Posttraumatic Stress Symptoms in Patients With Cancer During the COVID-19 Pandemic: A One-Year Longitudinal Study

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ABSTRACT

Background: Patients with cancer may be particularly vulnerable to psychological consequences of the COVID-19 pandemic. We studied the prevalence and evolution of posttraumatic stress symptoms (PTSS) in patients with cancer during the pandemic waves, and we investigated factors associated with high symptoms. **Methods:** COVIPACT is a 1-year longitudinal prospective study of French patients with solid/hematologic malignancies receiving treatment during the first nationwide lockdown. PTSS were measured every 3 months from April 2020 using the Impact of Event Scale–Revised. Patients also completed questionnaires on their quality of life, cognitive complaints, insomnia, and COVID-19 lockdown experience. **Results:** Longitudinal analyses involved 386 patients with at least one PTSS assessment after baseline (median age, 63 years; 76% female). Among them, 21.5% had moderate/severe PTSS during the first lockdown. The rate of patients reporting PTSS decreased at lockdown release (13.6%), increased again at second lockdown (23.2%), and slightly declined from the second release period (22.7%) to the third lockdown (17.5%). Patients were grouped into 3 trajectories of evolution. Most patients had stable low symptoms throughout the period, 6% had high baseline symptoms slowly decreasing over time, and 17.6% had moderate symptoms worsening during the second lockdown. Female sex, feeling socially isolated, worrying about COVID-19 infection, and using psychotropic drugs were associated with PTSS. PTSS were associated with impaired quality of life, sleep, and cognition. **Conclusions:** Approximately one-fourth of patients with cancer experienced high and persistent PTSS over the first year of the COVID-19 pandemic and may benefit from psychological support.

ClinicalTrials.gov identifier: NCT04366154

J Natl Compr Canc Netw 2023;21(3):265–272.e7
doi: 10.6004/jnccn.2023.7085

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Background

The COVID-19 pandemic spread worldwide in January 2020 and led to national measures such as lockdowns and curfews in many parts of the world as soon as March/April 2020. This stressful event has deeply and lastingly impacted populations in health, psychological, social, and financial aspects.[1,2] Posttraumatic stress disorder (PTSD) is defined as the direct or indirect exposure to a stressor (eg, actual or threatened death) followed by symptoms of intrusive memories, avoidance, and hyperarousal that persist for >1 month.[3] PTSD and related disorders, such as anxiety, distress, and depression, have been reported during past pandemics, such as Ebola virus, severe acute respiratory syndrome, and H1N1 influenza, and their effects are compounded by the public health measures required, such as quarantine.[4] The COVID-19 pandemic is unprecedented due to the repetition and duration of multiple waves of infections and lockdowns, and it may have deeper, long-term psychological consequences.

Some studies have reported high degrees of posttraumatic stress symptoms (PTSS) in the general population during the first wave of the COVID-19 pandemic, with a prevalence estimated at 27% in a meta-analysis.[5] However, very few studies repeated these assessments to investigate changes in PTSS over time.[6,7]

Patients who have cancer may be particularly prone to developing PTSS due to a high baseline level of anxiety and depression in relation to their cancer diagnosis,[8] the potential modification of cancer management in response to the COVID-19 pandemic,[9] and a high risk of developing a severe form of COVID-19 infection.[10–12] Several studies in various types of cancer reported PTSS in


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patients during the first wave of the pandemic, with a prevalence ranging from 9% to 35%.[13–15] However, to our knowledge, there has been no longitudinal study to date following patients with cancer over the different waves of the pandemic.

As soon as April 2020, we set up a 1-year longitudinal prospective clinical cohort of patients with cancer (COVIPACT). Previously published baseline results showed that 21% of patients with cancer experienced PTSS associated with poor quality of life (QoL) during the first lockdown.[16] An adjustment in medical oncology practice, such as cancellation or postponement of treatments or modification of follow-up, was implemented for approximately one-fourth of patients and was associated with the occurrence of PTSS. This article presents the longitudinal follow-up of the COVIPACT cohort. Our main objective was to describe the evolution of PTSS in patients with cancer over the first year of the COVID-19 pandemic and to identify factors associated with high PTSS. We also investigated the evolution of PTSS-related disorders (insomnia, cognitive complaints, and QoL)[3,17] over the pandemic in relation to PTSS to better understand the global impact of PTSS induced by the COVID-19 pandemic.

