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## THÈSE POUR LE DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

Prévalence du stress post-traumatique chez les étudiants à 1 mois de la levée de la quarantaine et facteurs associés – Etude COSAMe

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# **Avant-propos**

Cette thèse d'exercice a été réalisée au sein de la Fédération Régionale de Recherche en Santé Mentale et en psychiatrie (F2RSM) à partir des données de l'enquête COSAMe, un projet porté par le Centre National de Ressources et Résilience (CN2R) en partenariat avec le Fonds Innovation et Recherche de la Fédération Hospitalière Française (FHF) et le Ministère de l'Enseignement Supérieur de la Recherche et de l'Innovation, et promu par la F2RSM. Ce travail a été conduit sous la codirection des Docteurs Marielle WATHELET et Fabien D'HONDT.

#### Résumé

Prévalence du stress post-traumatique chez les étudiants à 1 mois de la levée de la quarantaine et facteurs associés – Etude COSAMe

Introduction. Le syndrome de stress post-traumatique (SSPT) est une conséquence connue de l'exposition à des catastrophes. Cependant, la survenue de SSPT en population générale, non directement touchée par la maladie à coronavirus 2019, fait débat. Cette étude avait pour objectif d'estimer la prévalence de SSPT chez les étudiants, fortement touchés par la détresse aiguë sévère (DAS) en début de pandémie, d'analyser les trajectoires de réponse psychologique (TRP) au contexte pandémique et d'identifier les facteurs associés au SSPT.

**Méthodes**. COSAMe est une étude transversale répétée ayant interrogé les étudiants universitaires français via en un questionnaire ligne du 17 avril au 4 mai (T1) et du 15 juin au 15 juillet (T2) 2020. Seuls les étudiants ayant participé à T2 ont été analysés. La prévalence de SSPT a été évaluée à l'aide de la PCL-5 (PTSD Checklist for DSM-5). Des caractéristiques sociodémographiques, médicales, socioéconomiques, et des informations relatives au soutien social et au degré d'exposition au contexte pandémique ont été recueillies. Des modèles de régression logistique multivariés ont identifé les facteurs de risque de SSPT. Dans le sous-groupe ayant répondu à T1, les TRP (résilience, chronicité, rétablissement et apparition différée de symptômes) ont été évaluées, ainsi que les facteurs de risque de chronicité chez les étudiants atteints de DAS à T1.

Résultats. L'échantillon était composé de 22 883 étudiants de 21 ans en moyenne dont 72,7% de femmes. La prévalence du SSPT était de 19,5%. Le genre féminin ou non binaire, les antécédents psychiatriques, l'exposition à un autre événement traumatique, les indicateurs d'isolement et de précarité ainsi que le sentiment d'être mal informé et un niveau élevé d'exposition au contexte pandémique étaient associés au SSPT. Parmi les 6 947 étudiants ayant répondu à T1, la TRP la plus fréquente était la résilience (73,2%), suivie du rétablissement (10,3%), de la chronicité (9,9%) et de l'apparition différée (6,5%). En cas de DAS, les étudiants à risque de chronicité étaient ceux souffrant d'anxiété habituelle, de troubles du sommeil, d'antécédents psychiatriques, d'exposition à un autre événement traumatique, vivant seuls ou ayant des liens sociaux altérés, fortement exposés au contexte pandémique et mal informés.

**Conclusion**. La forte prévalence du SSPT chez les étudiants universitaires souligne la nécessité d'impliquer la psychiatrie dans les plans de gestion de crise sanitaire liée à une pandémie.

#### **Abstract**

Prevalence of post-traumatic stress among students 1 month after the lifting of the quarantine and associated factors – COSAMe study

**Introduction.** Post-traumatic stress disorder (PTSD) is a known consequence of exposure to disasters. However, the occurrence of PTSD in the general population, not directly affected by the 2019 coronavirus disease, is debated. The objective of this study was to estimate the prevalence of PTSD in students, strongly affected by severe acute distress (SAD) at the start of the pandemic, to analyze the psychological response trajectories (TRP) to the pandemic context and to identify the factors associated with PTSD.

**Methods.** COSAMe is a repeated cross-sectional study based on data collected from April 17 to May 4 (T1), and from June 15 to July 15 (T2), 2020, through an online questionnaire sent to all French university students. Only students who participated in T2 were analyzed. The prevalence of PTSD was assessed using the PCL-5 (PTSD Checklist for DSM-5). Covariates were sociodemographic characteristics, medical information, social support indicators, socio-economic factors and level of exposure to the pandemic context. Multivariate logistic regression models identified the risk factors for PTSD. In the subgroup of students responding to T1 and T2, the TRP (resilience, chronicity, recovery and delayed onset of symptoms) to the context of pandemic were assessed, as well as the risk factors for chronicity in students with SAD at T1.

Results. A total of 22,883 students completed the survey. They were 21 years old on average and were mostly women (72.7%). The prevalence of PTSD was 19.5% at T2. Among the 6,947 students who responded to T1, the most common TRP was resilience (73.2%), followed by recovery (10.3%), chronicity (9.9%) and delayed onset trajectory (6.5%). Female or non-binary gender, psychiatric history, exposure to another traumatic event, having lived quarantine alone, foreign student status, poor quality of social ties, low feeling of integration, precariousness as well as low quality of the received information, and high level of exposure to COVID-19 were all significantly associated with PTSD. After SAD, students least likely to recover were those with severe trait-anxiety, sleep disorders, psychiatric history, exposure to another traumatic event, living alone or with low quality of social ties during the quarantine, highly exposed, and considering that they have been misinformed.

**Conclusion.** The high prevalence of PTSD among university students highlights the need to involve psychiatry in health crisis management plans linked to a pandemic.

