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IDEES ET CONDUITES SUICIDAIRES EN POPULATION ETUDIANTE :
UTILISATION DES SOINS EN SANTE MENTALE ET ASSOCIATION AVEC
LES MEDICAMENTS ANXIOLYTIQUES ET/OU HYPNOTIQUES

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1 Introduction

Le début de la vie adulte s'accompagne de nombreux changements dans le mode de vie ; ceux-ci peuvent provoquer un stress et augmenter le risque de troubles psychiatriques dans une période de la vie particulièrement vulnérable. L'arrivée dans la vie universitaire, conjugue ainsi une exposition à de nombreux facteurs de stress environnementaux et l'âge de survenue de la plupart des troubles psychiatriques. Les changements environnementaux peuvent concerner quasiment tous les aspects de la vie : les relations familiales et avec ses pairs avec parfois un certain isolement affectif, l'environnement de travail avec une plus grande pression sur les performances et un étayage moins important, une plus grande autonomie matérielle et financière avec parfois une certaine précarité, parfois la nécessité d'un travail étudiant, assez souvent la consommation de substances psychoactives et une irrégularité du rythme de vie.

Le suicide survient en particulier peu après l'apparition d'un trouble psychiatrique ; il en est la complication la plus redoutée (1). L'importance du risque suicidaire chez les jeunes gens en fait un problème majeur de santé publique. En effet, bien que la mortalité par suicide soit quatre à cinq fois plus élevée chez les personnes âgées de 45 à 54 ans, le suicide est la première ou la deuxième cause de mortalité chez les 15-34 ans (2). Les étudiants appartiennent également à la tranche d'âge la plus concernée par les tentatives de suicide. Dans une méta-analyse récente, la prévalence des idées et tentatives de suicide chez les étudiants était de, respectivement, 22,3% et 3,1% sur la vie entière et de 10,6% et 1,2% pour les douze derniers mois (3). Outre la souffrance induite, ces symptômes ont un impact à long terme : faible réussite académique, augmentation du risque de décès par suicide ultérieurement, y compris quinze années plus tard, dysfonctionnement relationnel, solitude, problèmes de santé psychiatriques et non psychiatriques, difficultés ou inactivité professionnelles, niveau socio-économique plus faible et problème de logement (3-6).

Il n'y a pas de consensus pour définir le suicide et ses aspects comme étant un trouble à part entière : les tentatives de suicides et comportements suicidaires font partie des troubles mentaux non classés ailleurs dans la CIM11 (Classification Internationale des Maladies, version 11) (7) ou parmi les troubles en annexe dans le DSM5 (Manuel de diagnostic statistique des

troubles mentaux, version 5) (8). De ce fait, la recherche portant sur les idées ou comportements suicidaires manque de donnée, en particulier pour en découvrir l'ensemble des facteurs prédictifs (9) et les soins les mieux adaptés. Les moyens thérapeutiques médicamenteux sont ainsi limités dans cette indication spécifique. De plus, l'accès aux soins chez les étudiants est souvent insuffisant, en particulier pour les soins psychiatriques.

Les médicaments de la classe des benzodiazépines et leurs apparentés ont une association encore incertaine avec les idées et conduites suicidaires. D'une part, ils sont couramment utilisés dans cette indication afin d'apaiser les souffrances qui provoquent ou découlent des idées suicidaires. D'autre part, ils sont suspectés d'augmenter le risque d'idées ou conduites suicidaires, sans que les mécanismes soient précisément élucidés. En effet, la modélisation du processus suicidaire, comme un continuum allant des idées passagères à l'acte suicidaire décidé et planifié, est complexe ; les facteurs de risque des différentes étapes sont souvent différents et parfois opposés, supposant des mécanismes différents.

Dans notre travail de thèse d'exercice, notre objet d'étude rassemblait les idées suicidaires et les antécédents de tentative de suicide. L'étude du suicide n'a pas été possible. Ce travail est constitué de deux études, présentées sous la forme de deux manuscrits, menées dans la cohorte nationale d'étudiants i-Share. Cette étude, basée à l'Université de Bordeaux et financée par le programme Investissements d'Avenir (ANR), a pour objectif d'étudier la santé d'environ 30 000 étudiants suivis pendant 10 ans. Elle a débuté en 2013 et comporte aujourd'hui environ 20 000 inscrits. Les étudiants volontaires renseignent régulièrement leur état de santé dans des questionnaires anonymes en ligne qui mesurent prospectivement plusieurs centaines de facteurs. Ces données concernent le parcours universitaire, les caractéristiques socio-économiques, l'environnement familial, le mode de vie et la santé physique ou mentale.

Le premier article présenté évalue l'utilisation des soins en santé mentale (consultations avec un psychiatre/psychologue/psychothérapeute et prescription de médicaments anxiolytiques/hypnotiques), ainsi que les facteurs associés à ces soins chez les étudiants présentant des idées et/ou des conduites suicidaires. Cet article est en cours de relecture par les co-auteurs.

Le second article évalue l'association entre utilisation de médicaments anxiolytiques et/ou hypnotiques et idées et/ou conduites suicidaires chez les étudiants, tout en prenant en compte de nombreux facteurs de confusion, notamment les troubles du sommeil et l'anxiété qui pourraient justifier leur prescription. Cet article est actuellement soumis pour publication.

Les travaux présentés dans ce manuscrit ont fait l'objet de communications dans des congrès scientifiques dont les références figurent ci-dessous.

Communication orale dans un congrès avec comité scientifique :

- Lecat N. Quel est le lien entre utilisation de psychotropes et conduites suicidaires chez les étudiants ? Finaliste du concours 180 secondes pour innover. Congrès Français de Psychiatrie, 8ème édition, Montpellier, 23-26 novembre 2016
- Lecat N, Tournier M. Association entre utilisation des soins et idées et conduites suicidaires dans une large population étudiante : la cohorte i-Share. 2ème Congrès de la Fédération Trauma Suicide Liaison Urgence (FTSLU), « Evaluer pour agir », Metz, 20-23 mars 2017
- Lecat N, Fourrier-Réglat A, Pariente A, Tzourio C, Tournier M. Etude de l'association entre idées et conduites suicidaires et utilisation de médicaments psychotropes dans une large population étudiante : la cohorte i-Share. 49^{me} Journées du GEPS, « Prévention du suicide : connexion synaptique, digitale, sociale », Montpellier, 10-12 janvier 2018

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- Lecat N, Pariente A, Tzourio C, Fourrier-Réglat A, Tournier M. The Use of Mental Health Care in Students with Suicide Risk: A Transversal Study in the i-Share Cohort. 26th European Congress of Psychiatry, « Mental Health : integrate, innovate, individualise », Nice, 3-6 march 2018
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2 Article 1. The use of mental health care in students with suicide ideation and/or behaviours: a study in the population-based i-Share cohort

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2.1 Abstract

BACKGROUND: While suicide ideation and behaviours are prevalent among university students, use of mental healthcare is poor in this population.

OBJECTIVE: We aimed at assessing the use of mental healthcare in students with suicide ideation/behaviours and to identify its associated factors.

METHODS: Study population was all the students participating to the i-Share cohort, included between April 2013 and March 2017. Suicide ideation/behaviours were defined as the presence of suicide ideation over the previous year or a lifetime suicide attempt at inclusion. Use of prescribed anxiolytic/hypnotic over the previous 3 months, consultations with a psychiatrist or a psychologist in the previous year and renunciation of healthcare were collected. Multivariate logistic regression models with backward stepwise were performed to assess factors associated with consultation with mental health professional and the use of anxiolytic/hypnotic drugs among students with suicide ideation/behaviours.

RESULTS: Among the 11,588 students who completed the baseline questionnaire, 2,916 (25.2%) presented with suicide ideation/behaviours. Among them 26.8% received mental health consultation versus 8.6% of other students ($p<0.0001$) and 19.0% used anxiolytics/hypnotics versus 7.4% ($p<0.0001$). In students with suicide ideation/behaviours, the use of mental health consultations and of these drugs was associated with being a female and history of diagnosed psychiatric disorders. Additional factors were associated with the use of a specific type of care.

DISCUSSION: The rate of use of mental healthcare in students with suicide ideation/behaviours was low and had specific correlates. The discrepancy between the high rate of suicide ideation/behaviours in students and the real use of mental health care (unmet needs) calls for action to improve both the access and use.

Key words: suicide; students; healthcare; foregoing healthcare; mental health

2.2 Introduction

According to the World Health Organization (1), suicide is the second cause of death among people 15-34 years old worldwide. A recent meta-analysis estimated that 3.2% of students presented with a lifetime suicide attempt, and 10.6% with suicidal ideation in the previous 12 months (2). Because of their age of onset, psychiatric disorders are particularly likely to occur in university students (3–5) and are the variable the most strongly associated with suicide of those that have been studied. They may be responsible of 47-74% of suicides (6). Early appropriate management of these disorders might reduce their short- and long-term impact, including suicide behaviours. The frequency of unmet need for access to care among students represents an important public health issue with respects to global care and mental healthcare in Europe (7–10). Consequently, prevention, identification of people at risk for psychiatric disorders and healthcare remain insufficient (11).

Multiple causes may explain this limited access to mental healthcare, like difficulty for students to convey mental distress (at any time or at the right time) to a professional (11), or inappropriate mental health services for detection and care of mental distress in students. Sociological and clinical factors were shown to be associated with unmet need of care, but no consensus was reached among scholars (9,12–16) except for stigma, although its importance may surprisingly be quite low and mentioned by only 12% of students at suicide risk (14). Stigma was more frequently reported when people were referred by other people (doctor, family) to mental health services and did not decide by themselves and was associated with high economic status and longer delay to consult in south-eastern Europe countries (12), residing in rural areas (17), and being a refugee (18) or internally displaced (19). Perceived stigma was also associated with self-stigma and shame for help-seeking (20). Barriers to mental healthcare concerned also the organization of the health services and students' inadequate knowledge of available services (19–21). Lastly, the lack of persistence and adherence to care was considered of a lack of care (22).

Moreover, while limited access to healthcare increases the risk of suicide (23,24), individuals at-risk for suicide are among the most reluctant help-seekers either by foregoing care or negating the need for help (7,25). The suicidal process is a factor in itself limiting access to

care. It locks the one who suffers in a spiral making him/her less and less capable of reasoning without bias. Students often do not access to care when their suffering begins; hence, distress persists over time and increases. Then, cognitive coping strategies can be altered leading to a unique illusory "suicidal solution"(26). At this point, it is sometimes too late to think of calling a friend or contacting a health care professional (27). As the need of care grows, the ability to seek help diminishes. Coping strategies are involved in the use of mental health services (10). Therefore, it seems imperative to take into account coping strategies and clinical information when assessing the access to care for people at risk of suicide.