Methods

Settings and Population

COVIPACT (NCT04366154) is a French longitudinal prospective study that enrolled patients between April 16 and May 29, 2020, and included outpatients aged ≥18 years and receiving oncologic treatment for solid or hematologic malignancy during the first nationwide lockdown at the day care hospital of 2 French cancer centers (the François Baclesse Center at Caen and the Henri Becquerel Center at Rouen).[16] Patients receiving oral treatments and simple surveillance were not included.

Data Collection and Survey

Demographics, clinical information, history of oncologic disease, and pandemic-induced adjustment in medical oncology practices were collected from medical records. Inclusion was based on a nonopposition form distributed to patients at the oncologic day care hospital. At baseline, enrolled patients were asked to complete validated self-questionnaires assessing PTSS, insomnia, QoL, and cognitive complaints. Follow-up questionnaires were sent by mail every 3 months over the course of 1 year, which approximately matched the waves of the pandemic and related restrictions. Questionnaires were completed in April and May 2020 during the first French lockdown (M0), in July and August 2020 during the release period (M3), in October and November 2020 during the second French lockdown (M6), in January and February 2021 after the second lockdown release (M9), and in April and May 2021 during the third French lockdown (M12). Patients were included in the present study if they completed the questionnaire on PTSS at baseline and at least one follow-up.

Questionnaires

The Impact of Event Scale–Revised (IES-R) is a 22-item self-questionnaire that highlights avoidance, intrusion, and hyperarousal PTSS in relation to a prespecified stressful event.[18,19] In COVIPACT, patients were asked to complete the IES-R questionnaire with regard to the COVID-19 pandemic. As previously recommended, a score of ≥33 out of 88 was used to identify moderate to severe PTSS.[19]

We used the Functional Assessment of Cancer Therapy–General (FACT-G) to assess QoL.[20] It includes 27 items that measure the physical, social, emotional, and functional components of health-related QoL in patients with cancer and yields a total score of 108.

Insomnia was assessed using the 7-item Insomnia Severity Index,[21] whose total score ranges from 0 to 28 and is interpreted as follows: absence of insomnia (0–7), subthreshold insomnia (8–14), moderate insomnia (15–21), and severe insomnia (22–28).

Cognitive complaints were evaluated by the Functional Assessment of Cancer Therapy–Cognitive Function (FACT-Cog),[22] especially the Perceived Cognitive Impairment subscale that contains 20 items and yields a maximum score of 72. Clinically significant symptoms of cognitive complaints were defined as ratings lower than the 10th percentile of a normative sample.[23]

Patients completed a questionnaire about their living conditions and feelings during the first lockdown, including their family environment, education, occupational status, fears about COVID-19 infection, social interactions, feelings of social isolation, and self-reported use of psychotropic drugs.

Statistical Analysis

Data were described by number and proportion for categorical variables and mean and standard deviation for continuous variables. We used a logistic mixed model to describe the evolution of moderate to severe PTSS (IES-R score ≥33) over time. Models included an intercept representing baseline symptoms, a discrete time representing change of symptoms over time, and a random intercept for each patient to account for interindividual variability. To explore associations of factors with PTSS at baseline and their change over time, factors were entered as both simple effect and in interaction with time. First, factors were entered individually in models minimally adjusted for study center and progressive disease at 6 months. Then, factors were retained simultaneously in the final multivariable model if $P<.10$. In secondary analyses, we used mixed models to describe the evolution of QoL, cognitive complaints, and insomnia over time according to PTSS. We identified distinct trajectories of IES-R using latent class

mixed models to identify patients with persistent or delayed PTSS over time. The optimal number of latent classes was chosen according to the Bayesian information criterion. The best statistical fit was reached with 4 trajectory groups, including 2 small trajectory groups of similar shape that were pooled a posteriori (supplemental eTable 1 and eFigure 1, available with this article at JNCCN.org). Multinomial logistic regression was then fitted to identify factors associated with each latent class trajectory.