# Liste des abréviations

Cl95% 95% Confidence Interval

**COVID-19** Maladie à coronavirus 2019

**DSM** Diagnostic and Statistical Manual of Mental Disorders

IES-R Impact of Event Scale – Revised

ISI Index of Severity of Insomnia

OR Odds Ratio

PCL-5 PTSD Checklist for DSM-5

PTSD Post-Traumatic Stress Disorder

**SARS** Severe Acute Respiratory Syndrome

**SSPT** Syndrome de Stress Post-Traumatique

**STAI Y-2** State-Trait Anxiety Inventory, Trait subscale

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#### Contexte

Bien que les premières descriptions retrouvées de symptômes de stress post-traumatique datent de plus de 4000 ans (1), la notion de SSPT a été introduite pour la première fois en 1980, dans la 3<sup>e</sup> version du Diagnostic and Statistical Manual of Mental diseases (DSM-III) (2). Un événement traumatique pouvant induire un SSPT était alors conceptualisé comme un facteur de stress catastrophique inhabituel pour un être humain.

La définition et les critères diagnostiques du SSPT ont été modifiés de nombreuses fois depuis, lors des différentes révisions du DSM : le DSM-III-R en 1987, le DSM-IV en 1994, le DSM-IV-TR en 2004 et enfin le DSM-V en 2013, passant de 12 critères diagnostiques dans le DSM-III à 20 critères dans le DSM-V (1).

Dans le DSM-V, le SSPT se définit comme un état de santé mentale, apparaissant ou persistant plus d'un mois après l'exposition directe ou indirecte d'un individu à la mort, à une menace de mort, à des violences sexuelles ou à une blessure grave. Il comprend des symptômes d'intrusion, d'évitement, d'hyperréactivité et de cognitions négatives. L'ensemble de ces symptômes doit avoir un retentissement négatif sur le fonctionnement de l'individu, et ne doit pas pouvoir être expliqué par un autre trouble mental ni par des substances exogènes.

Alors que le DSM-IV considérait que seules les victimes directes pouvaient souffrir d'un SSPT, la nouvelle version admet qu'un individu puisse être traumatisé s'il présente une proximité émotionnelle avec une victime directe ou s'il est exposé de façon répétée à des récits sordides dans le cadre de ses activités professionnelles.

La définition du SSPT est de nouveau sujet au débat en raison de l'ampleur de la pandémie de maladie à coronavirus 2019 (COVID-19) entraînant des mesures exceptionnelles de mises en quarantaine à large échelle pour limiter sa propagation. Si la possibilité de la survenue d'un SSPT

chez les personnes atteintes de COVID-19 et chez les professionnels de première ligne ne fait pas débat puisque la définition de l'événement traumatique est respectée, la survenue de SSPT en population générale partage les professionnels de santé. Si le contexte pandémique n'est pas perçu comme traumatique par certains, ou alors comme contexte favorisant l'exposition à d'autres événements traumatisants comme la violence domestique en raison de la quarantaine (3), d'autres professionnels s'inquiètent d'un « tsunami » de SSPT en population générale (4) du fait de l'intensité du stress auquel la population est exposée, que ce soit en raison de l'infodémie (terme employé pour désigner la propagation sur internet d'informations trompeuses ou erronées pendant un événement à l'échelle mondiale (5)) ou en raison des mesures restrictives et de leurs conséquences économiques et sociales.

# Introduction

In order to slow down the spread of coronavirus disease 2019 (COVID-19), many countries were placed under mass quarantine (6). In France, the government decided to confine its entire population from March 17 to May 11, 2020: people were to remain confined in their homes; any movement deemed non-essential was prohibited. As of 2 April 2020, 3.9 billion people worldwide were affected by quarantine measures, i.e. more than half of the world's population. This global quarantine is distinguished by its unprecedented extent, even though quarantine measures have already been implemented around the world in the past. This situation has rapidly raised concerns regarding the mental health of concerned populations. Indeed, the review of the literature on quarantine measures during previous epidemics by Brooks *et al.* has shown that the population targeted by the imposed quarantine measures is likely to develop psychological and psychiatric disorders, including post-traumatic stress symptoms (7).

According to the classification of psychiatric conditions proposed by the Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> edition (DSM-5), post-traumatic stress disorder (PTSD) is a reaction that can develop following exposure to actual or threatened death, serious injury, or sexual violation (8). PTSD, regardless of its trigger, causes clinically significant distress and impairment in the individuals' social interactions, capacity to work, or other important areas of functioning. Patients present a combination of symptoms that can be classified into four distinct diagnostic clusters: re-experiencing, avoidance, negative cognitions and mood, and arousal (8). DSM-5 now considers that a person is likely to suffer from PTSD not only as a direct victim but also because of emotional proximity to a direct victim or because of repeated confrontation with traumatic sordid tales (8,9). While professionals are unanimous on the possible occurrence of PTSD linked to the direct consequences of the infection (e.g., hospitalization or relative deceased from COVID-19), the occurrence of the "wave" of PTSD in the general population, not directly

affected by the COVID-19, is still a matter of debate (3).

Recent studies have assessed the psychological responses to the context of the COVID-19 pandemic among confined university students, considering this population at considerable risk of developing mental health issues (7,10–12). These studies found high rates of moderate or severe distress symptoms during the initial stage of the COVID-19 pandemic: 53.8% in the Chinese study of Wang *et al.*, 28.1% in the French study of Wathelet *et al.* (12,13). Both studies, like those performed during previous quarantines (Brooks), used the Impact of Events Scale-Revised (IES-R), which allows to assess immediate distress symptoms related to a traumatic event but is not a diagnostic tool for PTSD, the diagnosis of PTSD requiring symptoms to last for at least a month (8). Notably, evidence suggests that many people showing acute stress reactions do not develop PTSD (14,15). The recent review by Galatzer-Levy *et al.* indicated that, among response trajectories to potentially traumatic events, resilience (i.e. stable psychological health after the event) concerns 65.7% of the individuals, followed by recovery (i.e., prolonged but ultimately waning distress; 20.8%), chronicity (i.e. prolonged distress; 10.6%) and delayed onset (i.e. symptoms elevation above the diagnostic threshold that emerge following a significant delay; 8.9%) (15).

