ week 5=At least 4 x/ week	3=11 x or more/ month	
Frequency of drunkenness per year	Frequency of alcohol consumption until drunkenness in the last 12 months.	1=Never	1=Never	0=Never	# of subjects: 2182 (94.4%) # of missing: 129 (5.6%)
		2=1-2 x/ year	2=1-2 x/ year	1=1.5 x/ year	
		3=3-5 x/ year 4=6-9 x/ year	3=3-9 x/ year	2=6 x/ year	
		5=10-19 x/ year 6=20-39 x/ year 7=40 x or more/ year	4=More than 10 x/ year	3=12 x or more/ year	
Quantity of glasses consumed per occasion	1999: Average quantity of glasses consumed per occasion in the last week. 2009-2018: Quantity of glasses consumed on the last drinking occasion.	Quantity of wine, beer or cider, strong alcohol consumed per occasion. Resulted in 0-12 glasses/ occasion.		0=No glass	# of subjects: 2274 (9.8%) # of missing: 37 (1.6%)
			1=1-2 glasses/ occ.	1=1.5 glasses/ occ.	
			2=3-4 glasses/ occ.	2=3.5 glasses/ occ.	
			3=5-6 glasses/ occ.	3=5.5 glasses/ occ.	
			4=7-8 glasses/ occ. 5=9 glasses or more/ occ.	4=8 glasses or more/ occ.	
Frequency of binge drinking per month	1999: Frequency of consuming 5 or more glasses of alcohol on one occasion in the last 2 weeks. 2009-2018: Frequency of consuming 6 or more glasses on one occasion in the last 12 months.	1=Never last 2 weeks	1=Never 2=Once or less/ month	0=Never	# of subjects: 2208 (95.5%) # of missing: 103 (4.5%)
		2=Once last 2 weeks	3=Once/ month	1=Once/ month	
		3=2 x last 2 weeks 4=3-5 x last 2 weeks	4=Once/ week	2=5 x/ month	
		5=6-9 x last 2 weeks 6=10 x last 2 weeks	5=Every day	3=24 x or more/ month	
Alcohol consumption via AUDIT score	Consists of 10 questions: 3 on alcohol consumption, 3 on drinking behavior and dependence, 4 on drinking-related consequences or problems.	Not available.	Score of 0-7=low risk Score of 8-15=risky Score of 16-19=high risk Score of 20-40=high risk, harm, probably dependent	Continuous score	# of subjects: 1828 (99.5%) # of missing: 10 (0.5%)

Table C2: Distribution of subjects per category of original outcome per wave

Average alcohol consumption frequency per month	**1999 n (%)**	**2009 n (%)**	**2011 n (%)**	**2015 n (%)**	**2018 n (%)**	**Average %**
Never	130 (11.88)	118 (10.89)	123 (10.14)	61 (7.28)	54 (7.10)	9.85%
Once	445 (40.68)	266 (24.54)	308 (25.39)	154 (19.74)	144 (18.92)	26.70%
3 times	346 (31.63)	439 (40.50)	486 (40.07)	320 (41.03)	293 (38.50)	38.20%
11 times or more	173 (15.81)	261 (24.08)	296 (24.40)	245 (31.41)	270 (35.48)	25.24%
Respondents	1094	1084	1213	780	760	
Missing	54 (4.7)	19 (1.72)	1 (0.08)	6 (0.76)	8 (1.04)	
Total	***1148***	***1103***	***1214***	***786***	***768***	
Average frequency of drunkenness per year	**1999 n (%)**	**2009 n (%)**	**2011 n (%)**	**2015 n (%)**	**2018 n (%)**	**Average %**
Never	744 (68.01)	492 (51.41)	603 (55.37)	410 (57.26)	411 (58.8)	58.40%
1.5 times	212 (19.38)	281 (29.36)	291 (26.72)	214 (29.89)	199(28.47)	26.28%
6 times	98 (8.96)	118 (12.33)	153 (14.05)	63 (8.8)	64(9.16)	10.89%
12 times	40 (3.66)	66 (6.90)	42 (3.86)	29 (4.05)	25(3.58)	4.43%
Respondents	1094	957	1089	716	699	
Missing	54 (4.70)	146 (13.24)	125 (10.30)	70 (8.91)	69 (8.98)	
Total	***1148***	***1103***	***1214***	***786***	***768***	
Average number of glasses per occasion	**1999 n (%)**	**2009 n (%)**	**2011 n (%)**	**2015 n (%)**	**2018 n (%)**	**Average %**
No glass	523 (47.98)	118 (10.98)	123 (10.16)	61 (7.82)	54 (7.13)	14.96%
1.5 glass(es)	342 (31.38)	619 (57.58)	739 (61.02)	498 (63.85)	492 (64.99)	56.64%
3.5 glasses	141 (12.94)	231 (21.49)	250 (20.64)	171(21.92)	151 (19.95)	19.95%
5.5 glasses	41 (3.76)	66 (6.14)	62 (5.12)	30 (3.85)	40 (5.28)	5.05%
8 glasses	43 (3.94)	41 (3.81)	37 (3.06)	20 (2.56)	20 (2.64)	3.40%
Respondents	1090	1075	1211	780	757	
Missing	58 (5.1)	28 (2.5)	3 (0.2)	6 (0.7)	12 (1.5)	
Total	***1148***	***1103***	***1214***	***786***	***769***	
Average frequency of binge drinking per month	**1999 n (%)**	**2009 n (%)**	**2011 n (%)**	**2015 n (%)**	**2018 n (%)**	**Average %**
Never	926 (81.09)	795 (83.25)	978 (89.72)	643 (89.93)	637 (90.74)	86.42%
Once	119 (10.42)	118 (12.36)	86 (7.89)	54 (7.55)	40 (5.70)	9.06%
5 times	91 (7.97)	41 (4.29)	23 (2.11)	17 (2.38)	21 (2.99)	4.19%
24 times or more	6 (0.53)	1 (0.10)	3 (0.28)	1 (0.14)	4 (0.57)	0.33%
Respondents	1142	955	1090	715	702	
Missing	6 (0.52)	148 (7.18)	124 (10.21)	71 (9.03)	66 (8.59)	
Total	***1148***	***2061***	***1214***	***786***	***768***	