All statistical analyses were carried out using R version 4.1.0 (R Foundation for Statistical Computing) using packages GLMMadaptive (version 0.8-0), lme4 (version 1.1-27.1), and lcmm (version 1.9.3). A 2-sided P value $<.05$ was considered statistically significant.

Ethical Approval

Approval for the study was obtained from the local ethics committee (ref. 220C07; South Mediterranean II Committee for the Protection of Persons). The study was conducted in compliance with the French research standard (MR-003 "Research in the Field of Health Without Collection of Consent"; compliance commitment to MR-003 for the François Baclesse Center [no.2146328v.0, dated from January 26, 2018]). All patients received information, and none expressed any opposition to the use of their data. COVIPACT is registered as IDRCB:2020- A00879-30 (ClinicalTrials.gov identifier: NCT04366154).

Results

Baseline Characteristics

We included 734 patients, including 565 who completed the IES-R. As previously published, no statistically significant differences were observed between sociodemographic and clinical characteristics, except for ECOG performance status ≥2, which was more frequent in 734 patients (P=.03).[16] Among the 565 patients who completed the IES-R questionnaire at baseline, 386 completed at least 1 follow-up assessment and were included in the present longitudinal analysis (Figure 1). Mean follow-up was 9.7 months (range, 1.8–14.4 months). Most patients were female (76%), had breast cancer (50%), and had good general status (95% with ECOG performance status ≤1), and approximately half of the cohort had