If the pandemic context and the quarantine measures associated constitute a traumatic event for university students, one could consider that around 20% of them would present post-traumatic symptoms. Yet, first studies assessing PTSD prevalence among university students after the acute phase of the pandemic with diagnostic tools found very disparate rates: 2.7% according to Tang *et al.* (9) versus 30.8% according to Chi et al. (16) among samples of home-quarantined Chinese university students. Of note, these studies used the PCL-C (PTSD CheckList – Civilian Version) or an abbreviated version of the PCL-C which is based on the DSM-IV and which has already yielded widely varying prevalence estimates in similar samples (17).

Accordingly, we aimed to assess the prevalence of PTSD among French university students one

month after the quarantine using the PCL-5, recently revised to reflect DSM-5 changes to the PTSD criteria and exhibiting a good test-retest reliability among trauma-exposed college students (18). Data was collected during the second measurement time of the COSAMe study, a repeated cross-sectional university-based survey study conducted nationally since April 17, 2020. Beyond assessing PTSD rates, we also aimed to identify associated factors as well as the different response trajectories since the first measurement time.

# **Methods**

# Population and study design

In the context of the COSAMe study, the French Ministry of Higher Education, Research, and Innovation proposes to the 82 universities, at each measurement time, to send an email to their students (around 1,600,000 students targeted) offering them to participate in the survey by completing an online self-administered questionnaire. Due to the heterogeneity of sanitary measures from one country to another, only students residing in France during the quarantine are included. The survey is anonymous, and no compensation is offered.

The first measurement time (T1) took place during the quarantine, between April 17 and May 4, 2020. The second measurement time (T2) occurred one month after the quarantine was lifted, between June 15 and July 15, 2020. At T2, nearly 30,000 deaths were attributed to COVID-19 in France (19).

The present study included only the participants who responded to T2. Some of them had already responded to T1. To link the responses between T1 and T2, we used a pseudonymization method: each student was asked to answer personal but non-identifying questions, preserving the anonymity of the respondents.

This survey received the authorization of a French research ethics committee, the Comité de Protection des Personnes IIe de France VIII, before its initiation.

#### **Collected data**

We focused on the prevalence of PTSD at 1 month by asking participants to complete the PTSD Checklist for DSM-5 (PCL-5) (18). PCL-5 is a 20-item scale that explores PTSD symptom severity over the past month. The rating of the items ranges from 0 "not at all" to 4 "extremely" with a total

score between 0 and 80. A score greater than 32 is leading to the diagnosis of PTSD (18,20,21). The French version showed good internal consistency with a Cronbach's alpha between 0.79 and 0.94 (21).

Regarding factors associated with PTSD, we considered variables known to be linked to PTSD or variables likely to have worsened the quarantine experience to test their association with the outcome (7,9,22).

The following variables were available for all participants, either gathered at T1 or at T2 measurement time for new respondents:

- 1) sociodemographic characteristics: age, gender (male, female, other);
- 2) medical information: history of psychiatric follow-up, having experienced traumatic events non linked to the COVID-19 after the beginning of the pandemic, and insomnia assessed by the Index of Severity of Insomnia (ISI). ISI is composed of 7 items rated from 0 to 4 to obtain a score ranging from 0 to 28 interpreted as follows: 0 to 7 (absence of insomnia), 8 to 14 (mild insomnia), 15 to 21 (moderate insomnia), 22 to 28 (severe insomnia):
- 3) social support: being a foreign student, living alone during the quarantine, quality of social relationships during the quarantine (out of 10), feeling socially integrated before the quarantine (rated out of 10 on an 11-point Likert-type scale);
- 4) socio-economic factors: loss of income due to the quarantine, housing quality (rated out of 10);
- 5) quality of the information received (out of 10):
- 6) exposure to the pandemic context: based on a similar approach to the one used by Tang *et al.*, a COVID-19 exposure scale was constructed from DSM-V, including eight items coded as yes or no: living in a worst-hit area (i.e. in a department counting more than 50 deaths due to COVID-19 on March 29, 2020), symptoms consistent with COVID-19 since the beginning of the pandemic, having been in contact with an infected person, relative

deceased of the infection, subjective fear for relatives' health (out of 10), high exposure to media messages related to the pandemic (in minutes per day). The last 3 items were rated yes when the score was greater than the 3rd quartile. The total score was calculated by adding up the yes responses.

The following variables were only analyzed for students who participated at T1:

- 1) Presence of acute distress at T1, assessed by the 22-item Impact of Events Scale-Revised (IES-R) (23). Participants rate on a 5-point Likert scale the extent to which each of the 22 items applies to their experiences during the preceding 7 days, from 0 ("not at all") to 4 ("extremely"). The total score ranges from 0 to 88. Thresholds were established in the literature: the distress level is considered normal for scores between 0 and 23; mild, between 24 and 32; moderate, between 33 and 36; and severe, above 36 (13).
- 2) Presence of a severe trait-anxiety, assessed by the 20-item State-Trait Anxiety Inventory, Trait subscale (STALY-2) (24). Participants rate items from 1 to 4 to obtain a score ranging from 20 to 80. The intensity of anxiety increases with the score. Thresholds used in French literature are as follows: low below 46, moderate between 46 and 55, and high above 55 (25).
- 3) Seeking mental health care during the quarantine.

Finally, participants had to indicate which of the following events related to the pandemic context could be considered as traumatic, i.e. likely to endanger the life or the physical or the psychological integrity of a person who is exposed to it: news of a COVID-19 epidemic in China, news of a COVID-19 epidemic in France, closure of shops, bars and meeting places, closure of schools and universities, quarantine, having symptoms compatible with COVID-19, being infected with SARS-CoV2, being hospitalized for COVID-19, relative infected with SARS-CoV2, relative hospitalized for COVID-19, relative deceased from COVID-19.