AUDIT score	**2009 n (%)**	**2011 n (%)**	**2015 n (%)**	**2018 n (%)**
n	1086	1213	780	762
Minimum	0	0	0	0
Maximum	24	20	28	36

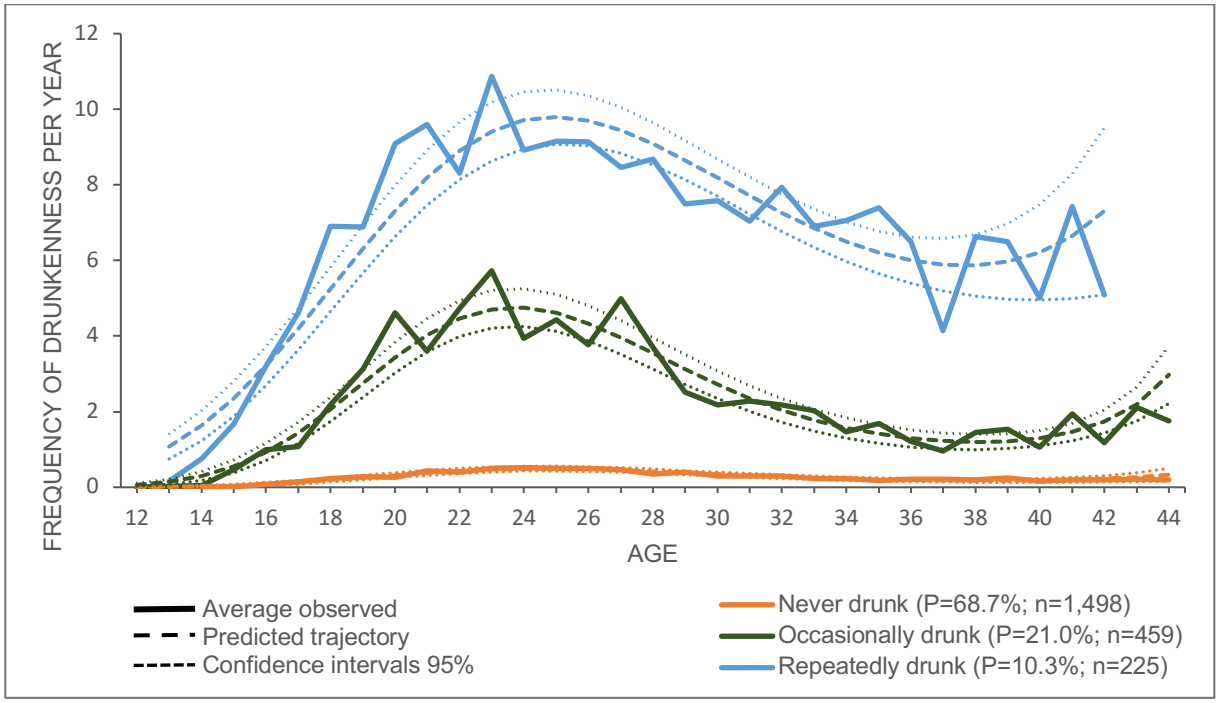

Figure C1: Alcohol consumption trajectories with frequency of drunkenness per year (model 333), n=2,182

Table C3: Comparison of eligible trajectory models for frequency of drunkenness per year

Model		**333**	**332**
BIC		**-7055.18**	**-7093.88**
2ΔBIC		Ref	77.4
Proportion P and group membership probability π and absolute difference between P and π	Never drunk		
	P (%)	68.65	69.80
	π (%)	65.33	66.82
	Occasionally drunk		
	P (%)	21.04	20.07
	π (%)	23.40	22.66
	Repeatedly drunk		
	P (%)	10.31	10.13
	π (%)	11.27	10.52
	Δ total (%)	6.64	5.96
AvePP (%)	Never drunk	91.64	92.42
	Occasionally drunk	80.85	80.95
	Repeatedly drunk	91.86	88.12
OCC	Never drunk	5.61	6.06
	Occasionally drunk	13.82	14.50
	Repeatedly drunk	88.87	63.11
95% Confidence intervals for π	Never drunk	61.99-68.66	63.91-69.73
	Occasionally drunk	20.60-26.20	20.00-25.32
	Repeatedly drunk	9.23-13.31	8.65-12.38