Current guidelines for prevention and care of suicide ideation and behaviours include psychiatric or psychological consultations and pharmacotherapy. Although most recommendations do not mention anxiolytic/hypnotic drugs in this situation (28–33), they are sometimes recommended to treat symptoms associated with suicidal risk (34,35) and their use is widespread when suicidal risk is identified. Thus, such use is considered as therapeutic response (35,36).

The population at risk of suicide who does not access to care is paradoxically very little studied (6), whereas a better understanding of their characteristics could support appropriate strategies against suicide. This study aimed at (1) assessing the use of mental healthcare (defined as either consultation with mental health professionals or prescribed anxiolytic or hypnotic drugs) in university students with suicide ideation and/or behaviours, and (2) identifying factors associated with this use in this specific population.

2.3 Methods

2.3.1 Study design and study population

This cross-sectional study was conducted on a national population-based cohort study, the ongoing Internet-based Students Health Research Enterprise (i-Share) project (37). This ongoing project assesses students' health in French-speaking universities and higher education institutions through self-administered online questionnaires. On a voluntary basis, students participate to the project and complete a baseline questionnaire online. Inclusion criteria for the i-Share cohort are the following: i) being officially registered at a university or higher education institute; ii) being at least 18 years old; and iii) being able to read and

understand French. All participants provided informed consent for participation. Students could opt for not answering the questionnaire on suicide ideation/behaviours, which was considered as missing data; therefore, these students were not included. The population of this specific study included all participants who fully completed the baseline questionnaire between April 2013 and March 2017.

2.3.2 Suicide ideation/behaviours and use of mental health care

The baseline questionnaire investigated the presence of suicidal ideations over the previous year as well as lifetime suicide attempts. The question to assess suicidal ideations was *“In the past 12 months, have you ever thought about committing suicide (having suicidal ideation)?”*. The question on lifetime suicide attempts was *“During your life, have you ever made a suicide attempt?”*. A variable *“suicide ideation/behaviours”* was defined as the presence of at least one of the two factors.

Mental healthcare use was also assessed at inclusion and corresponded to either at least one consultation with a mental health professional (psychiatrist, psychologist or psychotherapist) over the previous year, or to the use of at least one prescribed anxiolytic or hypnotic medication within the previous three months. In the questionnaire, anxiolytic drugs were defined as medications *“against anxiety or stress (during the day)”* and hypnotics as medications *“to sleep”*. Drug classes and names of products were unknown. Drugs were considered in the study only when they were reported as prescribed to the participant by a physician. Thus, drugs obtained over the counter were not considered.

Other collected variables

Covariates were collected to identify factors associated with the use of mental healthcare in students with suicide ideation/behaviours. They concerned students' characteristics: i) sociodemographic characteristics - age, sex, year of study (categorized in four groups: 1st, 2nd, 3rd or >3rd year of university), scholarship, siblings, accommodation (with his/her parent(s), university residence, apartment), living alone, being an orphan, divorced parents, paid employment; ii) dissatisfaction with living conditions - regarding recreational opportunities, relationships with parents, social life and financial resources; iii) use of non-mental health care over the previous year - at least one consultation with a general practitioner (GP), avoiding an

appointment with the GP or not buying prescribed medication although it was necessary/recommended; iv) lifetime health status - disability, at least one physician-diagnosed somatic disease including migraine, chronic inflammatory bowel disease, multiple sclerosis, type 1 diabetes, asthma or juvenile arthritis, at least one physician-diagnosed psychiatric disease including depression, attention deficit/hyperactivity disorder, obsessive compulsive disorder, anxiety disorders or anorexia, and exposure to a traumatic life event causing intense fear; v) family history - parental history of depression, anxiety disorders or alcohol use disorder; vi) health behaviours: body mass index or BMI ($\leq 18\text{kg/m}^2$, 18-30, $\geq 30\text{kg/m}^2$), regular physical exercise (at least 30 minutes of walking every day, daily biking, or doing sport at least twice a month, according to the WHO recommendations for physical activity (38)), practicing a team sport; vii) sleep disturbances - global sleep quality (poor/not poor), difficulty in falling asleep/maintaining sleep (more/less than once a week), feeling extremely sleepy during the day (more/less than three to five times per week), usual lack of sleep with at least one hour less than necessary (more than a few times a week/once a week or less); and viii) substance use - smoking status, alcohol use (more than four times a week/three times a week or less), cannabis use (more/less than once in the previous year), at least one lifetime use of another substance including ecstasy, MDMA, amphetamines, nitrous oxide, inhalant, cocaine, magic mushrooms (or other hallucinogenic plants), crack, free-base, heroin, LSD, or ketamine, or at least one use of doping products during competitions or exam periods.

2.3.3 Statistical methods

Characteristics of students were first described and compared according to the presence or not of suicide ideation/behaviours using univariate tests, the Pearson Chi2 test for qualitative variables and the Student test for quantitative variables. Then, among students with suicide ideation or behaviours, two multinomial logistic regression models were performed, both with stepwise backward, to identify factors independently associated with, on the one hand, at least one consultation with a mental health professional or, on the other hand, with the use of prescribed anxiolytic/hypnotic drugs. All previously cited covariates were included in both models. Covariates were defined *a priori* according to their clinical relevance and availability

in the database. Analyses were performed by using SAS (version 9.4; SAS Institute Inc, Cary, NC, USA) statistical software.

2.4 Results

2.4.1 Description of the i-Share population

Over the inclusion period, 12,112 students completed the i-Share baseline questionnaire, and only 524 of them did not answer the questions on suicide ideation/behaviours. Thus, the final study population included 11,588 students. Most of them were women (74.8%) and freshmen (39.8%). Mean age was 20.4 years old (SD 2.6). Suicide ideation/behaviours were identified in 2,916 (25.2%) students: 22.3% had suicidal ideations in the previous 12 months and 6.2% a lifetime suicide attempt. The prescription of anxiolytics/hypnotics was more prevalent among students with suicide ideation or behaviours (19.0% vs 7.4%, $p < 0.0001$), as well as mental health consultation (26.8% vs 8.6%, $p < 0.0001$).

2.4.2 Comparison of students with suicide ideation/behaviours who used or not anxiolytics/hypnotics drugs

Among students with suicide ideation/behaviours, 554 (19%) used anxiolytic and/or hypnotic on prescription. In comparison to those who did not, they were slightly older and more often women (Table 1). Other sociodemographic characteristics were similar in both groups, excepted for the divorce of their parents that was more frequent among students using drugs. These students had poorer psychiatric and non-psychiatric health status and more frequent sleep disturbances than students with suicide ideation/behaviours who did not use anxiolytics/hypnotics. They also had more dissatisfaction with their living conditions. They had less often a normal BMI although they declared to practice more physical activity, but less team sport. Substance use did not differ according to the use of anxiolytic and/or hypnotic, excepted for doping products during exams that were more often used among students with medication. They had also more frequent GP and mental health visits, despite a higher level of care renunciation.

2.4.3 Comparison of students with suicide ideation/behaviours who had or not mental health visits

Among students with suicide ideation/behaviours, 770 (26.8%) consulted a psychiatrist, a psychologist or a psychotherapist in the previous year. Some sociodemographic factors appeared to be associated with this care: being a woman, an orphan or having divorced parents (Table 2). Conversely, other factors were associated with foregoing this type of care: having siblings or being dissatisfied with recreational opportunities. Health status showed similar results to the previous comparison according to drug use, except for the practice of a team sport that was associated with absence of consultations. Many students with suicide ideation/behaviours consulted at least once their GP, especially when they also consulted a mental health specialist. Those who did not consult a mental health professional had a higher number of GP visits (4.5 vs. 3.6 over the preceding year). Foregoing consultations with a GP remained high and similar in both groups.

2.4.4 Factors associated with the use of care

Models performed to assess factors associated with the use of care (mental health visits and use of anxiolytics/hypnotics) were consistent (AUCs ROC were respectively 71% and 80%). Only six variables remained independently associated with consultation of mental health professional in the final model (Table 3); only dissatisfaction with recreational opportunities was associated with the absence of consultations. The use of anxiolytics/hypnotics was positively associated with nine independent variables, most of them being linked to health status, use of medical visits and sleep (Table 4). Diagnosed psychiatric conditions were strongly associated with both types of mental healthcare.

2.5 Discussion

The frequency of suicide ideation and behaviours found in students was higher than in prior studies and alarming regarding the prognosis of these symptoms in the short- and long-terms (39). This is to be considered in the light of the most striking finding of this study: nearly three quarters of students with suicidal ideation and/or behaviours did not use any mental healthcare in the previous year.

The high rate of students with suicidal ideation/behaviours who did not consult any mental health specialist was consistent with previous large surveys that were conducted in university students or non-attending university young adults in the United States (40,41) and in students in China (42). Those who did not consult any specialist were less likely to benefit from GP visits thus increasing their lack of care and reducing the probability of appropriate help. The lack of care is common among students and young adults, particularly in students with suicide ideation/behaviours (24). Yet, the large association between psychiatric disorders and the use of mental healthcare (either consultation or medication) highlighted the need for mental health care in students with suicide ideation/behaviours, which are strongly associated with psychiatric disorders (43). Surprisingly, proxies of income level (scholarship, accommodation, employment) had no impact on the use of mental health visits. Thus, barriers to this type of care did not seem to be merely financial, although visits with psychologist or psychotherapist are not reimbursed in France.

Foregoing mental healthcare could explain a part of the unmet need of care but, paradoxically, students who were prescribed anxiolytics or hypnotics reported more than the others having given up buying prescribed medication. This finding may be biased as, by definition, foregoing care can exist only if there is a prescription. Students also gave up more often GP visits whereas they consulted them more often. In the same way, students who waived buying drugs on prescription consulted more often a mental health professional. These diverging results are not necessarily inconsistent. Hence, students who reported renunciation of necessary health care might be students with the best insight and acutely aware of both their psychiatric needs and unmet needs. Stigma might also play an important role against insight and care seeking but it was not shown a such important factor (14).