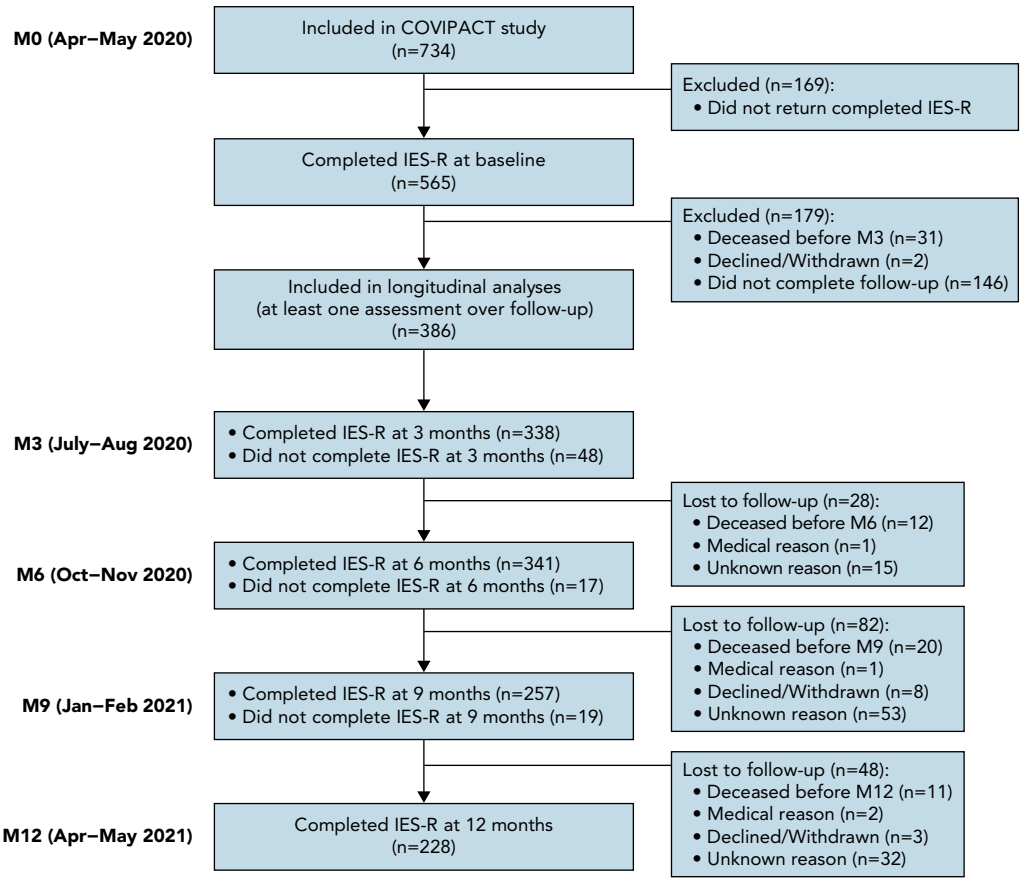

Figure 1. Flowchart of patients with cancer in the French COVIPACT study.
Abbreviations: IES-R, Impact of Event Scale–Revised; M0, first French lockdown; M3, first French lockdown release; M6, second French lockdown; M9, second French lockdown release; M12, third French lockdown.

Table 1. Baseline Patient Characteristics (N=386)

Characteristic	n (%)
Clinical characteristics	
Age, median [IQR] (min–max), y	63 [53–70] (28–87)
Age	
<70 y	287 (74%)
≥70 y	99 (26%)
Sex	
Male	94 (24%)
Female	292 (76%)
Study center	
François Baclesse center	296 (77%)
Henri Becquerel center	90 (23%)
ECOG performance status	
0 or 1	366 (95%)
>1	20 (5%)
Months since diagnosis, median [IQR] (min–max)	14 [4.5–54] (0.7–410)
Type of cancer	
Breast	193 (50%)
Digestive	44 (11%)
Lung, head and neck	64 (17%)
Urologic and gynecologic	71 (18%)
Other solid and hematologic	14 (4%)
Metastatic cancer[a]	
Yes	204 (54%)
No	173 (46%)
Missing/Not provided	9
History of anxiety and depression	
Yes	32 (8%)
No	354 (92%)
Adapted cancer treatment or care during first lockdown	
Yes	112 (29%)
No	274 (71%)

(*continued on next column*)

Table 1. Baseline Patient Characteristics (N=386) (cont.)

Characteristic	n (%)
Self-reported characteristics	
Level of education[a]	
Less than high school	189 (52%)
High school diploma	57 (16%)
Postsecondary education	117 (32%)
Missing/Not provided	23
Current occupation status[a]	
Active	95 (26%)
Retired	189 (51%)
Not active	86 (23%)
Missing/Not provided	16
COVID-19–induced financial consequences[a]	
Moderate/Severe	31 (8%)
Little	43 (12%)
None	291 (80%)
Missing/Not provided	21
Living alone during first lockdown[a]	
Yes	56 (15%)
No	316 (85%)
Missing/Not provided	21
Feeling of social isolation during first lockdown[a]	
Moderate/Severe	164 (44%)
Not much	206 (56%)
Missing/Not provided	16
Fear of COVID-19 infection during first lockdown[a]	
Moderate/Severe	245 (66%)
Not much	126 (34%)
Missing/Not provided	15
Increased use of psychotropic drugs during first lockdown[a]	
Yes	94 (26%)
No	267 (74%)
Missing/Not provided	25

Abbreviation: IQR, interquartile range.
[a]Percentages are of nonmissing data.

metastatic disease (Table 1). During the first lockdown, 15% of patients were living alone, 44% reported feeling socially isolated, and 66% worried about COVID-19 infection (Table 1). Clinical characteristics of the 386 patients retained in the longitudinal analysis and those of the initial 565 patients were similar (supplemental eTable 2). The IES-R score was also comparable between groups at baseline (mean [SD], 21.5 [15.5] and 20.8 [15.9], respectively).