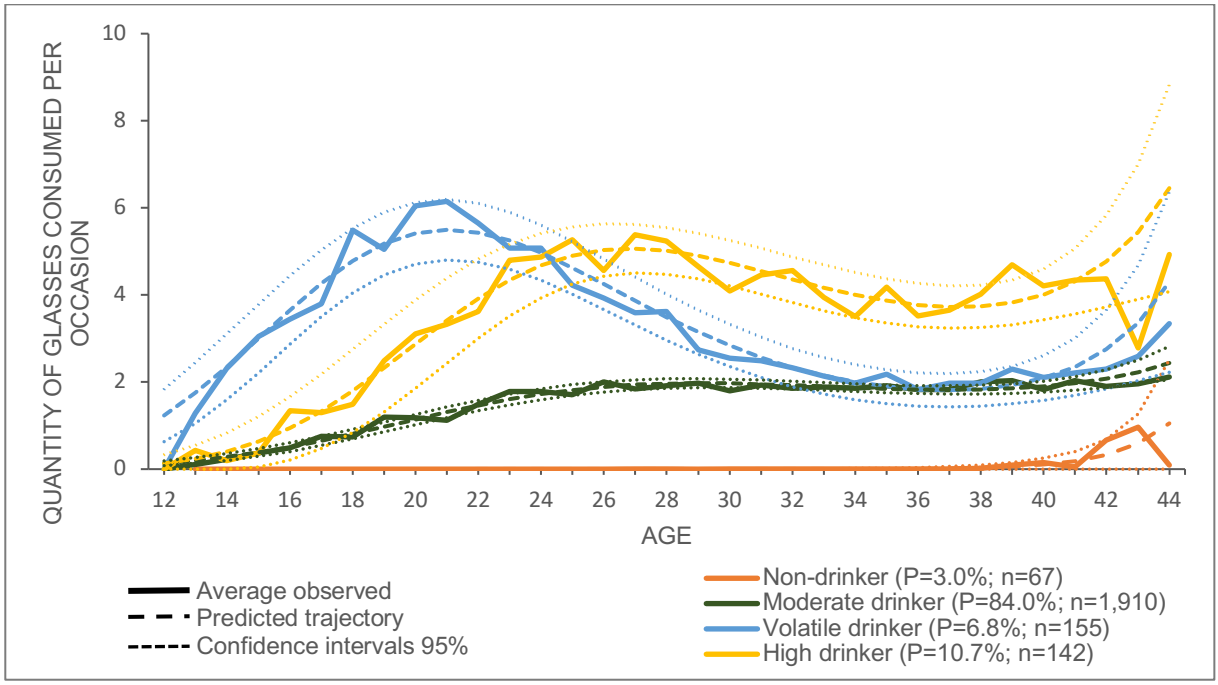

Figure C2: Alcohol consumption trajectories with quantity of glasses consumed per occasion (model 1333), n=2,274

Table C4: Comparison of eligible trajectory models for glasses consumed per occasion

Model		**1303**	**1333**
BIC		**-8331.11**	**-8337.11**
2ΔBIC		Ref	11.99
Proportion P and group membership probability π and absolute difference between P and π	Non-drinker		
	P (%)	2.95	2.95
	π (%)	4.32	4.29
	Moderate drinker		
	P (%)	83.73	83.99
	π (%)	71.86	71.77
	Volatile drinker		
	P (%)	2.90	6.82
	π (%)	5.15	13.29
	High drinker		
	P (%)	10.42	6.24
	π (%)	18.67	10.66
	Δ total (%)	23.74	24.45
AvePP (%)	Non-drinker	80.54	80.07
	Moderate drinker	82.70	82.59
	Volatile drinker	71.10	71.98
	High drinker	68.61	70.12
OCC	Non-drinker	91.58	89.64
	Moderate drinker	1.87	1.87
	Volatile drinker	45.34	16.77
	High drinker	9.52	19.67
95% Confidence intervals for π	Non-drinker	3.14-5.51	3.11-5.47
	Moderate drinker	66.64-77.08	67.39-76.15
	Volatile drinker	2.34-7.95	8.41-18.16
	High drinker	12.58-24.77	6.48-14.83

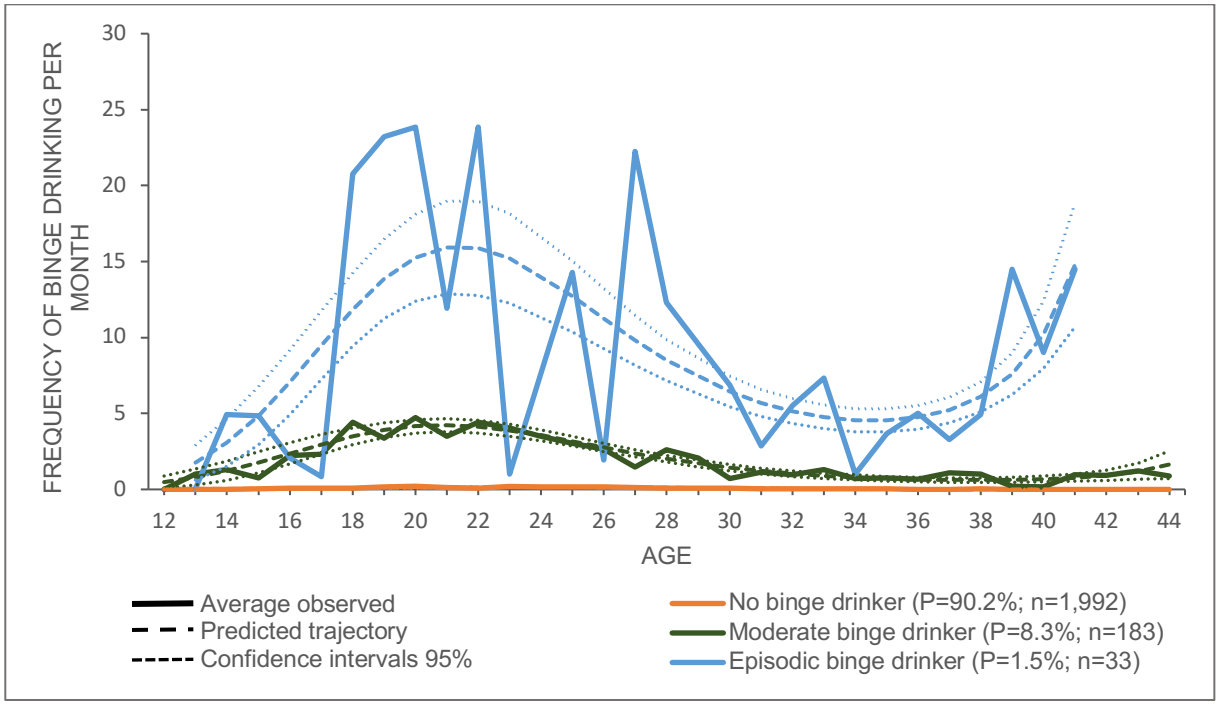

Figure C3: Alcohol consumption trajectories with frequency of binge drinking per month (model 233), n=2,208