#### Statistical analyses

Participants who fully completed the questionnaires were analyzed.

Qualitative variables were summarized using percentages, and quantitative variables were summarized using means and standard deviations.

To identify factors associated with PTSD, bivariate analyses were performed to compare characteristics of students with or without PTSD, using Student's t-tests to compare means and Chi-2 tests to compare proportions. Then, multivariable logistic regression analysis was performed, including all explanatory variables available for the whole sample. Associations between risk factors and outcomes were presented as odds ratios (OR) and 95% confidence intervals (95%CI).

Finally, based on the subgroup that responded to T1 and T2, we assessed the prevalence of the different response trajectories to a potentially traumatic event as defined in the article of Galatzer-Levy *et al.*, i.e. resilient, chronic, recovery, and delayed-onset trajectories (15). Thus, trajectories were defined as follows: 1) resilience for students who had neither severe distress at T1 nor PTSD at T2, 2) chronicity for students with both severe distress at T1 and PTSD at T2, 3) recovery for students with severe distress at T1 but who did not develop PTSD at T2 and 4) delayed-onset for students who did not report severe distress at T1 but presented PTSD at T2. In order to identity factors associated with the inability to recover, we conducted analyses on students presenting severe acute distress at T1 only. A multivariable logistic regression model was used, including the same variables as in the previous model as well as the variables available for this sub-group: sleep disorders, use of mental health care and anxiety-trait.

Data analysis was performed using R 3.6.1. The significance level was set at  $\alpha$  = 0.05, and all tests were 2-tailed.

#### Results

#### Sample characteristics

A total of 22,883 students completed the questionnaire at the second measurement time. Their characteristics are presented in *Table 1*.

The majority of respondents were women (72.7%). The average age was 21 (± 4) years old. Regarding medical information, 10.6% of the students reported a history of psychiatric follow-up, and 14.1% of them declared having been exposed to a traumatic event unrelated to the pandemic since the start of the pandemic. Concerning social ties, 6.0% of the participants were foreign students and 11.6% lived alone during the quarantine. The feeling of integration into society before the quarantine was high for 62.5% of the students, medium for 30%, and low for 7.4% of them, and the quality of the social bond during guarantine was considered high for 42.4% of the participants, medium for 38.9% and low for 18.7% of them. Regarding socio-economic factors, 18.3% of the students reported a loss of income linked to the consequences of the pandemic, and the quality of housing during confinement was considered high by 84% of the students, medium for 12.8%, and low for 3.2%. The quality of the information received during confinement was considered good for 36.6% of the respondents, average for 46.3%, and poor for 17.1%. Finally, regarding exposure to COVID-19 during confinement, more than a quarter (28.1%) of the students resided in an affected department, respondents declared having been in contact with infected people for 14.4% of them, knowing a person deceased from COVID-19 for 5.8%, and having had symptoms consistent with COVID-19 for 23.1%. A worry was considered important for those whose score (out of 10) was above the 3rd quartile. Thus, 21.1% of the students were very worried about their relatives' health (score higher than 8) and 24.7% for their health (score higher than 5). Those whose time watching the news about pandemic exceeded the 3rd quartile were considered to be highly exposed to media messages. Thus, they were 23.1% to spend more than 45 minutes per day consulting the information.

#### Post-traumatic stress disorder and associated factors

Among the participants, 4456 students (19.5% CI95% [19.0-20.0]) had a PCL-5 score above 32.

In bivariate analysis, all characteristics were significantly associated with PTSD as assessed by the PCL-5 score. The age was very slightly different from one group to another (20.8  $\pm$  4.1 in the group without PTSD vs 21.2 ± 4.0 in the group with PTSD, p<.001). Rates of PTSD according to gender were 15.7% among men, 20.5% among women, and 36.5% among non-binary persons (p<.001). Concerning medical information, having a history of psychiatric follow-up and having been exposed to a traumatic event not linked with the pandemic since the start of the pandemic were associated with PTSD (21.3% vs 8.0%, p<.001, and 33.1% vs 9.5%, p<.001, respectively). Regarding social support, being "isolated" was always associated with PTSD, students concerned by PTSD being more likely to declare: living alone (16.6% vs 10.4%, p<.001), being a foreign student (10.5% vs 4.9%, p<.001), feeling less integrated before the guarantine (66.4%, 27.9% and 5.7% for respectively high, medium and low integration in the group without PTSD vs 46.6%, 39.0% and 14.4% for high, medium and low integration in the group with PTSD, p<.001), and declaring poor quality of social ties during the quarantine (46.0%, 38.7% and 15.3% for respectively high, medium and low quality of social ties in the group without PTSD vs 27.6%, 39.7% and 32.7% for high, medium and low quality in the group with PTSD, p<.001). Precariousness was also associated with PTSD, students with PTSD being more likely to report loss of income (24.6% vs 16.8%, p<.001) or poor housing quality (7.2% of low housing quality in the group with PTSD, 21.5% of medium quality and 71.3% of good quality vs 2.2%, 10.6% and 87.1% of low, medium and good quality in the group without PTSD, p<.001). The lack of information was also more important in the group with PTSD (22.9%, 48.1% and 29.0% of respectively low, medium, and good quality of received information in the group with PTSD vs 15.7%, 45.8%, and 38.4% of low, medium and good quality in the other group, p<.001). Finally, any form of exposure was more frequent in the group with PTSD than in the other: living in a worst-hit area (30.5% vs 27.6%, p<.001), having been in contact with affected people (17.3% vs 13.7%, p<.001), having had symptoms consistent with COVID-19 (32.7% vs 20.8%, p<.001), knowing someone deceased from COVID-19 (8.9% vs 5.1%, p<.001), having been highly exposed to media messages (30.6% vs 21.3%, p<.001), feeling highly worried about relatives' health (39.2% vs 16.7%, p<.001) or for their health (42.1% vs 20.5%, p<.001).