The use of mental health consultation was associated with the presence of a diagnosed psychiatric disorder or a disability, being an orphan, a parental history of psychiatric disorder and dissatisfaction with social life. These factors correspond to adverse events that might have enhanced the awareness of the student or of his/her relatives. They are known risk factors for psychological distress, psychiatric disorders and suicide behaviours. Students with suicide ideation/behaviours who did not report mental health consultations were more often dissatisfied with their recreational opportunities. Dissatisfaction regarding their recreational

opportunities might decrease the probability to consult, for instance because of lack of time or of money. At the opposite, mental health management might increase the ability to take time for recreation and to relax and then decrease the probability of dissatisfaction to recreation. A surprising finding was the absence of association between sex and the use of mental health care in students, contrary to previous studies (9,44).

Regarding the prescription of anxiolytics and/or hypnotics drugs, the use of medication against anxiety is fifty percent more frequent than the use of medication to sleep, and is strongly associated with mental health consultation(s). It is noteworthy that students who did not met mental health professionals used similarly to other students, medications borrowed from a relative or from another source. Mental health consultations increased only the probability to use a personal treatment, either on prescription or obtained over the counter. The use of prescribed anxiolytics/hypnotics was more frequent in students with suicide ideation/behaviours who presented medical conditions, either psychiatric or non-psychiatric, or an objective symptom such as poor sleep. They were more likely to have medical visits and, therefore, to receive a drug prescription.

Strengths of this study include the large number of participants with a high proportion of students displaying suicide ideation/behaviours plus the availability of a wide range of life conditions and health informations. The associations with mental health care were found with significant ORas meaning at least 30% increase or decrease and corresponding to clinically relevant information. Moreover, this study brought new knowledge and a first approach of factors associated with access to mental healthcare among students with suicide ideation/behaviours. However, findings are to be interpreted in the light of some methodological limitations. As the study was cross-sectional, it cannot assess causality except for some variables that occurred obviously more than one year prior to inclusion (and the assessment of health care use). There might be a time gap between a lifetime suicide attempt and the presence of mental health visits in the previous year and of anxiolytics/hypnotics use in the preceding three months. However, a lifetime suicide attempt is a marker of psychiatric vulnerability and is associated with a persistent risk of suicide behaviours over years (45,46). The self-reported assessment exposed to several biases such as participation bias, information bias (social desirability, memorization) and confounding bias. However, the associations

would be impacted by these biases only if they were differential. Moreover, the whole survey was anonymized in order to minimize social desirability bias and confounding bias was taken into account through multivariate statistical models.

2.6 Conclusion

Worryingly, whereas students reported a particularly high level of suicidal ideation/behaviours, nearly three quarter of them did not use mental healthcare, including either anxiolytics/hypnotics or mental health visits. Medical conditions, psychiatric and non-psychiatric ones, and social isolation seemed strongly associated with both types of mental healthcare. Only one variable, 'dissatisfaction with recreational opportunities', was associated with not being treated. This finding might help targeting interventions on students who are very busy and proposing intervention that circumvent lack of time as a barrier to treatment, such as interventions using mobile phone technology.

Ethics approval

The i-Share project from which this study was derived was approved by the Commission Nationale de l'Informatique et des Libertés (CNIL) [DR-2013-019].

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2.8 Tables

Table 1. Description of students with suicidal ideation/behaviours according to their use of mental healthcare.

| | N ^a | Without anxiolytics/hypnotics prescription (n=2,362) | With anxiolytics/hypnotics prescription (n=554) | Khi-2 / t-Test p | N ^a | Without mental health consultation (n=2,101) | With mental health consultation (n=770) | Khi-2 / t-test p |
|------------------------------|----------------|---|--|---------------------|----------------|---|--|---------------------|
| | | n (%) | n (%) | | | n (%) | n (%) | |
| Age [mean (SD)] | 2,916 | 20.35 (2.6) | 20.64 (2.8) | 0.02 | 2,871 | 20.3 (2.5) | 20.61 (3.1) | 0.03 |
| Sex (woman) | 2,916 | 1,788 (75.7) | 466 (84.1) | <0.0001 | 2,871 | 1,597 (76.0) | 621 (80.7) | 0.009 |
| Year of study | 2,916 | | | | 2,871 | | | |
| 1 | | 1,028 (43.5) | 261 (47.1) | 0.5 | | 905 (43.1) | 358 (46.5) | 0.1 |
| 2 | | 456 (19.3) | 100 (18.1) | | | 406 (19.3) | 138 (17.9) | 0.4 |
| 3 | | 320 (15.6) | 74 (13.4) | | | 289 (13.8) | 103 (13.4) | 0.8 |
| >3 | | 558 (23.6) | 119 (21.5) | | | 501 (23.9) | 171 (22.2) | 0.4 |
| Scholarship | 2,834 | 1,535 (66.9) | 363 (67.2) | 0.9 | 2,791 | 1,373 (67.3) | 499 (66.5) | 0.7 |
| Siblings | 2,886 | 2,121 (90.8) | 490 (89.1) | 0.2 | 2,842 | 1,900 (91.4) | 675 (88.3) | 0.01 |
| Accommodation | 2,916 | | | 0.6 | 2,871 | | | 0.85 |
| With his/her parent(s) | | 701 (29.7) | 167 (30.1) | | | 632 (30.1) | 221 (28.7) | |
| University residence | | 353 (14.9) | 75 (13.5) | | | 304 (14.5) | 117 (15.2) | |
| Apartment | | 1,218 (51.6) | 285 (51.4) | | | 1,083 (51.6) | 399 (51.8) | |
| Orphan (at least one parent) | 2,916 | 142 (6.0) | 37 (6.7) | 0.6 | 2,871 | 112 (5.3) | 61 (7.9) | 0.01 |
| Divorced parents | 2,810 | 864 (38.0) | 231 (43.2) | 0.03 | 2,770 | 761 (37.6) | 321 (43.2) | 0.008 |
| Paid employment | 2,916 | 813 (34.4) | 197 (35.6) | 0.6 | 2,871 | 719 (34.2) | 276 (35.8) | 0.4 |

Table 1. Description of students with suicidal ideation/behaviours according to their use of mental healthcare (continued).

| | | Without | With | | | Without mental health | With mental health | |
|---|----------------|---|---|----------------|----------------|------------------------|----------------------|----------------|
| | N ^a | anxiolytics/hypnotics prescription (n=2,362) | anxiolytics/hypnotics prescription (n=554) | Khi-2 / t-Test | N ^a | consultation (n=2,101) | consultation (n=770) | Khi-2 / t-test |
| | | n (%) | n (%) | p | | n (%) | n (%) | p |
| Dissatisfaction with living conditions | 2,916 | | | | | | | |
| Relationship with parents | | 421 (17.8) | 146 (26.4) | <0.0001 | 2,871 | 385 (18.3) | 172 (22.3) | 0.02 |
| Financial resources | | 665 (28.2) | 172 (31.1) | 0.2 | 2,871 | 608 (28.9) | 216 (28.1) | 0.6 |
| Recreational opportunities | | 744 (31.5) | 210 (37.9) | 0.004 | 2,871 | 705 (33.6) | 229 (29.7) | 0.05 |
| Social life | | 596 (25.2) | 191 (34.5) | <0.0001 | 2,871 | 543 (25.8) | 229 (29.7) | 0.04 |
| Health status | | | | | | | | |
| Somatic illness ^b | 2,916 | 949 (40.2) | 308 (55.6) | <0.0001 | 2,871 | 869 (41.4) | 363 (47.1) | 0.006 |
| Psychiatric illness ^c | 2,916 | | | | 2,871 | | | |
| Diagnostic | | 832 (35.2) | 418 (75.5) | <0.0001 | | 700 (33.3) | 530 (68.8) | <0.0001 |
| Supported | | 575 (24.3) | 361 (65.2) | <0.0001 | | 450 (21.4) | 470 (61.0) | <0.0001 |
| Hospitalization | | 166 (7.0) | 136 (24.6) | <0.0001 | | 125 (6.0) | 173 (22.5) | <0.0001 |
| Parental history of depression/anxiety/alcohol use disorder | 2,496 | 1,251 (62.2) | 363 (74.9) | <0.0001 | 2,461 | 1,088 (60.9) | 506 (75.0) | <0.0001 |
| Disability | 2,916 | 90 (3.8) | 38 (6.9) | 0.002 | 2,871 | 73 (3.5) | 52 (6.8) | <0.0001 |
| Traumatic event that caused intense fear | 2,886 | 1,030 (44.1) | 285 (51.8) | 0.001 | 2,845 | 915 (44.0) | 378 (50.0) | 0.008 |
| Health behaviour | | | | | | | | |
| Physical regular activity | 2,909 | 2,167 (92.0) | 50 (90.4) | 0.2 | 2,864 | 1,887 (90.1) | 684 (89.0) | 0.4 |
| Practicing a team sport | 2,916 | 260 (11.0) | 42 (7.6) | 0.02 | 2,871 | 237 (11.3) | 59 (7.7) | 0.005 |

Table 1. Description of students with suicidal ideation/behaviours according to their use of mental healthcare (continued).

| | Without | | With | | Without mental health | | With mental health | |
|---|----------------|---|---|----------------|-----------------------|------------------------|----------------------|----------------|
| | N ^a | anxiolytics/hypnotics prescription (n=2,362) | anxiolytics/hypnotics prescription (n=554) | Khi-2 / t-Test | N ^a | consultation (n=2,101) | consultation (n=770) | Khi-2 / t-test |
| | | n (%) | n (%) | p | | n (%) | n (%) | p |
| BMI | 2,739 | | | 0.002 | 2,698 | | | 0.08 |
| ≤ 18 kg/m ² | | 203 (9.2) | 74 (14.2) | | | 187 (9.5) | 86 (11.8) | |
| 18 - 30 kg/m ² | | 1,922 (86.7) | 422 (80.8) | | | 1,703 (86.6) | 607 (83.2) | |
| ≥ 30 kg/m ² | | 92 (4.2) | 26 (5.0) | | | 78 (4.0) | 37 (5.1) | |
| Sleep disturbances | | | | | | | | |
| Poor quality of sleep | 2,916 | 687 (29.1) | 262 (47.3) | <0.0001 | 2,871 | 638 (30.4) | 292 (37.9) | 0.0001 |
| Difficulty falling asleep/maintaining sleep | 2,916 | 1,299 (55.0) | 404 (72.9) | <0.0001 | 2,871 | 1,189 (56.6) | 485 (63.0) | 0.002 |
| Daytime sleepiness | 2,916 | 1,316 (55.7) | 396 (71.5) | <0.0001 | 2,871 | 1,195 (56.9) | 489 (63.5) | 0.001 |
| Usual lack of sleep | 2,916 | 1,387 (58.7) | 377 (68.1) | <0.0001 | 2,871 | 1,249 (59.5) | 484 (62.9) | 0.1 |
| Substance use | | | | | | | | |
| Doping products | 2,916 | 599 (25.4) | 177 (31.6) | 0.002 | 2,871 | 555 (26.4) | 215 (27.9) | 0.4 |
| Tobacco | 2,916 | 888 (37.6) | 226 (40.8) | 0.2 | 2,871 | 793 (37.7) | 304 (39.5) | 0.4 |
| Alcohol | 2,916 | 124 (5.3) | 26 (4.7) | 0.6 | 2,871 | 106 (5.1) | 42 (5.5) | 0.7 |
| Cannabis | 2,313 | 802 (42.5) | 167 (39.3) | 0.2 | 2,275 | 514 (30.7) | 195 (32.5) | 0.5 |
| Another drugs ^d | 2,912 | 875 (37.1) | 210 (37.9) | 0.7 | 2,867 | 765 (36.5) | 300 (40.0) | 0.2 |