Evolution of PTSS Over Time

During the first lockdown, 21.5% of patients had moderate to severe PTSS (Figure 2). The rate changed significantly over time ($P<.001$) with a marked decrease during the lockdown release (13.6% at M3), followed by a return to the same level as during the first lockdown during the second lockdown (23.2% at M6). The rate of patients with PTSS remained stable after the second lockdown (22.7% at M9) and slightly decreased at the end of follow-up (17.5% at M12). We observed a similar trend when using the IES-R scale as a continuous measure. All 3 PTSD components (avoidance,

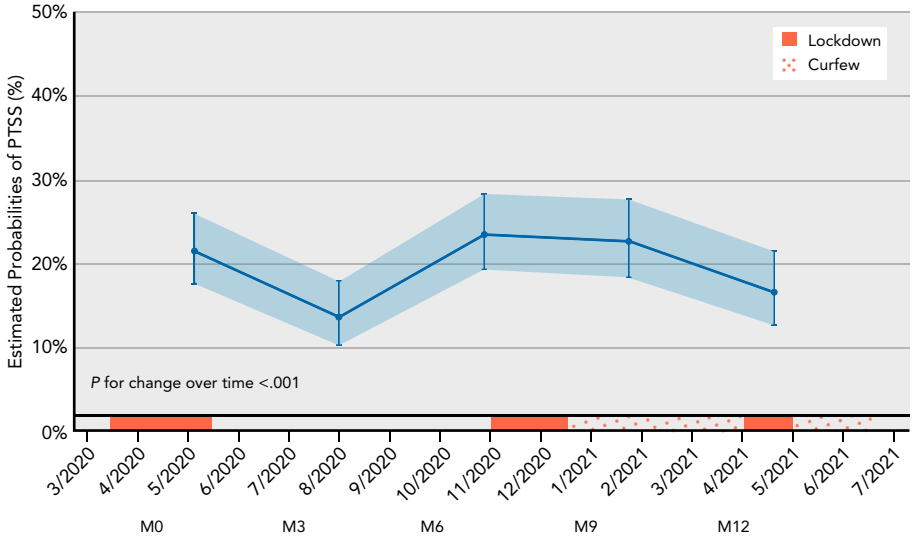

Figure 2. Trajectory of PTSS in patients with cancer during the COVID-19 pandemic in the French COVIPACT study (n=386).
Estimates and 95% confidence intervals are from a logistic mixed model on PTSS (defined as IES-R score ≥33) with discrete time and a random patient effect.
Abbreviations: IES-R, Impact of Event Scale–Revised; M0, first French lockdown (April–May 2020); M3, first French lockdown release (July–August 2020); M6, second French lockdown (October–November 2020); M9, second French lockdown release (January–February 2021); M12, third French lockdown (April–May 2021); PTSS, posttraumatic stress symptoms.

intrusion, and hyperarousal) followed a similar trajectory over time (data not shown).

Female patients, patients who felt socially isolated during the first lockdown, those who had fears of COVID-19 infection, and those who reported increased use of psychotropic drugs during this period had more PTSS at baseline. These associations remained broadly constant over time (supplemental eFigure 2), except for sex, whose effect tended to decrease over time (although not significantly; *P* for change =.32). In addition, patients who experienced any adjustment in medical oncology practices during the first lockdown tended to have more PTSS at baseline (*P*=.053), but the difference decreased over time (*P* for change =.002) toward no difference at M3 and thereafter. All these associations observed in minimally adjusted models remained similar when factors were considered simultaneously in a multivariable model (supplemental eTable 3).

We grouped patients into 3 homogeneous trajectory classes of IES-R change over time (Figure 3). Most patients were in the "stable low IES-R" class (n=295; 76.4%), characterized by a low IES-R score throughout follow-up. Other patients had a persistently moderate IES-R score over time, with either a subtle decrease during follow-up ("decreased moderate IES-R": n=23; 6%) or a steep increase at second lockdown ("increased moderate IES-R": n=68; 17.6%). As observed in the primary analysis, feelings of social isolation, fear of COVID-19 infection, and use of psychotropics were associated with the class trajectories (supplemental eTable 4).