Table C5: Comparison of trajectory models with frequency of binge drinking per month

Model		**333**	**233**
BIC		**-2912.42**	**-2920.97**
2ΔBIC		Ref	8.55
Proportion P and group membership probability π and absolute difference between P and π	No binge drinker		
	P (%)	90.31	90.22
	π (%)	88.61	88.33
	Moderate binge drinker		
	P (%)	8.20	8.29
	π (%)	9.95	10.21
	Episodic binge drinker		
	P (%)	1.49	1.49
	π (%)	1.44	1.46
	Δ total (%)	3.50	3.84
AvePP (%)	No binge drinker	97.58	97.44
	Moderate binge drinker	92.89	93.75
	Episodic binge drinker	89.19	90.07
OCC	No binge drinker	5.18	5.03
	Moderate binge drinker	118.24	131.91
	Episodic binge drinker	564.71	612.20
95% Confidence intervals for π	No binge drinker	86.97-90.24	86.65-90.01
	Moderate binge drinker	8.41-11.49	8.63-11.80
	Episodic binge drinker	0.86-2.02	0.87-2.05

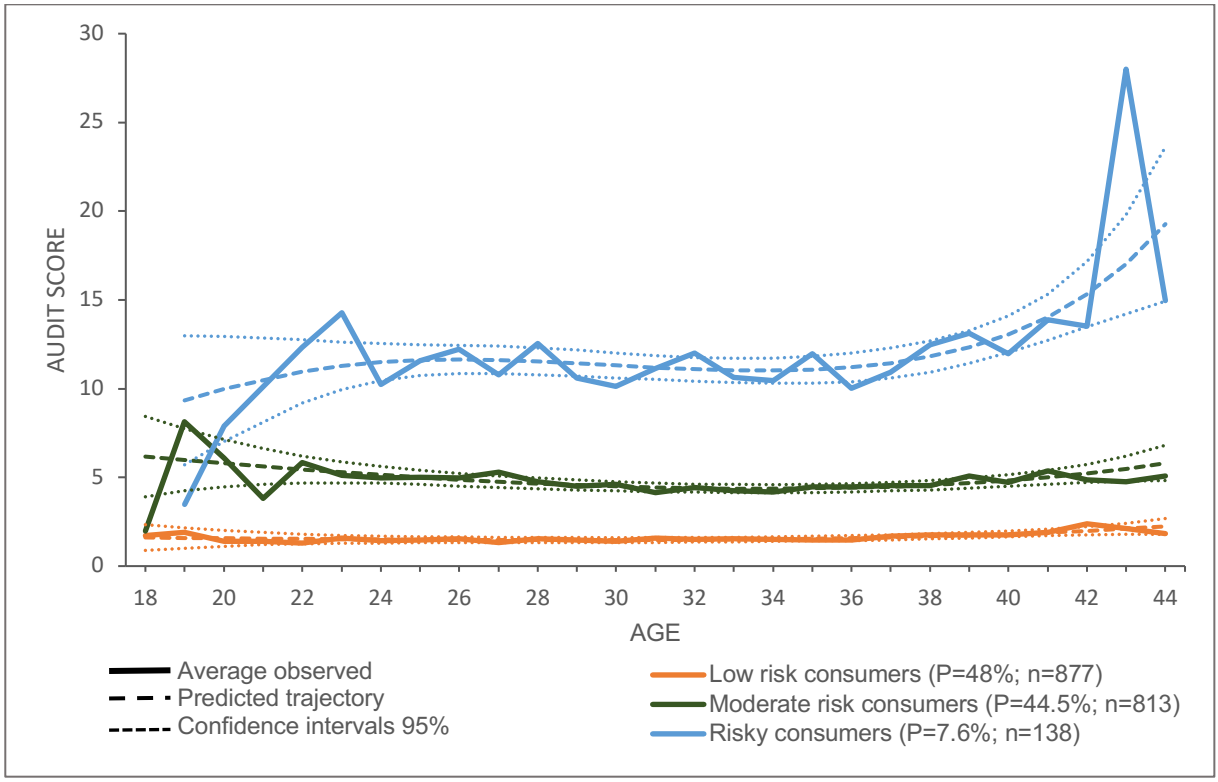

Figure C4: Alcohol consumption trajectories with AUDIT score (model 220), n=1,828