Table 2. Use of mental healthcare over the previous year in students with suicidal ideation/behaviours

| | N ^a | Without anxiolytics/hypnotics prescription (n=2,362) | With anxiolytics/hypnotics prescription (n=554) | Khi-2 / t- Test | N ^a | Without mental health consultation (n=2,101) | With mental health consultation (n=770) | Khi-2 / t- test |
|--|----------------|---|--|--------------------|----------------|---|--|--------------------|
| | | n (%) | n (%) | p | | n (%) | n (%) | p |
| Consultation with a general practitioner | 2,916 | 2,013 (85.2) | 527 (95.1) | <0.0001 | 2,871 | 1,798 (85.6) | 704 (91.4) | <0.0001 |
| Number of consultations (mean, SD) | | 3.11 (3.3) | 5.59 (4.9) | <0.0001 | | 4.50 (4.2) | 3.26 (3.6) | <0.0001 |
| Consultation with a psychiatrist/psychologist/psychotherapist | 2,871 | 473 (20.3) | 297 (54.4) | <0.0001 | 2,871 | 0 | 2,871 (100) | |
| Number of consultations (mean, SD) | | 2.00 (6.5) | 9.08 (14.7) | <0.0001 | | 0 | 12.48 (14) | |
| Renunciation of necessary health care | | | | | | | | |
| Of GP consultation | 2,916 | 1,143 (48.4) | 302 (54.5) | 0.01 | 2,871 | 1,051 (50.0) | 370 (48.0) | 0.4 |
| Of prescribed medications | 2,916 | 682 (28.9) | 244 (44.0) | <0.0001 | 2,871 | 617 (29.4) | 294 (38.2) | <0.0001 |
| Anxiolytics use | 2,916 | 371 (15.7) | 463 (83.6) | <0.0001 | 2,871 | 448 (21.3) | 369 (48.0) | <0.0001 |
| Frequency of use | | | | <0.0001 | | | | <0.0001 |
| Daily | | 88 (3.7) | 218 (39.4) | | | 141 (6.7) | 160 (20.8) | |
| Several times a week | | 84 (3.6) | 74 (13.4) | | | 85 (4.1) | 71 (9.2) | |
| Several times a month | | 89 (3.8) | 75 (13.5) | | | 98 (4.7) | 59 (7.7) | |
| Less than once a month | | 110 (4.7) | 96 (17.3) | | | 124 (5.9) | 79 (10.3) | |
| Source of anxiolytics | | | | | | | | |
| Medical prescription | | NA | 441 (79.6) | | | 138 (8.7) | 254 (33.0) | <0.0001 |
| Over the counter | | 308 (13.0) | 77 (13.9) | 0.6 | | 250 (11.9) | 122 (15.8) | 0.005 |
| Borrowed from relatives | | 53 (2.2) | 21 (3.8) | 0.04 | | 50 (2.4) | 21 (2.7) | 0.6 |
| Another source | | 32 (1.4) | 2 (0.4) | 0.05 | | 25 (1.2) | 8 (1.0) | 0.7 |

Table 2. Use of mental healthcare over the previous year in students with suicidal ideation/behaviours (continued)

| | N ^a | Without anxiolytics/hypnotics prescription (n=2,362) | With anxiolytics/hypnotics prescription (n=554) | Khi-2 / t- Test p | N ^a | Without mental health consultation (n=2,101) | With mental health consultation (n=770) | Khi-2 / t- test p |
|-------------------------|----------------|---|--|-------------------------|----------------|---|--|-------------------------|
| Hypnotics use | | 250 (10.6) | 332 (59.9) | <0.0001 | | 330 (15.7) | 237 (30.8) | <0.0001 |
| Frequency of use | | | | <0.0001 | | | | <0.0001 |
| Daily | | 43 (1.8) | 122 (22.0) | | | 82 (3.9) | 80 (10.4) | |
| Several times a week | | 67 (2.8) | 58 (23.8) | | | 65 (3.1) | 58 (7.5) | |
| Several times a month | | 67 (2.8) | 68 (12.3) | | | 80 (3.8) | 49 (6.4) | |
| Less than once a month | | 73 (3.1) | 84 (15.2) | | | 103 (4.9) | 50 (6.5) | |
| Source of hypnotics | | | | | | | | |
| Medical prescription | | NA | 292 (52.7) | | | 133 (6.3) | 153 (20.0) | <0.0001 |
| Over the counter | | 196 (8.3) | 75 (13.5) | 0.0001 | | 177 (8.4) | 86 (11.2) | 0.02 |
| Borrowed from relatives | | 54 (2.3) | 35 (6.3) | <0.0001 | | 62 (3.0) | 23 (3.0) | 0.9 |
| Another source | | 17 (0.7) | 3 (0.5) | 0.6 | | 14 (0.7) | 5 (0.7) | 0.9 |

Table 2. Use of mental healthcare over the previous year in students with suicidal ideation/behaviours (continued)

| | | | | | | | | |
|--|-------|------------|------------|---------|-------|------------|------------|---------|
| Anxiolytics and/or hypnotics use | 2,916 | 481 (20.4) | 554 (100) | <0.0001 | 2,871 | 590 (28.1) | 422 (54.8) | <0.0001 |
| Frequency of use | | | | <0.0001 | | | | <0.0001 |
| Daily | | 111 (4.7) | 252 (45.5) | | | 175 (8.3) | 182 (23.6) | |
| Several times a week | | 114 (4.8) | 93 (16.8) | | | 116 (5.5) | 88 (11.4) | |
| Several times a month | | 120 (5.1) | 97 (17.5) | | | 137 (6.5) | 70 (9.1) | |
| Less than once a month | | 136 (5.8) | 112 (20.2) | | | 162 (7.7) | 82 (10.7) | |
| Source of anxiolytics/hypnotics | | | | | | | | |
| Medical prescription | | NA | 554 (100) | | | 249 (11.9) | 297 (38.6) | <0.0001 |
| Over the counter | | 394 (16.7) | 125 (22.6) | 0.001 | | 342 (16.3) | 162 (21.0) | 0.003 |
| Borrowed from relatives | | 91 (3.9) | 45 (8.1) | <0.0001 | | 92 (4.4) | 38 (4.9) | 0.5 |
| Another source | | 40 (1.7) | 4 (0.7) | 0.09 | | 31 (1.5) | 12 (1.6) | 0.9 |
| Frequency of use of prescribed anxiolytics/hypnotics | | | | | | | | <0.0001 |
| At least once a day | | NA | 252 (45.5) | | | 93 (4.4) | 157 (20.4) | |
| Several times a week | | NA | 93 (16.8) | | | 44 (2.1) | 49 (6.4) | |
| Several times a month | | NA | 97 (17.5) | | | 50 (2.4) | 43 (5.6) | |
| Less than once a month | | NA | 112 (20.2) | | | 62 (3.0) | 48 (6.2) | |

^a number of students with available information

Table 3. Factors independently associated with mental health visits (final model of multivariate logistic regression)

| (N=2,255) | ORa | IC95% | |
|---|-----|-------|-----|
| Psychiatric disorders ^a | 4.2 | 3.4 | 5.1 |
| Disability | 1.9 | 1.2 | 2.9 |
| Orphan | 1.6 | 1.04 | 2.4 |
| Parental history of depression/anxiety/alcohol use disorder | 1.4 | 1.1 | 1.7 |
| Dissatisfaction / social life | 1.3 | 1.1 | 1.7 |
| Dissatisfaction / recreational opportunities | 0.7 | 0.5 | 0.8 |

^a including diagnosed depression, attention deficit/hyperactivity disorder, obsessive compulsive disorder, anxiety disorders or anorexia

Table 4. Factors associated with the use of prescribed anxiolytic/hypnotic medication (final model of multivariate logistic regression)

| (N=2,232) | ORa | IC95% | |
|---|-----|-------|-----|
| Psychiatric disorders ^a | 3.5 | 2.7 | 4.6 |
| Consultation of a mental health practitioner | 3.1 | 2.4 | 3.9 |
| Consultation of a general practitioner | 2.3 | 1.3 | 3.9 |
| Dissatisfaction / relationship with parents | 1.6 | 1.2 | 2.1 |
| Renunciation of buying prescribed medications | 1.4 | 1.1 | 1.8 |
| Difficulty falling asleep | 1.4 | 1 | 1.8 |
| Daytime sleepiness | 1.4 | 1.1 | 1.8 |
| Somatic illness ^b | 1.3 | 1.1 | 1.7 |
| Poor quality of sleep | 1.3 | 1 | 1.7 |

^a including depression, attention deficit/hyperactivity disorder, obsessive compulsive disorder, anxiety disorders or anorexia; ^b including migraine, chronic inflammatory bowels disease, multiple sclerosis, type 1 diabetes, asthma, juvenile arthritis

3 Article 2. Association between anxiolytic/hypnotic drugs and suicidal ideation or behaviours in a population-based cohort of students

Running head: Anxiolytics/hypnotics and suicide behaviours in students

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3.1 Abstract

Objective: As recent studies suggested that benzodiazepines might induce suicidal ideation and/or behaviour, the objective was to investigate the association between the use of anxiolytic/hypnotic drugs and suicidal ideation/behaviours in the students of the i-Share cohort taking into account many confounders, in particular anxiety and sleep disorders.