Table 1: Characteristics of the global sample and of the subgroups according to the presence of a PTSD or not

	Global sample	PTS	SD	
	N = 22883	No Yes		р
		N = 18427	N = 4456	
Sociodemographic characteristics		18427	4456	
Age, m (sd)*	20.9 (4.1)	20.8 (4.1)	21.2 (4.0)	<.001
Gender, n (%)				<.001
Male	5906 (25.8)	4981 (27.0)	925 (20.8)	
Female	16640 (72.7)	13232 (71.8)	3408 (76.5)	
Others	337 (1.5)	214 (1.2)	123 (2.8)	
<u>Medical information</u>				
Psychiatric history, n (%)	2417 (10.6)	1467 (8.0)	950 (21.3)	<.001
Exposure to another traumatic event, n (%)	3221 (14.1)	1745 (9.5)	1476 (33.1)	<.001
Social support				
Living alone, n (%)	2646 (11.6)	1908 (10.4)	738 (16.6)	<.001
Foreign student, n (%)	1365 (6.0)	898 (4.9)	467 (10.5)	<.001
Quality of social ties, n (%)				<.001
High (7-10)	9706 (42.4)	8474 (46.0)	1232 (27.6)	
Medium (4-6)	8894 (38.9)	7126 (38.7)	1768 (39.7)	
Low (0-3)	4283 (18.7)	2827 (15.3)	1456 (32.7)	
Feeling integrated, n (%)				<.001
High (7-10)	14310 (62.5)	12232 (66.4)	2078 (46.6)	
Medium (4-6)	6872 (30.0)	5136 (27.9)	1736 (39.0)	
Low (0-3)	1701 (7.4)	1059 (5.7)	642 (14.4)	
Socio-economic factors				
Loss of income, n (%)	4184 (18.3)	3090 (16.8)	1094 (24.6)	<.001
Housing quality, n (%)				<.001
High (7-10)	19229 (84.0)	16052 (87.1)	3177 (71.3)	
Medium (4-6)	2921 (12.8)	1961 (10.6)	960 (21.5)	
Low (0-3)	733 (3.2)	414 (2.2)	319 (7.2)	
Quality of information received, n (%)				<.001
High (7-10)	8375 (36.6)	7082 (38.4)	1293 (29.0)	
Medium (4-6)	10586 (46.3)	8444 (45.8)	2142 (48.1)	
Low (0-3)	3922 (17.1)	2901 (15.7)	1021 (22.9)	
<u>Exposure</u>				
Department of residence affected, n (%)	6439 (28.1)	5079 (27.6)	1360 (30.5)	<.001
Contact with affected people, n (%)	3303 (14.4)	2532 (13.7)	771 (17.3)	<.001
Symptoms consistent with Covid-19, n (%)	5291 (23.1)	3835 (20.8)	1456 (32.7)	<.001
Deceased relative, n (%)	1337 (5.8)	942 (5.1)	395 (8.9)	<.001
High concern for relatives' health, n (%)	4824 (21.1)	3079 (16.7)	1745 (39.2)	<.001
High concern for own health, n (%)	5656 (24.7)	3780 (20.5)	1876 (42.1)	<.001
High exposure to media messages, n (%)	5282 (23.1)	3917 (21.3)	1365 (30.6)	<.001

<sup>\*</sup> m (sd): mean (standard deviation)

In multivariate analysis (Table 2), all factors remained significantly associated with PTSD. Age was slightly associated with PTSD (OR [CI95%] = 0.99 [0.98-0.99], p=.003), and concerning gender, as compared to men, being a woman was at-risk of PTSD (1.32 [1.21-1.45], p<.001) as well as being a non-binary person (1.76 [1.35-2.31], p<.001). Declaring a psychiatric history or an exposition to another traumatic event were associated with an increased risk of PTSD (2.26 [2.05-2.51], p<.001, and 3.37 [3.08-3.67], p<.001, respectively). Indicators of social support were all associated with PTSD: having lived guarantine alone (1.22 [1.09-1.37], p<.001), being a foreign student (1.70 [1.48-1.95], p<.001), a medium (1.42 [1.30-1.55], p<.001) or poor (2.38 [2.15-2.62], p<.001) quality of social ties compared to those declaring a good quality, and a medium (1.56 [1.44-1.69], p<.001) or low (2.21 [1.95-2.51], p<.001) feeling of integration compared to those reporting a good integration. Precariousness as assessed by loss of income (1.20 [1.09-1.31], p<.001) and a medium (1.60 [1.45-1.76], p<.001) or poor quality housing (1.90 [1.59-2.26], p<.001) compared to good quality housing was associated with PTSD. A medium or low quality of information received was also associated with increased risk of PTSD, compared to good quality (1.26 [1.15-1.37], p<.001 and 1.50 [1.35-1.66], p<.001, respectively). Finally, the more the students were exposed, the more at-risk of PTSD (OR [CI95%] from 1.38 [1.24-1.54], p<.001 for those with one exposure vs no exposure, to 10.82 [2.33-76.57], p=.005 for those with 7 exposures vs no exposure).