Table C6: Comparison of trajectory models with the AUDIT score

Model		**120**	**220**	**122**	**222**
BIC		**-8600.12**	**-8600.30**	**-8600.51**	**-8600.70**
2ΔBIC		Ref	0.37	0.79	1.16
Proportion P and group membership probability π and absolute difference between P and π	Low risk consumers				
	P (%)	46.99	47.98	46.44	47.32
	π (%)	48.04	47.97	47.61	47.56
	Moderate risk consumers				
	P (%)	45.46	44.47	45.73	44.86
	π (%)	43.66	43.76	43.77	43.85
	Risky consumers				
	P (%)	7.55	7.55	7.82	7.82
	π (%)	8.29	8.27	8.62	8.58
	Δ total (%)	3.59	1.44	3.93	2.01
AvePP (%)	Low risk consumers	88.87	88.18	88.86	88.26
	Moderate risk consumers	83.17	84.22	82.94	83.86
	Risky consumers	91.62	91.48	91.41	91.24
OCC	Low risk consumers	8.64	8.09	8.78	8.29
	Moderate risk consumers	6.38	6.86	6.25	6.65
	Risky consumers	120.95	119.09	112.81	110.98
95% Confidence intervals for π	Low risk consumers	43.64-52.43	43.65-52.28	43.26-51.96	43.29-39.87
	Moderate risk consumers	39.62-47.71	39.78-47.75	39.74-47.81	39.87-47.83
	Risky consumers	6.60-9.99	6.58-9.96	6.91-10.33	6.88-10.28

Appendix D: Detailed information on variable creation

Table D1: Responses, waves and coding mechanism used for the determinants

Variable	Responses and waves used	Coding mechanism
Individual factors		
Sex (male, female)	- time-invariant	At any point.
Education ≤Bac +2 (yes, no)	- Parents' responses 1999 - Subject's responses 2009, 2011, 2014, 2018	Highest degree across all survey waves
Grade repetition (yes, no)	- Parents' responses 1991, 1999 - Subject's responses 2009, 2011	Using all available survey waves.
Externalizing symptoms ≤14 years (yes, no)	- Parents' responses 1991, 1999 - Subject's responses 1999, 2011 - In 1991 and 1999 question asked about symptoms in last 6 months, in 2011 about symptoms before age of 15	Using 1991 or 1999 connected with age in those years, if missing 2011. Since the question only refers to externalizing symptoms in the last 6 months except for in 2011, we can't use other years to reduce missing data for subjects that did not experience externalizing symptoms.
Anxio-depressive symptoms (yes, no)	- Parents' responses 1991 and 1999 - Subject's responses 1999, 2011 - In 1991 and 1999 question asked about symptoms in last 6 months, in 2011 in last 12 months	Using 1991 or 1999, if missing 2011. We can't use other years to reduce missing data since this is not lifetime anxio-depressive symptoms.
Suicidal ideation (yes, no)	- Parents' responses 1991, 1999 - Subject's responses 1999, 2011 - CBCL and MINI asked about suicidal thoughts in last 6 months, remaining questions asked about lifetime suicidal thoughts	Using 1991 or 1999, if missing 2011. The question was only available for these years anyways.
Regular smoker (yes, no)	- Parents responses 1999 - Subject's responses 1999, 2011	Using 1999, if missing used 2011.
Age at first experimentation with cannabis ≤16 (yes, no)	- Parents' responses about cannabis use 1999 - Subject's responses about age of cannabis use 1999, 2009, 2018 - Subject's responses about cannabis use 1999, 2009, 2011, 2014, 2018	Using all years for question about age of cannabis use if age is below that in 1999. For subjects that never experimented with cannabis, we used all available years to reduce missing data.
Experimentation with other psychoactive drugs (yes, no)	- Parents' response 1999 - Subject's response 1999, 2009, 2011, 2014, 2018	Using 1999, if missing used 2011 for both categories or all available years for 'no lifetime usage of other drugs' to reduce missing data.

Parental factors		
Age left home ≤17 (yes, no)	- Parents' responses 1991 about children's current living situation - Subject's responses about age of having left home 1999, 2009, 2011 - Subject's responses 1999, 2009, 2011, 2014, 2018 about current living situation	Using all years for question about age of having left home if age was below that in 1999. For subjects that never left home, we used all available years to reduce missing data.
Parental divorce or separation ≤16 years (yes, no)	- Using GAZEL data, parents' yearly responses 1989 to 2015 - GAZEL subjects were asked about divorce or separation in last 12 months 1991 and yearly 1994 to 2015 and about family situation yearly 1989 to 2015	Age of TEMPO subjects was calculated for each year of GAZEL. If their parents had divorce or separation between 1989 and 1999 and subjects were less than 17 years old, it was counted as 'yes'. For subjects whose parents reported never having had divorce or separation, we used all available years to reduce missing data.
Parental depression ≤16 years (yes, no)	- Using GAZEL data, parents' yearly responses 1989 to 1999 - GAZEL subjects were asked about frequent depressive episodes in last 12 months	Age of TEMPO cohort was calculated for each year of GAZEL and if their parents had depression between 1989 and 1999 and they were less than 17 years old, it was counted.
Parental profession (blue-collar worker, white-collar worker)	- Using record of parents' profession 1989 - Higher occupations consist of cultivators and intermediate professions, artisans, merchants, heads of enterprises and executives	Using 1989 because we have information on both parents that is not available for 1991 or later waves. We prioritized higher profession of parent and collapsed categories into employees and workers/ higher occupations.
Parental alcohol consumption (heavy drinker, drinker, abstainer)	- TEMPO subject's responses 2011 on alcohol problem among parents - GAZEL subject's responses 1991 on quantity and frequency of alcohol consumption in last week	Using TEMPOs answers 2011 combined with GAZELs answers in 1991, prioritizing more severe drinking behavior.
Parental tobacco consumption (smoker, ex-smoker, non-smoker)	- TEMPO subject's responses 2011 on parental tobacco consumption - GAZEL subject's responses 1991 on current tobacco consumption	Using TEMPOs answers 2011 combined with GAZELs answers in 1991, prioritizing more severe smoking behavior.