Method: 12,112 participants who completed the baseline questionnaire in the i-Share cohort between April 2013 and March 2017 were included. Suicidal ideation/behaviours and the use of prescribed anxiolytic/hypnotic drugs over the previous 3 months were measured at baseline and follow-up time points. 2,919 students completed the follow-up questionnaire. Suicidal ideation/behaviours were defined at inclusion as suicidal ideation over the previous year or a lifetime suicide attempt. Psychiatric disorders were assessed through validated scales, such as GAD-7 for anxiety and PHQ-9 for depression. Multivariate logistic regression models were performed.

Results: At inclusion, 25.2% of students had suicidal ideation/behaviours and 10.3% used anxiolytics/hypnotics. Suicidal ideation/behaviours at baseline were associated with a more frequent use of anxiolytics/hypnotics in the previous 3 months (OR 1.42; 95%CI 1.19-1.70), after adjustment for covariates including anxiety, depression, sleep, impulsivity, and substance use. The use of anxiolytics/hypnotics at baseline was not associated with the occurrence, persistence or remission of suicidal ideation/behaviours one year later. On the converse, suicidal ideation/behaviours at baseline were associated with a new anxiolytic/hypnotic treatment one year later (OR 1.79; 95%CI 1.18-2.7).

Conclusions: Anxiolytic/hypnotic drug use was associated with suicidal ideation/behaviours in students independently of many risk factors of suicide and most psychiatric disorders that require such treatment raising drug safety concerns.

Declaration of interests: Authors have no conflict of interest to disclose.

Key words: Suicide; students; anxiolytic; hypnotic

3.2 Introduction

Young adults are vulnerable to suicidal ideations/behaviours with a short- and long-term impact. According to the World Health Organization [1], suicide is the second cause of death among people 15-34 years old worldwide. Suicide attempts are also particularly frequent between 15 and 24 years. Thus, a very recent meta-analysis estimated that 3.2% of students presented with a lifetime suicide attempt, and 10.6% with suicidal ideation in the previous 12 months [2]. It therefore appears relevant to identify risk and protective factors for suicidal ideation and behaviour in this population. Furthermore, many medication drugs are associated with warnings from regulatory agencies related to suicide risk. Paradoxically, many of them are psychotropic drugs used to treat psychiatric disorders or symptoms known to increase the occurrence of suicidal ideation or behaviour [3, 4]. Some recent studies have shown that benzodiazepines or Z-drugs have frequently been used prior to suicide death [5, 6], thus suggesting that these drugs might induce suicidal ideation and/or behaviour [5, 7–10]. Although these studies found a positive and significant association, they did not demonstrate any causality owing to methodological issues, particularly confounding by indication, as these drugs might be prescribed because of a suicidal risk [11, 12]. Indeed, no study has shown a prospective association while controlling for depression, insomnia and anxiety symptoms [11]. Furthermore, previous studies did not take into account substance use or temperament traits such as impulsivity, aggression and coping strategies, which also moderate suicide risk [13]. Finally, mechanisms that might be involved in a potential causal association remain unclear; they might be direct (disinhibition, impairment of judgement) or indirect (via depression, rebound insomnia or anxiety) [11]. Some authors suggested that measuring this association might lead to a nocebo effect if patients knew about this potential and rare adverse event [14]. As the use of these drugs is not infrequent in young adults [15, 16], and as suicidal ideation/behaviours are a major public health concern in this population, it is of utmost importance to clarify the role of anxiolytic and hypnotic drugs with respect to suicide risk, taking into account numerous confounding factors.

The study was conducted to assess the association between the use of prescribed anxiolytic or hypnotic drugs and suicidal ideations or behaviours in a cohort of university students that allowed to take into account numerous risk factors for suicide behaviours, in particular

psychiatric symptoms or disorders that might require these treatments such as depression, anxiety, impulsivity, aggression, substance use and insomnia in order to minimize confounding by indication. Secondary objectives were to assess in an exploratory way the association (i) between the use of anxiolytic or hypnotic drugs at baseline and the occurrence, persistence or remission of suicidal ideations or behaviours at follow-up, and (ii) between the history of suicidal ideations or behaviours at baseline and the occurrence of anxiolytic or hypnotic drugs use at follow-up.

3.3 Method

3.3.1 Study design and study population

Repeated cross-sectional assessments were conducted in a national prospective population-based cohort study with public funding, the ongoing Internet-based Students Health Research Enterprise (i-Share) project [17]. This ongoing project assesses students' health in French-speaking universities and higher education institutions by self-administered online questionnaires. On a voluntary basis, students register in the study and complete a mandatory baseline questionnaire online. An optional mental health survey is sent to these participants three months after completing the baseline questionnaire in order to specifically investigate psychiatric disorders, personality and temperament traits using psychometric scales. A follow-up questionnaire is then sent to participants one year after inclusion to assess health care use and suicidal ideations/behaviours among other items. Inclusion criteria for the i-Share cohort are the following: i) officially registered at a University or higher education institute, ii) at least 18 years old, iii) able to read and understand French. All participants provided informed consent for participation. The study population included all participants who fully completed the baseline questionnaire between April 2013 and March 2017. Within the cohort, three populations were studied independently: all included students (*i.e.* students having completed the baseline questionnaire), those also having completed the optional mental health questionnaire and those having completed both baseline and follow-up questionnaires.

3.3.2 Exposure to anxiolytic/hypnotic drugs and suicidal ideation/behaviours

The main variables were exposure to anxiolytic/hypnotic drugs and suicidal ideation/behaviours; points of measurement over the study period are shown in Figure 1.

They were explored through the baseline and follow-up questionnaires. Drug use was assessed within the previous three months at each contact. Anxiolytic drugs were defined as medications “against anxiety or stress (during the day)” and hypnotics as medications “to sleep”. Drug classes and names of products were unknown. Drugs were considered only when they were reported as prescribed to the participant by a physician. Thus, drugs obtained over the counter were not taken into account. The variable of interest was the use of at least one prescribed anxiolytic or hypnotic drug over the 3-month period.

The baseline questionnaire investigated the presence of suicidal ideations over the previous 12 months (“Over the 12 preceding months, have you ever thought about killing yourself (suicidal ideation)?”) as well as lifetime suicide attempts (“Over your lifetime, did you ever attempt suicide?”). Time windows were different since suicidal ideations are more common and considered as less severe than suicide attempts. Suicide attempts are the main risk factor for suicide, even several years after. The variable “suicidal ideation/behaviours” was defined as the presence of at least one of the two factors. In order to select students at high and current suicide risk, a variable “suicidal ideation and behaviours” was considered for sensitivity analyses and corresponded to students who had both suicide ideations over the previous 12 months and at least a lifetime suicide attempt. The follow-up questionnaire investigated the presence of suicidal ideation and attempts over the previous 12 months. Incident suicidal ideation/behaviours were identified in the sub-population having completed the follow-up questionnaire and defined as the presence of suicidal ideation and/or behaviours at follow-up (ideations and/or attempt over the previous year) and none at baseline. In the same sub-population, persistent suicidal ideation/behaviours corresponded to the presence of suicidal ideation/behaviours at baseline and the presence of suicidal ideation and/or suicide attempt over the previous year at follow-up.

3.3.3 Other collected variables

Covariates were collected through the baseline and the mental health questionnaires. We selected *a priori* risk factors for suicidal ideation/behaviours that could also be associated with use of anxiolytics or hypnotics were selected to limit confounding. They related to participants’ characteristics: i) sociodemographic characteristics: age, sex, year of study

(categorized in four groups: 1st, 2nd, 3rd or higher year of university), scholarship, siblings, accommodation (with his/her parent(s), university residence, apartment), living alone, being an orphan, divorced parents, paid employment; ii) dissatisfaction with living conditions: regarding recreational opportunities, relationships with parents, social life and financial resources; iii) use of health care over the previous year: at least one consultation with a general practitioner (GP), at least one consultation with a psychiatrist, psychologist or psychotherapist, avoiding an appointment with the GP or not buying prescribed medication although it was necessary/recommended; iv) health status: disability, at least one physician-diagnosed somatic disease including migraine, chronic inflammatory bowel disease, multiple sclerosis, type 1 diabetes, asthma or juvenile arthritis, at least one physician-diagnosed psychiatric disease including depression, attention deficit/hyperactivity disorder, obsessive compulsive disorder, anxiety disorders or anorexia, and exposure to a traumatic life event causing intense fear; v) family history: parental history of depression, anxiety disorders or alcoholism; vi) health behaviours: unhealthy BMI ($\leq 18\text{kg/m}^2$, 18-30, $\geq 30\text{kg/m}^2$), regular physical exercise (at least 30 minutes of walking every day, daily biking, or doing sport at least twice a month, according to the WHO recommendations for physical activity [18]), practicing a team sport; vii) sleep disturbances: global sleep quality (poor/not poor), difficulty in falling asleep/maintaining sleep (more/less than once a week), feeling extremely sleepy during the day (more/less than 3 to 5 times per week), usual lack of sleep with at least one hour less than necessary (more than a few times a week/once a week or less); and viii) substance use: smoking status, alcohol use (more than 4 times a week/3 times a week or less), cannabis use (more/less than once in the previous year), at least one lifetime use of another substance including ecstasy, MDMA, amphetamines, nitrous oxide, inhalant, cocaine, magic mushrooms (or other hallucinogenic plants), crack, free-base, heroin, LSD, or ketamine, or at least one use of doping products during competitions or exam periods. The use of other psychotropic medication drugs was not available in the database.

The mental health questionnaire consisted of nine psychometric scales: a perceived stress assessment adapted to the student population [19]; a scale assessing coping strategies divided in three parts: search for social support, emotional coping, festive and addictive coping [20]; the Spielberger trait anxiety inventory (STAI-YA) [21]; the adolescent version of the Barratt

Impulsivity Scale (BIS-11-A) [22]; the Life History of Aggression (LHA) [23]; the Patient Health Questionnaire (PHQ-9) [24, 25] to assess a current major depressive episode of at least moderate intensity (score ≥ 10); the Mood Disorder Questionnaire (MDQ) to screen bipolar disorders (at least 7 lifetime manic or hypomanic symptoms, several co-occurring symptoms, and moderate or serious associated functional impairment) [26]; the Rosenberg self-esteem scale [27]; and a short version of Cloninger's Temperament and Character Inventory (TCI) with 56 items that allow the creation of 6 scores, including temperament traits (novelty-seeking, harm avoidance, dependence on reward and persistence), and character traits (determination and cooperation) [28]. Concerning MDQ and PHQ-9 scores, validated thresholds made it possible to obtain binary variables (presence/absence). For the other scales, quantitative scores were transformed into binary variables (high/low) using the median obtained in the study population as threshold, since thresholds validated in different populations might not be appropriate in students.