Table 2: Factors associated with PTSD in the global sample according to the multivariable logistic regression analysis

	Adjusted OR [CI95%]	р
Sociodemographic characteristics	[010070]	
Age	0.98 [0.98-0.99]	.003
Gender		
Male	1 [ref]	
Female	1.32 [1.21-1.45]	<.001
Others	1.76 [1.35-2.31]	<.001
Medical information		
Psychiatric history (Yes vs No)	2.26 [2.05-2.51]	<.001
Exposure to another traumatic event (Yes vs No)	3.37 [3.08-3.67]	<.001
Social support		
Living alone (Yes vs No)	1.22 [1.09-1.37]	<.001
Foreign student (Yes vs No)	1.70 [1.48-1.95]	<.001
Quality of social ties		
High (7-10)	1 [ref]	
Medium (4-6)	1.42 [1.30-1.55]	<.001
Low (0-3)	2.38 [2.15-2.62]	<.001
Feeling integrated		
High (7-10)	1 [ref]	
Medium (4-6)	1.56 [1.44-1.69]	<.001
Low (0-3)	2.21 [1.95-2.51]	<.001
Socio-economic factors		
Loss of income (Yes vs No)	1.20 [1.09-1.31]	<.001
Housing quality		
High (7-10)	1 [ref]	
Medium (4-6)	1.60 [1.45-1.76]	<.001
Low (0-3)	1.90 [1.59-2.26]	<.001
Quality of information received		
High (7-10)	1 [ref]	
Medium (4-6)	1.26 [1.15-1.37]	<.001
Low (0-3)	1.50 [1.35-1.66]	<.001
Exposure score		
0	1 [ref]	
1	1.38 [1.24-1.54]	<.001
2	2.02 [1.81-2.26]	<.001
3	3.07 [2.71-3.47]	<.001
4	4.62 [3.95-5.41]	<.001
5	6.87 [5.32-8.87]	<.001
6	8.17 [4.79-14.06]	<.001
7	10.82 [2.33-76.57]	.005

# Response trajectories to a potentially traumatic event and factors associated with chronic trajectories

Among the 6,947 respondents to both T1 and T2, response trajectories were as follows: 1) chronicity for 690 students (9.9% Cl95% [9.2-10.6]) who had severe acute distress at T1 and developed a PTSD at T2; 2) recovery for 719 students (10.3% [9.6-11.1]) who had severe acute distress at T1 but did not develop PTSD at T2, 3) delayed-onset for 450 students (6.5% [5.9-7.1]) who did not report severe acute distress at T1 but a PTSD at T2, and 4) resilience concerned 5088 students (73.2% [72.2-74.3]), i.e. no severe distress at T1 or PTSD at T2, resilience being the modal response.

Thus, among the 1409 students (20.3% [19.3-21.2]) presenting a severe acute distress at T1, 690 students (49.0% [46.3-51.6]) were not capable of recovery. According to the results presented in *Table 3*, among the students presenting severe distress at T1, the students least likely to recover were those with severe trait-anxiety (OR [Cl95%] = 2.17 [1.70-2.78], p<.001), sleep disorders (2.12 [1.39-3.27], p<.001), psychiatric history (1.51 [1.07-2.15], p=.021), exposure to another traumatic event (2.55 [1.39-3.27], p<.001), those living alone (1.44 [1.01-2.05], p=.043) or with low quality of social ties during the quarantine (1.54 [1.12-2.11], p=.008), those who were highly exposed (1.74 [1.22-2.48], p=.002), and those considering that they have been misinformed (1.58 [1.13-2.22], p=.008).

Table 3 : Factors associated with PTSD in the students presenting an acute severe distress at T1 according to the multivariable logistic regression analysis

	m (sd)* or N, (%)	Adjusted OR [CI95%]	р
Sociodemographic characteristics		_	
Age	20.7 (3.4)	0.99 [0.95-1.02]	.549
Gender			
Male	183 (13.0)	1 [ref]	
Female	1196 (84.9)	0.92 [0.65-1.29]	.621
Others	30 (2.1)	1.34 [0.56-3.30]	.513
Medical information			
Severe anxiety-trait (Yes vs No)	742 (52.7)	2.17 [1.70-2.78]	<.001
Psychiatric history (Yes vs No)	296 (21.0)	1.51 [1.07-2.15]	.021
Exposure to another traumatic event (Yes vs No)	295 (20.9)	2.55 [1.90-3.44]	<.001
Sleeping disorder (Yes vs No)	143 (10.1)	2.12 [1.39-3.27]	<.001
Use of mental health care (Yes vs No)	223 (15.8)	0.91 [0.62-1.34]	.633
Social support			
Living alone (Yes vs No)	202 (14.3)	1.44 [1.01-2.05]	.043
Foreign student (Yes vs No)	71 (5.0)	1.26 [0.73-2.19]	.402
Quality of social ties			
High (7-10)	452 (32.1)	1 [ref]	
Medium (4-6)	610 (43.3)	1.07 [0.82-1.40]	.610
Low (0-3)	347 (24.6)	1.54 [1.12-2.11]	.008
Feeling integrated			
High (7-10)	735 (52.2)	1 [ref]	
Medium (4-6)	527 (37.4)	1.26 [0.98-1.63]	.067
Low (0-3)	147 (10.4)	1.03 [0.68-1.56]	.899
Socio-economic factors			
Loss of income (Yes vs No)	319 (22.6)	0.90 [0.68-1.19]	.472
Housing quality			
High (7-10)	1106 (78.5)	1 [ref]	
Medium (4-6)	250 (17.7)	1.14 [0.94-1.56]	.369
Low (0-3)	53 (3.8)	1.63 [0.85-3.23]	.149
Quality of information received			
High (7-10)	427 (30.3)	1 [ref]	
Medium (4-6)	707 (50.2)	1.22 [0.94-1.59]	.132
Low (0-3)	275 (19.5)	1.58 [1.13-2.22]	.008
Exposure score			
0	367 (26.0)	1 [ref]	
1	455 (32.3)	1.04 [0.77-1.40]	.788
2	329 (23.3)	1.29 [0.93-1.78]	.128
3+	253 (18.3)	1.74 [1.22-2.48]	.002

<sup>\*</sup> m (sd): mean (standard deviation)

#### **Traumatic events**

Figure 1 reports proportions of students considering each COVID-19 related even as potentially traumatic. More than 3 quarters of the students considered as traumatic the direct consequences of infection by Sars-CoV2 such as death (88.3%) or hospitalization, whether it concerns a relative (82.1%) or oneself (76.8%). Then, most of the participants considered that the infection contracted by a relative (68.8%) or by oneself (60.8%) and that presenting symptoms compatible with COVID-19 could be traumatic (53.2%). Interestingly, quarantine came in 5th position, with two-thirds (66.4%) of students considering it potentially traumatic, ahead of being infected with Sars-CoV2. Finally, a minority of respondents considered the following events to be potentially traumatic: news of the COVID-19 epidemic in France (37.0%), closure of schools and universities (33.2%), closure of bars, shops, and meeting places (27.9%) and news of the COVID-19 epidemic in China (10.8%).