Appendix E: Attrition among TEMPO subjects

Table E1: Distribution of subjects with different amount of data points on alcohol consumption frequency

Number of data points	Frequency	Percentage	Cumulated frequency	Cumulated percentage
Only 1	947	41.6	947	41.6
Only 2	525	23.0	1472	64.6
Only 3	457	20.1	1929	84.7
Only 4	181	7.9	2110	92.6
Only 5	168	7.4	2278	100

Appendix F: Multiple imputation

Table F1: Absolute missing values and proportion

Variable	Absolute missing (n)	Proportion missing (%)
Individual factors		
Sex		
Education ≤Bac+2	162	7.1
Grade repetition	48	2.1
Externalizing symptoms ≤14 years	48	2.1
Anxio-depressive symptoms	44	1.9
Suicidal ideation	237	10.4
Regular smoker	243	10.7
Age at first experimentation with cannabis ≤16	361	15.8
Experimentation with other psychoactive drugs	62	2.7
Parental factors		
Age left home ≤17 years	43	1.9
Parental divorce or separation ≤16 years	33	1.4
Parental depression ≤16 years	33	1.4
Parental profession	33	1.4
Parental alcohol consumption	150	6.6
Parental tobacco consumption	71	3.1

Appendix G: Population included and excluded

Table G1: Comparison of population included and excluded

	Population included n=2,278	Population excluded n=1,118	p-value	Phi-coefficient
Sex			<.001	0.170
Male	42.1%	59.8%		
Female	57.9%	38.5%		
Parental profession			<.001	-0.0969
Blue-collar worker	6.0%	11.6%		
White-collar worker	94.0.%	88.4%		
Year of birth			<.001	
median	1980	1979		
Parental divorce or separation ≤1991			<.001	-0.0825
Yes	6.0%	10.7%		
No	94.0%	89.3%		
Parental depression ≤1991			0.145	-0.0256
Yes	12.3%	14.2%		
No	87.7%	85.8%		

Note: Chi-squared tests for categorical and one-way ANOVA for continuous variables were used

Appendix H: Final trajectory model

Table H1: Model selection results for number of trajectory groups

Number of groups	BIC	2ΔBIC
1	-15718.81	
2	-12268.00	6901.62
3	-12030.98	474.04
4	-11903.64	254.68
5*	-11622.99	561.3
6	-11601.65	42.68

Note: *chosen number of trajectories for our trajectory model

Appendix I: Sensitivity analysis

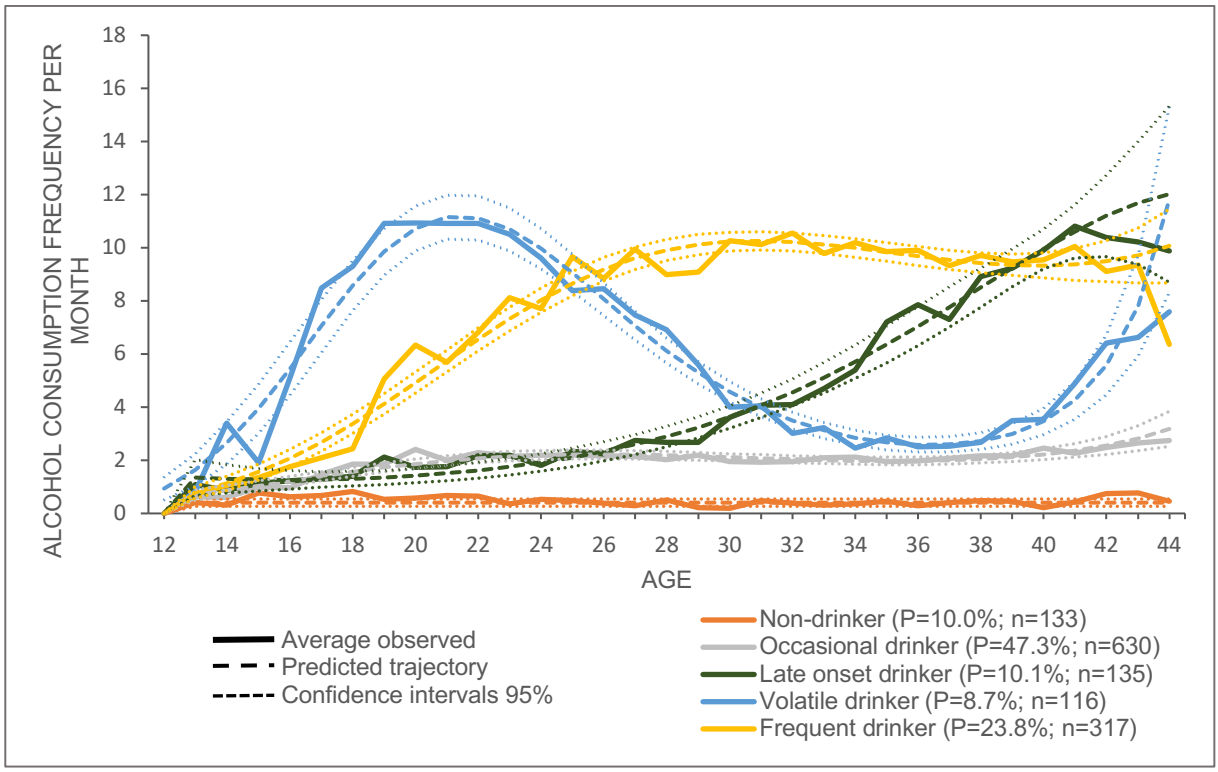

Figure I1: Alcohol consumption trajectories with at least two data points

Table I1: Comparison of total population with subjects that have at least two data points