3.3.4 Statistical method

All statistical analyses were performed by using SAS (version 9.4; SAS Institute Inc, Cary, NC, USA) statistical software. First, we carried out descriptive analyses of the study population. Participants who had also completed the mental health questionnaire were compared with those who did not using univariate tests, the Pearson χ^2 test for qualitative variables and the Student test for quantitative variables. In the same way, completers of the follow-up questionnaire were compared with non-completers. Then, several multinomial logistic regression models were performed to assess the association between prescribed anxiolytic/hypnotic drugs and suicidal ideation/behaviours. The first model assessed the association between suicidal ideation/behaviours and the use of prescribed anxiolytic/hypnotic drugs at baseline in the whole population, adjusting for all covariates explored through the baseline questionnaire. Three sensitivity analyses were performed for this model: i) for the first one, "suicidal ideation/behaviours" was replaced by "suicidal ideation and behaviours"; ii) the second one was conducted in participants having completed the optional mental health questionnaires to add these covariates to the model; and iii) for the third one, all covariates were included in a propensity score in order to assess over-adjustment risk. The three other models were performed for participants who had completed

the follow-up questionnaire. The first one assessed the association between incident suicidal ideation/behaviours (absence at baseline and presence at follow-up) and the use of prescribed anxiolytics/hypnotics at baseline, adjusting for all covariates explored through the baseline questionnaire, in students without suicidal ideation/behaviours at baseline. The second one assessed the association between persistent suicidal ideation/behaviours (presence at baseline and at follow-up) and the use of prescribed anxiolytics/hypnotics at baseline, adjusting for all covariates explored through the baseline questionnaire, in students with suicidal ideation/behaviours at baseline. The last one investigated the association between the use of prescribed anxiolytic/hypnotic drugs at follow-up and suicidal ideation/behaviours at baseline, adjusting for all covariates explored through the baseline questionnaire. For these models, sensitivity analyses were performed including covariates in propensity scores.

All covariates were defined *a priori* according to their clinical relevance. Variables with more than 20% missing data were eliminated from all models. All interactions were tested and verification of the suitability of the model was carried out with the Hosmer-Lemeshow test, as well as an evaluation of its discriminating power by computing the area under the ROC curve.

3.4 Results

A total of 12,112 students completed the i-Share baseline questionnaire. Among them, 3,585 students fully completed the mental health questionnaire and were then identified as the “mental health subgroup”. Finally, 2,919 students completed the follow-up questionnaire and were considered as the “follow-up subgroup”. Flow chart is shown in Figure 2.

3.4.1 Description of study population

Among the 12,112 students enrolled in the i-Share cohort, 97.5% students answered questions on suicide ideations and attempts (n=11,588). Suicidal ideation/behaviours were identified in 2,916 students (25.2%), nearly 22% reporting suicidal ideations in the past 12 months, and 6.2% a lifetime suicide attempt (Table 1). These students are described in Table 2 according to the presence or not of suicidal ideation/behaviours. In both groups, most participants were women and more than one-third were in the first year. Both groups were

similar in terms of age (mean 20.4 years; SD 2.6). Students with or without suicidal ideation/behaviours at baseline had different characteristics with regard to nearly all sociodemographics, health care use and health status, apart from age, having siblings and a paid job. In particular, the use of prescribed anxiolytic and/or hypnotic was nearly three times higher among students with a suicide risk (Table 2).

3.4.2 Description of the sub-population who completed the mental health questionnaires

The sub-sample who completed the mental health questionnaire was compared to the students who did not (data not shown). Completers were slightly different from the others. The main differences concerned scholarship (62 % among whole group vs 67 % among mental health subgroup, $p < 0.0001$) and smoking (34 % vs 26 %, $p < 0.0001$). Almost all mental health scores were very different in students with or without suicidal ideation/behaviours at baseline, with poorer mental health in students with suicidal ideation/behaviours than in those without (Table 3). However, seeking social support as a coping strategy and planning difficulties were similar across the groups, as well as some temperament traits such as novelty-seeking, harm avoidance and reward dependence.

3.4.3 Cross-sectional association between use of anxiolytic/hypnotic drugs and suicidal ideation/behaviours

Suicidal ideation/behaviours at baseline were associated with the use of prescribed anxiolytic/hypnotic medications at baseline, after adjustment for all covariates (Table 4). This association persisted in sensitivity analyses after adjustment for mental health characteristics in the subgroup of students who completed the mental health questionnaire and when using a propensity score method (aOR 1.36; IC95% 1.12-1.65). As an interaction was found between having divorced parents and the use of anxiolytics/hypnotics, the model assessing the association between suicidal ideation and behaviours and the use of these drugs was stratified on having or not divorced parents. Suicidal ideation and behaviours were also associated with the use of anxiolytic/hypnotic drugs, but only among students who had divorced parents.

3.4.4 Longitudinal associations between use of anxiolytic/hypnotic drugs and suicidal ideation/behaviours

At the follow-up, incident suicidal ideation/behaviours were 7.1% and almost 47% of students with suicidal ideation/behaviours at baseline had still suicidal ideation/behaviours. The subsample who completed the follow-up questionnaire was compared to students who did not (data not shown). Completers were slightly different from the others. The main differences concerned scholarship (60 % among non-completers vs 78 % among follow-up subgroup, $p < 0.0001$), smoking (35 % vs 26 %, $p < 0.0001$).

No association was found between the prescription of anxiolytic/hypnotic medication at baseline and incident suicidal ideation/behaviours one year later in students without suicide risk at inclusion or the persistence at follow-up of suicidal ideation/behaviours (Table 4). This was found also when using a propensity score method (aOR 1.09; IC95% 0.73-1.63). On the contrary, there was a significant association between suicidal ideation/behaviours at baseline and a new use of prescribed anxiolytic/hypnotic drugs at follow-up (aOR 1.9; 95%CI 1.1-3.3; $p = 0.02$). This model showed a 90% increase in new use of prescribed anxiolytic/hypnotic at follow-up after a self-reported suicidal ideation/behaviours at baseline. This was found also when using a propensity score method (aOR 1.80; IC95% 1.20-2.71).

3.5 Discussion

3.5.1 Main findings

This study conducted in a large student population was the first one to show an association between the use of prescribed anxiolytic/hypnotic medication and suicidal ideations/behaviours, even when taking into account psychiatric disorders and symptoms including depression, anxiety, perceived stress, sleeping disorders, impulsivity and substance use. Another striking finding is the high number of students found to have suicidal ideation/behaviours.

Indeed, more than one out of five students reported suicidal ideations over the year preceding the baseline questionnaire. This rate was higher than in a recent meta-analysis assessing suicidal ideations among college students (10.6%, 95%CI [9.10;12.25]) [2], but similar to the frequency described among US undergraduate students (24%) [29] or in medical students over

the same duration (24.2%, 95%CI [13.0;40.5]) [30]. The frequency of lifetime suicide attempts was also nearly two-fold higher in the present study than in the findings of the meta-analysis (1.2%, 95%CI [0.83;1.59]) [2] but lower in a study with same design (9%) [29]. As inclusion in the i-Share cohort is voluntary and its objective is to assess students' health conditions, students concerned about health or having health problems, especially mental health disorders, might be over-represented in the sample. However, we cannot exclude an especially high frequency of suicide behaviours in French students compared with other countries, as already reported for deliberate self-harm [31].

Suicidal ideation/behaviours at baseline were associated with the use of a prescribed anxiolytic or hypnotic drug at inclusion while taking into account all other variables including psychiatric disorders, anxiety, sleep disturbances, impulsivity and substance use, allowing minimizing confounding and particularly confounding by indication. The association persisted with suicidal ideation and behaviours but only when students' parents were divorced. Thus, when students presented a history of suicide attempt and recent suicidal ideations, they were more likely to use prescribed medications if their parents were divorced. Parents' divorce might represent a risk factor for seeking mental health care in students at risk of suicide. They might be offered care more easily or they might be more likely to seek professional support to offset poor parental support.

Suicidal ideation/behaviours at baseline were also associated with a new prescription of anxiolytic/hypnotic drugs at follow-up. Students with mental distress, and particularly suicidal ideation and/or attempt, were likely to seek mental health care and, among other treatments, to receive a prescription of anxiolytic/hypnotic drugs. This request for health care might be deferred and be formulated later than suicidal ideations, because students might lack information about the availability of health care services [32], or they might be worried about or suspicious of psychiatry and psychotropic drugs. They might wait until their distress is overwhelming before consulting. Moreover, only a few students with suicidal ideation/behaviours sought health care. Conversely, we did not find any association between the use of prescribed anxiolytic/hypnotic medication within the three months preceding the baseline questionnaire and the occurrence of suicidal ideation/behaviours or the persistence

or remission at follow-up of suicidal ideation/behaviours already identified at the time of inclusion [33]. This suggests that the use of these drugs did not attenuate them.

3.5.2 Study limitations and strengths

These longitudinal analyses were performed in an exploratory way and several methodological limitations might have hampered the identification of such an association. First, the study lacked statistical power as only 10 students had no suicidal ideation/behaviours at baseline, used these drugs at baseline and presented with suicidal ideation/behaviours at follow-up. Second, a depletion of susceptible bias might be suspected, since considering only the occurrence of incident suicidal ideation/behaviours excluded all students who presented with suicidal ideations in the year prior to inclusion and who used anxiolytic/hypnotic drugs in the preceding three months; in other words, all students likely to present suicidal ideations and/or behaviours when exposed to these drugs.

Some other limitations should be taken into account. First, the abovementioned selection bias might have modified the association only if it was differential. Second, students less likely to participate might have been students with suicidal ideation/behaviours [34] and non-users of prescribed medications, which would tend to reduce the strength of the association that we identified. Third, there may have been a competitive risk because students who died by suicide were not identified. In fact, there was a 97% risk that a maximum of two students might have died from suicide during the follow-up. Fourth, the vagueness of the questions concerning drug use may have created an information bias. However, to minimize this risk, we considered only prescribed medications in order to exclude over-the-counter drugs such as herbal medicine and to select high-potency drugs. Finally, a residual confounding by indication bias might have led us to conclude erroneously about an association between drug use and suicide risk, since these drugs and suicide risk might be independently associated with the condition treated. Although most indications of these drugs were adjusted for, as well as other confounding factors, further studies are warranted to investigate clinical events occurring when such treatments are initiated and during the following weeks [35].