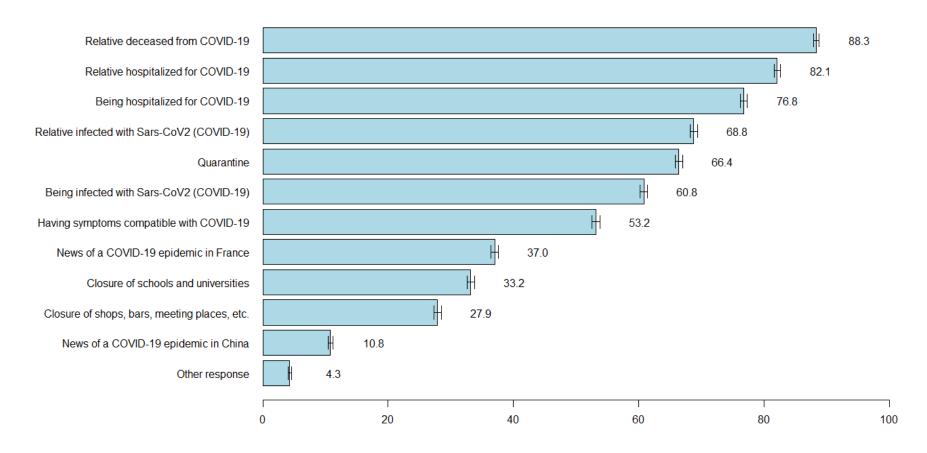


Figure 1: Proportions of students considering the COVID-19 related events as potentially traumatic

## **Discussion**

One to two months after the end of the quarantine due to the COVID-19 pandemic in France, we found that 19.5% of the French university students reported severe post-traumatic stress symptoms. Age, female or non-binary gender, psychiatric follow-up history, exposition to another traumatic event, having lived quarantine alone, being a foreign student, poor quality of social ties, a low feeling of integration, loss of income and poor quality housing as well as low quality of the information received, and high level of exposure to COVID-19 were all significantly associated with PTSD. Response trajectories to the context of COVID-19 pandemic and the associated quarantine were resilience for 73.2% of the students, followed by recovery (10.3%), chronicity (9.9%), and delayed-onset trajectory (6.5%). Among students presenting severe acute distress during the quarantine, the individuals least likely to recover were those with high trait anxiety, sleep disorders, psychiatric history, exposure to another traumatic event, those living alone or with low quality of social ties during the quarantine, those who were highly exposed, and those considering that they have been misinformed.

The rate of PTSD assessed in this study is much higher than the prevalence before quarantine, estimated at 0.7% in the general French population (26). This result confirms the harmful impact of COVID-19 and the associated quarantine on the mental health, as shown by other studies on COVID-19 (9,27–33) as well as on previous quarantine measures (34). It also reinforces concerns about the mental health of young adults and more particularly of students, already identified as worrying before the pandemic (10). In particular, the PTSD rate in our sample was higher than PTSD rates found in other populations using PCL-5 one month after the COVID-19 outbreak: 7% in the China hardest-hit areas a month after the COVID-19 outbreak according to Liu *et al.*, 3.8% among front-line health care workers in China according to Yin *et al.* (35), and 1.2% among Canadian pregnant women according to Berthelot *et al.* (36).

Risk factors associated with PTSD were the same as these of severe acute distress as found during the first measurement time of the COSAMe study. This result is also consistent with other studies on COVID-19 and on previous quarantine measures in which female gender, history of mental problems, poor social support, indicators of precariousness, and exposure to the event were identified as risk factors for psychological disorders (9,27,29,32,34,37).

Response trajectories to the pandemic context and in particular the quarantine were similar to those found by Galatzer-Levy *et al.*, resilience being the modal response (15). Half of the students with self-reported severe acute distress had not recovered one to two months after the end of the quarantine. Risk factors associated with PTSD in this subgroup were mostly similar to those cited above except for age, gender and precariousness, no significantly associated with chronicity among individuals presenting a severe acute distress at T1. Identified risk factors, including sleeping disorders and high trait anxiety, are consisted with literature findings (31,38).

If acute stress disorder is described as a modest predictor of PTSD (39), the IES-R scale appears to be a useful tool, easy to administer, and interpret during the acute phase. It could help to identify students who deserve specific attention, half of the students with severe acute distress developing PTSD versus 8% of those without severe acute distress. Indeed, it is particularly important to take early care of students at risk of PTSD insofar as the consequences in terms of mental health are major, PTSD individuals being 2 to 5 times more at risk of suicidal ideation, suicide attempt, and deaths by suicide (40). But taking care of these students seems also useful to break the vicious circle between COVID-19 and PTSD. Considering that chronic stress is related to an altered response of the immune system, Liang *et al.* warned about the context of the COVID-19 pandemic favoring the occurrence of PTSD in the general population, PTSD altering the immune response, and thus the susceptibility to infections (41,42).