		Model from subjects with at least two data points (n= 1,331) (Model 03333)						
		ND	OD	LD	VD	FD	*NA*	*Total*
Model from population (n= 2,278) (Model 33133)	ND	99	0	0	0	0	14	113
	OD	34	629	1	0	0	738	1,402
	LD	0	0	134	0	3	0	137
	VD	0	1	0	114	1	57	173
	FD	0	0	0	2	313	138	453
	Total	133	630	135	116	317	947	2278

Note: ND=Non-drinker ; OD=Occasional drinker ; LD=Late onset drinker ; VD=Volatile drinker ; FD=Frequent drinker ; NA=not attributed

Appendix J: Descriptive analysis

Table J1: Characteristics of the study population and per trajectory group

	Total population n=2,278	**Non-drinker n=113**	**Occasional drinker n=1,402**	**Late onset drinker n=137**	**Volatile drinker n=173**	**Frequent drinker n=453**	**p-value‡**
Individual factors							
Sex							<.001*
Male	42.1%	22.1%	37.4%	36.5%	55.5%	58.1%	
Female	57.9%	77.9%	62.6%	63.5%	44.5%	41.9%	
Education ≤Bac+2							<.001*
Yes	50.1%	47.8%	56.2%	34.3%	55.0%	34.7%	
No	49.9%	52.2%	43.8%	65.7%	45.0%	65.3%	

Grade repetition							0.025*
Yes	59.5%	66.7%	57.3%	67.7%	55.9%	64.2%	
No	40.5%	33.3%	43.7%	32.3%	44.1%	35.8%	
Externalizing symptoms ≤14 years							0.199*
Yes	15.3%	16.2%	14.1%	19.3%	19.7%	16.1%	
No	84.7%	83.8%	85.9%	80.7%	80.3%	83.9%	
Anxio-depressive symptoms†							0.261
Yes	23.9%	25.9%	25.0%	25.2%	23.7%	19.9%	
No	76.1%	74.1%	75.0%	74.8%	76.3%	80.1%	
Suicidal ideation†							0.017*
Yes	10.5%	14.6%	9.7%	18.3%	8.2%	10.4%	
No	89.5%	85.4%	90.3%	81.7%	91.8%	89.6%	
Regular smoker†							<.001*
Yes	25.8%	19.4%	22.0%	21.4%	39.2%	34.8%	
No	74.2%	80.6%	78.0%	78.6%	60.8%	65.3%	
Age at first experimentation with cannabis ≤16							<.001*
Yes	11.9%	7.3%	9.4%	10.1%	32.7%	13.1%	
No	88.1%	92.7%	90.6%	89.9%	67.3%	86.9%	
Experimentation with other psychoactive drugs†							<.001*
Yes	8.6%	3.6%	6.0%	10.9%	17.0%	13.9%	
No	91.4%	96.4%	94.0%	89.1%	83.0%	86.1%	
Parental factors							
Age left home ≤17 years							0.023*
Yes	4.8%	8.9%	3.7%	5.9%	5.8%	6.6%	
No	95.2%	91.1%	96.3%	94.1%	94.2%	93.4%	
Parental divorce or separation ≤16 years							0.565
Yes	9.5%	8.0%	10.3%	6.6%	8.3%	9.1%	
No	90.5%	92.0%	89.7%	93.4%	91.7%	90.9%	
Parental depression ≤16 years							0.551
Yes	20.5%	26.5%	20.6%	20.4%	19.5%	19.3%	
No	79.5%	73.5%	79.4%	79.6%	80.5%	80.7%	
Parental profession†							0.060*
Blue-collar worker	6.0%	11.5%	6.3%	4.4%	5.3%	4.4%	
White-collar worker	94.0%	88.5%	93.7%	95.6%	94.7%	95.6%	
Parental alcohol consumption†							0.325
Heavy drinker	11.2%	13.7%	10.1%	11.5%	9.8%	14.6%	
Drinker	86.8%	83.3%	87.8%	87.7%	88.3%	83.8%	
Abstainer	1.9%	2.9%	2.1%	0.8%	1.8%	1.6%	
Parental tobacco consumption†							<.001*
Smoker	23.7%	21.4%	23.4%	29.2%	22.6%	24.0%	
Ex-smoker	20.5%	18.8%	18.4%	27.7%	16.7%	26.7%	
Non-smoker	55.8%	59.8%	58.3%	43.1%	60.7%	49.3%	

Note: ‡ Bivariate analysis was conducted using Chi2-tests. †=in childhood or adolescence of the TEMPO subjects.
*p≤0.2

Appendix K: Complete case and bivariate analyses

Table K1: Multivariate logistic regression results with adjusted ORs with complete cases