The main strengths of the study are its large number of participants and the number of explored variables. Many risk factors were assessed with validated tools including psychiatric

disorders and symptoms, substance abuse and chronic somatic diseases. Many suicide protective factors such as social and family support and coping strategies were also investigated. This study was in fact conducted in a large cohort who completed many relevant items. The use of a composite criterion (ideation and/or behaviours) makes it possible to consider those who have made an attempt without a suicidal ideation, which can be associated with the use of medication in youth [36].

In conclusion, this large community-based cohort study found a cross-sectional association between the use of anxiolytics/hypnotics and suicidal ideation/behaviours, with an approximately 50% increase in the risk of suicidal ideations/behaviours. This association was independent from many risk factors of suicide and from most psychiatric disorders that require such treatments. Even if residual confounding cannot be excluded, these findings should alert prescribers of this potential risk and at least of the lack of demonstrated effectiveness of these drugs on suicidal ideation/behaviours and encourage them to balance expected benefit and risks when prescribing anxiolytics or hypnotics, even to young patients.

Ethics approval

The i-Share project from which this study was derived was approved by the Commission Nationale de l'Informatique et des Libertés (CNIL) [DR-2013-019].

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3.7 Tables

Table 1. Suicidal ideation/behaviours at baseline and at follow-up

| | Number of students with available information | Students with suicidal ideation/behaviours | |
|--|---|--|------|
| | | N | (%) |
| At baseline (n=12,112) | | | |
| Suicidal ideations in previous 12 months | 11,664 | 2,603 | 22.3 |
| Lifetime suicide attempt | 11,791 | 732 | 6.2 |
| Total suicidal ideation/behaviours ^a | 11,588 | 2,916 | 25.2 |
| Suicidal ideation and behaviours ^b | 11,867 | 419 | 3.5 |
| At time of follow-up in whole population (n=2,919) | | | |
| Suicidal ideations in previous 12 months | 2,799 | 483 | 17.3 |
| Suicide attempt in previous 12 months | 2,812 | 18 | 0.6 |
| Suicide attempt and/or ideations in previous 12 months | 2,799 | 491 | 17.5 |
| At time of follow-up in students with suicide risk at baseline (n=718) | | | |
| Persistent suicidal ideation/behaviours ^c | 685 | 321 | 46.9 |
| At time of follow-up in students with no suicide risk at baseline (n=2,106) | | | |
| Suicidal ideations in previous 12 months | 2,029 | 139 | 6.8 |
| Suicide attempt in previous 12 months | 2,037 | 6 | 0.3 |
| Incident suicidal ideation/behaviours ^d | 2,029 | 145 | 7.1 |

^a suicidal ideations in preceding year and/or lifetime suicide attempt; ^b suicidal ideations in preceding year and lifetime suicide attempt; ^c Suicidal ideation/behaviours at baseline and suicidal ideations and/or attempt in preceding year at follow-up; ^d No suicidal ideation/behaviours at baseline and suicidal ideations and/or attempt in preceding year at follow-up.

Table 2. Whole study population according to presence of suicidal ideation/behaviours at baseline (n=11,588)

| | n ^a | Students without suicidal ideation/behaviours (n=8,672) n (%) | Students with suicidal ideation/behaviours (n=2,916) n (%) | Khi-2 T-test p |
|---|----------------|--|---|----------------------|
| Prescribed anxiolytics/hypnotics in preceding 3 months | 11,588 | 643 (7.4) | 554 (19.0) | <0.0001 |
| Sociodemographic characteristics | | | | |
| Age [mean (SD)] | 11,588 | 20.4 (2.6) | 20.4 (2.7) | 0.67 |
| Sex (woman) | 11,588 | 6,412 (73.9) | 2,254 (77.3) | 0.0003 |
| Year of study | 11,588 | | | <0.0001 |
| 1 | | 3,321 (38.3) | 1,289 (44.2) | |
| 2 | | 1,691 (19.5) | 556 (19.1) | |
| 3 | | 1,324 (15.3) | 394 (13.5) | |
| 4 or more | | 2,336 (26.9) | 677 (23.2) | |
| Scholarship | 11,316 | 5,361 (63.2) | 1,898 (67.0) | 0.0003 |
| Siblings | 11,459 | 7,838 (91.4) | 2,611 (90.5) | 0.1 |
| Accommodation | 11,588 | | | <0.0001 |
| With his/her parent(s) | | 2,770 (31.9) | 868 (29.8) | |
| University residence | | 943 (10.9) | 428 (14.7) | |
| Apartment | | 4,655 (53.7) | 1,503 (51.5) | |
| Orphan (at least one parent) | 11,588 | 413 (4.8) | 179 (6.1) | 0.004 |
| Divorced parents | 11,235 | 2,502 (29.7) | 1,095 (39.0) | <0.0001 |

Table 2. Whole study population according to presence of suicidal ideation/behaviours at baseline (n=11,588) (continued)

| | | | | |
|---|--------|--------------|--------------|---------|
| Paid employment | 11,588 | 2,951 (34.0) | 1,010 (34.6) | 0.6 |
| Dissatisfaction with living conditions | | | | |
| Relationship with parents | 11,588 | 634 (7.3) | 567 (19.4) | <0.0001 |
| Financial resources | 11,588 | 1,614 (18.6) | 837 (28.7) | <0.0001 |
| Recreational opportunities | 11,588 | 1,885 (21.7) | 954 (32.7) | <0.0001 |
| Social life | 11,588 | 1,215 (14.0) | 787 (27.0) | <0.0001 |
| Use of health care over previous year | | | | |
| Consultation with general practitioner | 11,587 | 7,436 (85.7) | 250 (87.1) | 0.07 |
| Consultation with mental health professional | 11,467 | 741 (8.6) | 770 (26.8) | <0.0001 |
| Avoiding general practitioner consultation | 11,588 | 2,804 (32.3) | 1,445 (49.6) | <0.0001 |
| Not buying prescribed medications | 11,588 | 1,726 (19.9) | 926 (31.8) | <0.0001 |
| Health status | | | | |
| Somatic illness ^b | 11,588 | 3,030 (34.9) | 1,257 (43.1) | <0.0001 |
| Psychiatric illness ^c | 11,588 | 1,417 (16.3) | 1,250 (42.9) | <0.0001 |
| Parental history of depression/anxiety/alcohol use disorder | 10,243 | 3,321 (42.9) | 1,614 (64.7) | <0.0001 |
| Disability | 11,588 | 230 (2.7) | 128 (4.4) | <0.0001 |
| Traumatic event that caused intense fear | 11,481 | 2,646 (30.8) | 1,315 (45.6) | <0.0001 |

Table 2. Whole study population according to presence of suicidal ideation/behaviours at baseline (n=11,588) (continued)

| Health behaviour | | | | |
|---|--------|--------------|--------------|---------|
| Physical regular activity | 11,566 | 8,135 (94.0) | 2,667 (91.7) | <0.0001 |
| Practising a team sport | 11,588 | 1,235 (14.2) | 302 (10.4) | <0.0001 |
| BMI | 10,962 | | | <0.0001 |
| ≤ 18 kg/m ² | | 706 (8.6) | 277 (10.1) | |
| 18 - 30 kg/m ² | | 7,323 (89.7) | 2,344 (85.6) | |
| ≥ 30 kg/m ² | | 194 (2.36) | 118 (4.3) | |
| Sleep disturbances | | | | |
| Poor quality of sleep | 11,588 | 1,556 (17.9) | 949 (32.5) | <0.0001 |
| Difficulty falling asleep/maintaining sleep | 11,585 | 3,522 (40.6) | 1,703 (58.4) | <0.0001 |
| Daytime sleepiness | 11,586 | 3,586 (41.4) | 1,712 (58.7) | <0.0001 |
| Usual lack of sleep | 11,588 | 4,227 (48.7) | 1,764 (60.5) | <0.0001 |
| Substance use | | | | |
| Doping products | 11,588 | 1,874 (21.6) | 776 (26.6) | <0.0001 |
| Tobacco | 11,588 | 2,468 (28.5) | 1,114 (38.2) | <0.0001 |
| Alcohol | 11,588 | 351 (4.1) | 150 (5.1) | 0.01 |
| Cannabis | 9,187 | 2,143 (31.2) | 969 (41.9) | <0.0001 |
| Other drugs ^d | 11,570 | 3,016 (34.8) | 1,085 (37.3) | 0.02 |

^a: Number of students with available information; ^b including migraine, chronic inflammatory bowels disease, multiple sclerosis, type 1 diabetes, asthma, juvenile arthritis; ^c including depression, attention deficit/hyperactivity disorder, obsessive compulsive disorder, anxiety disorders or anorexia; ^d at least one lifetime use of another substance among ecstasy, MDMA, amphetamines, nitrous oxide, inhalant, cocaine, magic mushrooms (or other hallucinogenic plants), crack, free-base, heroin, LSD, or ketamine

Table 3. Mental health characteristics according to presence of suicidal ideation/behaviours at baseline (n=3,585)

| N=3,585 | Students without | Students with | Khi-2 p |
|---------------------------------------|---------------------------------|-------------------------------|------------|
| | suicide risk (n=2,566) n (%) | suicide risk (n=898) n (%) | |
| High level of perceived stress | 1,250 (46.5) | 577 (64.3) | <0.0001 |
| Coping strategies | | | |
| Emotional | 1,315 (48.9) | 591 (65.8) | <0.0001 |
| Festive-addictive | 1,320 (49.1) | 475 (52.9) | 0.05 |
| Seeking social support | 1,707 (63.5) | 571 (63.6) | 0.9 |
| High level of impulsivity | | | |
| Motor | 1,546 (57.5) | 574 (63.9) | 0.0008 |
| Cognitive | 1,350 (50.2) | 605 (67.4) | <0.0001 |
| Planning difficulties | 1,541 (57.4) | 490 (54.6) | 0.2 |
| Low self-esteem | 1,103 (41.1) | 537 (59.8) | <0.0001 |
| High level of anxiety | 1,283 (47.8) | 559 (62.3) | <0.0001 |
| Bipolar disorder | 102 (3.8) | 108 (11.7) | <0.0001 |
| Major depressive episode | 421 (15.7) | 372 (41.4) | <0.0001 |
| High level of aggression | 1,243 (46.3) | 558 (62.1) | <0.0001 |
| Temperament and character | | | |
| Novelty-seeking | 1,425 (53.0) | 492 (54.8) | 0.4 |
| Persistence | 1,318 (49.1) | 486 (54.1) | 0.009 |
| Harm avoidance | 1,369 (51) | 460 (51.2) | 0.9 |
| Determination | 1,214 (45.2) | 653 (72.7) | <0.0001 |
| Reward dependence | 1,718 (63.9) | 576 (64.1) | 0.9 |
| Cooperation | 1,343 (50.0) | 564 (62.8) | <0.0001 |