There are some limitations to our study. On the one hand, unlike previous studies on the rates of PTSD in students, our study used a validated diagnostic tool based on the DSM-V. However, the

PCL-5 is normally only a scale that provides a provisional diagnosis of PTSD. The diagnosis should then be confirmed by a clinician. Nevertheless, the PCL-5 showed strong reliability and validity and a cut-off of 31 to 33 was shown to be optimally effective in diagnosing PTSD (20,43). On the other hand, the results might be overestimated due to a self-selection bias. Indeed, we found a higher rate of PTSD in new respondents than in the subgroup already present at T1 (19.5% vs 16.5%), suggesting that students who do best appear less inclined to participate in mental health surveys. However, it is also known that studies focusing on stigmatized behaviors or diseases being are avoided by the concerned subjects (44,45). In addition, the prevalence rate of PTSD measured in this study corresponds to that expected from the response trajectories to a potentially traumatic event, if we consider quarantine as such an event (15).

Indeed, there is an intense debate as to whether or not quarantine can be considered a traumatic event (3). If the definition of PTSD has been revised several times and broadened in the DSM-5, the COVID-19 pandemic further upsets the notion of a traumatic event. If we stick to the definition of the DSM-5, because confinement does not constitute, for the individual, exposure to a threat of death, serious injury, or sexual violence, it cannot be considered as a potentially traumatic event (14). For some authors, if quarantine is linked to PTSD, it could be due to traumatic events lived at home and not quarantine in itself (3,46). However, adjusting for traumatic events unrelated to Covid-19 experienced since the start of the pandemic (14.1% of the students), both the pandemic in itself and the quarantine appear to have a role. The level of exposure to the COVID-19 pandemic and the consequences of social isolation were both associated with PTSD. Interestingly, quarantine was considered more potentially traumatic by the students than being infected with Sars-CoV2.

In summary, we found a high prevalence of PTSD among French university students a month after the end of the quarantine linked to the COVID-19 pandemic. Because of its consequences on mental health and on the maintenance of susceptibility to infections in the general population,

these results reinforce Chevance *et al.*'s statement that it will be necessary to include psychiatry in plans design to face pandemics (47).

# **Perspectives**

Au-delà des débats sur la définition de SSPT, notre étude retrouve un profond mal-être chez les étudiants français, plus d'un mois après la fin du confinement. La prévalence de la dépression, de l'anxiété et des idées suicidaires au cours de la crise sanitaire pourront être estimées à partir des données complémentaires de l'enquête COSAMe afin de préciser le fardeau de la maladie mentale chez les étudiants dans ce contexte de pandémie de COVID-19.

Outre les conséquences de la pandémie de COVID-19, le 21ème siècle fait aussi face à l'émergence d'une pandémie de maladies mentales. D'après l'Organisation Mondiale de la Santé, environ 15% de la charge de morbidité mondiale est liée aux troubles mentaux, responsables de près de 15 % de la perte d'années de vie corrigées de l'incapacité (48). La tranche d'âge la plus touchée est celle des jeunes adultes (48).

Par ailleurs, en raison du contexte écologique, entre autres, l'émergence d'autres zoonoses est à redouter à l'avenir (49). Il apparaît donc capital d'intégrer la préparation psychologique et sociale ainsi que la psychiatrie dans les plans de gestion de crise sanitaire permettant de juguler les pandémies d'une telle ampleur.

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Mots-clés: Syndrome de stress post-traumatique, COVID-19, étudiants, quarantaine

#### Résumé:

**Introduction.** Le syndrome de stress post-traumatique (SSPT) est une conséquence connue de l'exposition à des catastrophes. Cependant, la survenue de SSPT en population générale, non directement touchée par la maladie à coronavirus 2019, fait débat. Cette étude avait pour objectif d'estimer la prévalence de SSPT chez les étudiants, fortement touchés par la détresse aiguë sévère (DAS) en début de pandémie, d'analyser les trajectoires de réponse psychologique (TRP) au contexte pandémique et d'identifier les facteurs associés au SSPT.

**Méthodes**. COSAMe est une étude transversale répétée ayant interrogé les étudiants universitaires français via en un questionnaire ligne du 17 avril au 4 mai (T1) et du 15 juin au 15 juillet (T2) 2020. Seuls les étudiants ayant participé à T2 ont été analysés. La prévalence de SSPT a été évaluée à l'aide de la PCL-5 (PTSD Checklist for DSM-5). Des caractéristiques sociodémographiques, médicales, socioéconomiques, et des informations relatives au soutien social et au degré d'exposition au contexte pandémique ont été recueillies. Des modèles de régression logistique multivariés ont identifé les facteurs de risque de SSPT. Dans le sousgroupe ayant répondu à T1, les TRP (résilience, chronicité, rétablissement et apparition différée de symptômes) ont été évaluées, ainsi que les facteurs de risque de chronicité chez les étudiants atteints de DAS à T1.

Résultats. L'échantillon était composé de 22 883 étudiants de 21 ans en moyenne dont 72,7% de femmes. La prévalence du SSPT était de 19,5%. Le genre féminin ou non binaire, les antécédents psychiatriques, l'exposition à un autre événement traumatique, les indicateurs d'isolement et de précarité ainsi que le sentiment d'être mal informé et un niveau élevé d'exposition au contexte pandémique étaient associés au SSPT. Parmi les 6 947 étudiants ayant répondu à T1, la TRP la plus fréquente était la résilience (73,2%), suivie du rétablissement (10,3%), de la chronicité (9,9%) et de l'apparition différée (6,5%). En cas de DAS, les étudiants à risque de chronicité étaient ceux souffrant d'anxiété habituelle, de troubles du sommeil, d'antécédents psychiatriques, d'exposition à un autre événement traumatique, vivant seuls ou ayant des liens sociaux altérés, fortement exposés au contexte pandémique et mal informés.

**Conclusion**. La forte prévalence du SSPT chez les étudiants universitaires souligne la nécessité d'impliquer la psychiatrie dans les plans de gestion de crise sanitaire liée à une pandémie.

**Composition du Jury:** 

Président : Monsieur le Professeur Philippe AMOUYEL

Assesseurs : Monsieur le Professeur Guillaume VAIVA

Directeurs de thèse : Monsieur le Docteur Fabien D'HONDT

Madame le Docteur Marielle WATHELET