	Non-drinker (ref=OD)	**Late onset drinker (ref=OD)**	**Volatile drinker (ref=OD)**	**Frequent drinker (ref=OD)**	**p-value**
	OR (95% CI)	**OR** (95% CI)	**OR** (95% CI)	**OR** (95% CI)	
Individual factors					
Sex					<.0001***
Males vs. Females	0.60 (0.35-1.02)	1.13 (0.70-1.83)	2.22 (1.47-3.34)	3.25 (2.37-4.45)	
Education ≤Bac+2					<.0001***
Yes vs. No	0.75 (0.45-1.24)	0.47 (0.29-0.77)	0.52 (0.34-0.80)	0.31 (0.22-0.44)	
Grade repetition					0.490
Yes vs. No	1.42 (0.85-2.39)	1.40 (0.85-2.33)	0.97 (0.63-1.48)	1.05 (0.76-1.46)	
Externalizing symptoms ≤14 years					0.894
Yes vs. No	1.17 (0.61-2.23)	1.33 (0.74-2.39)	1.08 (0.64-1.81)	1.02 (0.67-1.53)	
Suicidal ideation†					0.754
Yes vs. No	1.16 (0.47-2.85)	1.31 (0.60-2.84)	0.63 (0.25-1.56)	0.90 (0.49-1.66)	
Regular smoker†					0.002**
Yes vs. No	0.89 (0.47-1.66)	1.19 (0.67-2.10)	1.82 (1.15-2.89)	1.97 (1.37-2.83)	
Age at first experimentation with cannabis ≤16					0.000***
Yes vs. No	0.77 (0.33-1.78)	1.19 (0.60-2.33)	2.87 (1.79-4.59)	1.14 (0.74-1.77)	
Experimentation with other psychoactive drugs†					0.002**
Yes vs. No	0.66 (0.20-2.25)	1.90 (0.85-4.21)	2.68 (1.48-4.86)	2.29 (1.35-3.88)	
Parental factors					
Age left home ≤17 years					0.197
Yes vs. No	2.70 (1.18-6.19)	1.48 (0.55-4.00)	1.44 (0.62-3.32)	1.41 (0.73-2.73)	
Parental profession†					0.528
Blue-collar vs. White-collar worker	1.63 (0.72-3.67)	0.54 (0.16-1.82)	0.94 (0.39-2.23)	0.78 (0.39-1.57)	
Parental alcohol consumption†					
Heavy drinker vs. Drinker	1.10 (0.52-2.34)	1.04 (0.49-2.20)	1.08 (0.56-2.07)	1.28 (0.79-2.06)	0.989
Abstainer vs. Drinker	1.64 (0.36-7.58)	0.71 (0.09-5.57)	1.08 (0.29-4.04)	1.29 (0.46-3.63)	
Parental tobacco consumption†					0.113
Smoker vs. Non-smoker	1.12 (0.63-2.01)	1.66 (0.92-2.97)	0.92 (0.55-1.54)	1.24 (0.85-1.83)	
Ex-smoker vs. Non-smoker	0.85 (0.45-1.63)	2.22 (1.28-3.85)	1.05 (0.62-1.78)	1.52 (1.03-2.22)	

Note: Ref=reference. OD=Occasional drinker. †=in childhood or adolescence of the TEMPO subjects. *p≤0.05, **p≤0.01, ***p≤0.001

Table K2: Multinomial logistic regression results with crude ORs

	Non-drinker (ref=OD)	**Late onset drinker (ref=OD)**	**Volatile drinker (ref=OD)**	**Frequent drinker (ref=OD)**	**p-value**
	OR (95% CI)	**OR** (95% CI)	**OR** (95% CI)	**OR** (95% CI)	
Individual factors					
Sex					<.0001***
Males vs. Females	0.47 (0.30-0.75)	0.96 (0.67-1.38)	2.08 (1.51-2.86)	2.31 (1.86-2.87)	
Education ≤Bac+2					<.0001***
Yes vs. No	0.71 (0.49-1.05)	0.41 (0.28-0.59)	0.95 (0.69-1.31)	0.41 (0.33-0.52)	
Grade repetition					0.026*
Yes vs. No	1.49 (0.96-2.31)	1.56 (1.00-2.43)	0.94 (0.68-1.32)	1.34 (1.04-1.71)	
Externalizing symptoms ≤14 years					0.202
Yes vs. No	1.18 (0.70-2.00)	1.45 (0.92-2.29)	1.49 (1.00-2.24)	1.17 (0.87-1.57)	
Suicidal ideation†					0.020*
Yes vs. No	1.58 (0.89-2.82)	2.08 (1.29-3.37)	0.83 (0.46-1.48)	1.08 (0.75-1.57)	
Regular smoker†					<.0001***
Yes vs. No	0.85 (0.51-1.42)	0.96 (0.62-1.49)	2.28 (1.63-3.19)	1.88 (1.47-2.41)	
Age at first experimentation with cannabis ≤16					<.0001***
Yes vs. No	0.75 (0.36-1.59)	1.08 (0.59-1.98)	4.66 (3.14-6.92)	1.45 (1.01-2.07)	
Experimentation with other psychoactive drugs†					<.0001***
Yes vs. No	0.59 (0.21-1.64)	1.94 (1.08-3.47)	3.22 (2.04-5.09)	2.54 (1.79-3.62)	
Parental factors					
Age left home ≤17 years					0.027*
Yes vs. No	2.54 (1.25-5.15)	1.63 (0.76-3.52)	1.59 (0.79-3.19)	1.82 (1.14-2.91)	
Parental profession†					0.069
Blue-collar vs. White-collar worker	1.93 (1.04-3.57)	0.68 (0.29-1.58)	0.83 (0.41-1.69)	0.69 (0.42-1.13)	
Parental alcohol consumption†					
Heavy drinker vs. Drinker	1.43 (0.79-2.59)	1.15 (0.65-2.02)	0.97 (0.56-1.67)	1.52 (1.10-2.10)	0.339
Abstainer vs. Drinker	1.50 (0.45-5.05)	0.37 (0.05-2.77)	0.89 (0.27-2.96)	0.84 (0.36-1.94)	
Parental tobacco consumption†					0.001**
Smoker vs. Non-smoker	0.89 (0.55-1.45)	1.69 (1.11-2.58)	0.93 (0.63-1.38)	1.21 (0.93-1.58)	
Ex-smoker vs. Non-smoker	0.99 (0.60-1.66)	2.04 (1.33-3.15)	0.87 (0.56-1.35)	1.71 (1.32-2.24)	

Note: Ref=reference. OD=Occasional drinker. †=in childhood or adolescence of the TEMPO subjects. *p≤0.05, **p≤0.01, ***p≤0.001