Table 4. Association between use of anxiolytic or hypnotic drugs at baseline and suicidal ideation/behaviours at baseline or at follow-up (multivariate models)

| | N ^a | Use of anxiolytic or hypnotic drugs at baseline | | | |
|--|----------------|---|-------|-----|--------|
| | | aOR ^b | 95%CI | | p |
| Suicidal ideation/behaviours at baseline | 7,218 | 1.46 | 1.2 | 1.8 | 0.0001 |
| Suicidal ideation and behaviours at baseline ^d | | | | | |
| Parents not divorced | 5,162 | 1.26 | 0.8 | 2.0 | 0.3 |
| Parents divorced | 2,201 | 2.48 | 1.5 | 4.1 | 0.0005 |
| Suicidal ideation/behaviours at baseline in students having completed mental health survey ^c | 2,277 | 1.57 | 1.1 | 2.3 | 0.01 |
| Incident suicidal ideation/behaviours at follow-up in students with no suicide risk at baseline | 1,353 | 1.25 | 0.6 | 2.9 | 0.6 |
| Persistent suicidal ideation/behaviours at follow-up in students with suicidal ideation/behaviours at baseline | 685 | 1.04 | 0.6 | 2.0 | 0.9 |

^a Number of students with available information; ^b Odds ratio adjusted on all covariates: sociodemographic characteristics, dissatisfaction with living conditions, use of health care over previous year, health status, health behaviours, sleep disturbances and substances use; ^c Odds ratio adjusted on all these covariates and on perceived stress, coping strategies, trait-anxiety, impulsivity, aggression, current major depressive episode, bipolar disorder, self-esteem, temperament and character traits; ^d a significant interaction led to stratification on having divorced parents or not.

3.8 Figures

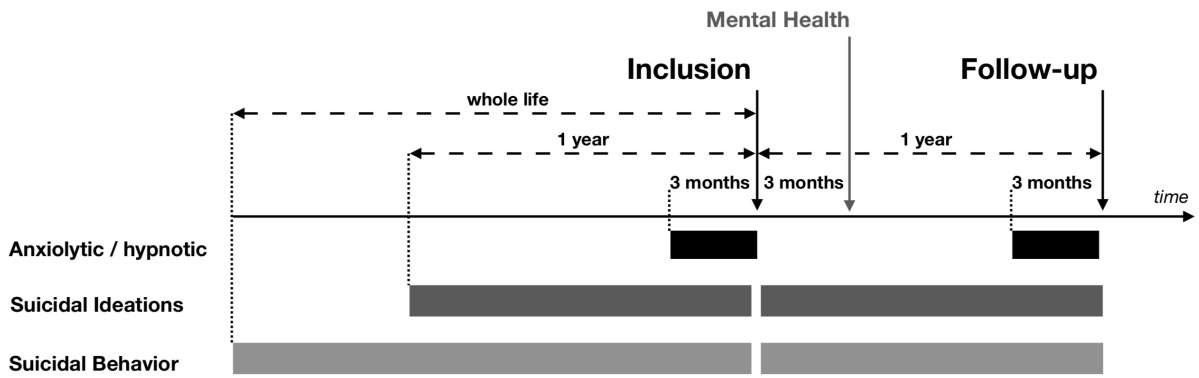


Figure 1 : Description of the main variable measures in the i-Share study

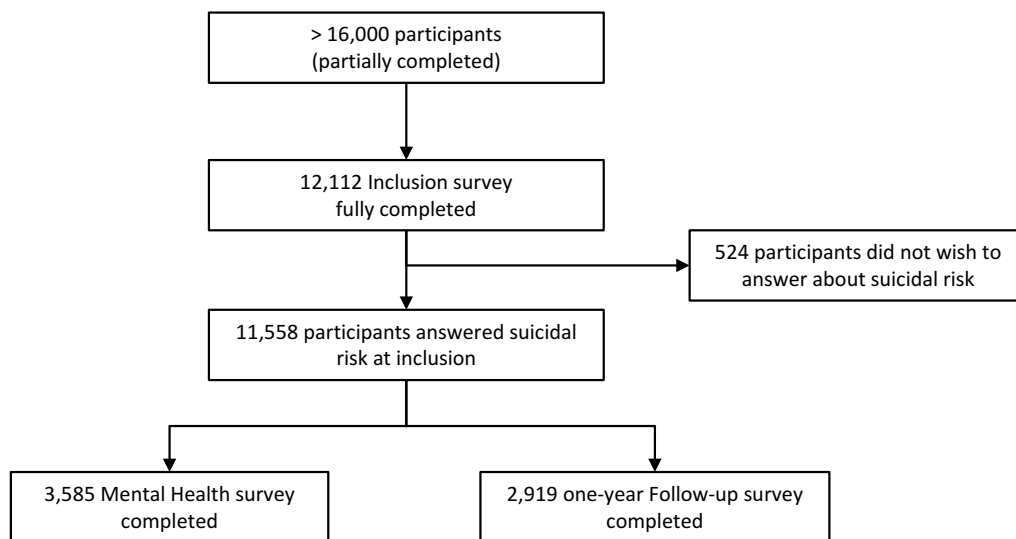


Figure 2 : Flow chart of the study population

4 Conclusion

La cohorte i-Share, de laquelle sont issus tous les résultats, montre un niveau d'idées suicidaires dans l'année et de tentative de suicide dans la vie plus important que dans d'autres cohortes de populations similaires (10). Ces prévalences sont inquiétantes au regard de leurs souffrances associées et de leur pronostic (4) et justifient que ces étudiants puissent bénéficier d'une évaluation et de soins en santé mentale appropriés.

Le premier article montre que seulement un quart des étudiants qui présentent des idées et/ou des conduites suicidaires bénéficient de ces soins mais aussi qu'il est difficile d'établir un profil type de celui ou celle qui n'accède pas au soin, malgré le besoin manifeste. Cette première étude étaye la nécessité d'études ultérieures, s'intéressant à ce thème avec une méthodologie différente. En effet, nous avons notamment mesuré que la recherche de soins par les étudiants de la cohorte n'apparaît pas déterminée par leurs caractéristiques socio-économiques, avec une place particulière de la souffrance sociale. Ainsi, la complexité des facteurs associés aux idées et aux tentatives de suicide (11) chez ces adultes jeunes laisse la voie libre à des investigations au plus proche de la phénoménologie de ces individus en souffrance, par exemple grâce à des évaluations sur smartphone.

La question du soin approprié est associée à la question du repérage du risque suicidaire, puisque l'isolement social l'augmente, en particulier chez les jeunes (12), et que la prise en charge psychiatrique le diminue (13). Cependant, le rôle de la prescription des médicaments de la classe des benzodiazépines et de leurs apparentés reste à préciser. La plupart des recommandations ne les citent pas pour la prévention du risque suicidaire (14–18), et ils sont même suspectés de l'aggraver (19), au moins chez certaines personnes. Le second article ne permet pas d'évaluer l'augmentation du risque suicidaire liée à l'utilisation de ces médicaments, par manque de puissance. Mais il permet néanmoins d'identifier une association entre leur usage et l'existence d'idées et/ou de conduites suicidaires, indépendante de nombreux facteurs de risque, notamment l'anxiété, les troubles du sommeil et la dépression. Cela fait craindre une balance bénéfice/risque défavorable pour l'utilisation de ces médicaments dans cette population de jeunes adultes à risque suicidaire élevé. Il est

d'ailleurs notable que leur utilisation n'est pas associée à une décroissance des idées suicidaires une année plus tard.

5 Références

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Serment d'Hippocrate

Au moment d'être admis à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité.

J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences. Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences.

Je donnerai mes soins à l'indigent et à quiconque me le demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admis dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçu à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.

Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité.

Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonoré et méprisé si j'y manque.

RÉSUMÉ

Contexte : Les jeunes adultes sont particulièrement à risque de suicide, conduites et idées suicidaires ; ils sont confrontés à des nombreux facteurs de risque et sont à l'âge auquel l'incidence des troubles psychiatriques est la plus élevée. Peu de données en France concerne le lien entre idées et conduites suicidaires et utilisation des soins de santé mentale chez les étudiants.

Objectifs : Un premier manuscrit a évalué l'utilisation des soins de santé mentale chez les étudiants ayant des idées et/ou des conduites suicidaires ; un second a étudié l'association entre prescription d'anxiolytiques/hypnotiques et idées et/ou conduites suicidaires.

Méthode : Ces études ont utilisé la base de données de la cohorte d'étudiants i-Share. L'utilisation des soins a été évaluée transversalement et l'association entre anxiolytiques/hypnotiques et idées/conduites suicidaires transversalement et longitudinalement. Les idées suicidaires ont été évaluées au cours de la dernière année et les tentatives de suicide au cours de la vie. De nombreuses caractéristiques sociodémographiques ou cliniques ont été prises en compte. Des modèles de régression logistique multivariés ont été réalisés pour identifier les facteurs associés aux soins et l'association entre médicaments et idées/conduites suicidaires.

Résultats : 12 112 étudiants ont été inclus. Un quart des étudiants présentaient des idées/conduites suicidaire. L'utilisation de soins de santé mentale concernait moins du quart de ces étudiants. Peu de facteurs associés à l'absence de soin en santé mentale ont été retrouvés. Prescription d'anxiolytiques/hypnotiques et idées/conduites suicidaires étaient associées indépendamment de la plupart des facteurs de confusion dont les principales indications de ces traitements.

Conclusion : Ces données mettent en garde à la fois sur le défaut d'utilisation des soins et sur un impact incertain des anxiolytiques/hypnotiques sur les idées/conduites suicidaires, chez les jeunes adultes.

MOTS-CLÉS :

étudiants idées conduites suicidaires anxiolytiques hypnotiques soins consultations