PTSD-Related Symptoms

At all times, PTSS were strongly associated with insomnia, cognitive complaints, and poor global QoL (all *P*<.001; supplemental eFigure 3). In particular, at M6, when the differences between patients with and without PTSS were the greatest, 55% of patients with PTSS reported moderate to severe insomnia, and 40% had cognitive complaints, compared with 25% and 23% of patients without PTSS, respectively. In addition, there was an average difference of 8 points on the FACT-G global score of QoL throughout follow-up between patients with and without PTSS.

Discussion

This longitudinal prospective study of French patients with cancer followed over 1 year showed high levels of PTSS over the repeated waves of COVID-19 infections and associated lockdown periods, affecting almost one-fourth of patients who received medical oncology treatment. Female patients, patients who felt socially isolated during the first lockdown, those worrying about COVID-19 infection, and those who reported increased use of psychotropics during this period had more PTSS. PTSS were associated with more insomnia, more cognitive complaints, and worse QoL.

We observed 21.5% of moderate to severe PTSS at baseline at the beginning of the pandemic, which is similar to results of an Italian study of patients with lymphoma treated during the same period.[13] A higher rate (35%) was observed in patients with breast cancer in Wuhan (China), which may be explained by the exclusively female population and

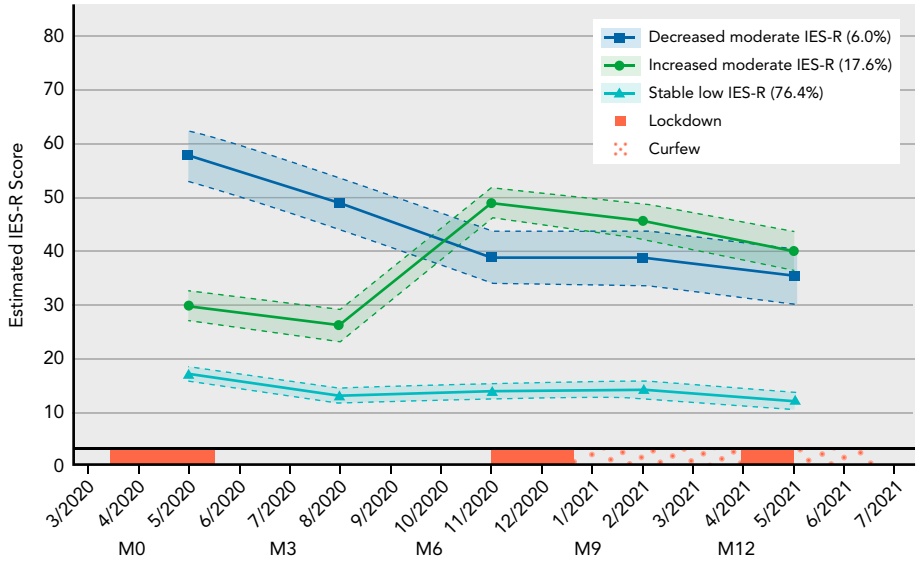

Figure 3. Distinct trajectories of IES-R change over time in patients with cancer in the French COVIPACT study (n=386). Trajectory classes were identified by latent class linear mixed model on IES-R score. The optimal number of latent classes from 2 to 6 was chosen according to Bayesian information criterion. Four trajectory groups were identified, including one with a small sample size (n=5), which was combined a posteriori with another group with a similar trajectory, yielding 3 trajectory groups with distinct IES-R change over time. Each individual was assigned to the latent class with the highest probability of membership. The mean IES-R score estimate and 95% confidence interval over time are displayed for each latent class.
Abbreviations: IES-R, Impact of Event Scale–Revised; M0, first French lockdown (April–May 2020); M3, first French lockdown release (July–August 2020); M6, second French lockdown (October–November 2020); M9, second French lockdown release (January–February 2021); M12, third French lockdown (April–May 2021).

the study location at the COVID-19 epicenter.[14] Overall, the rate of PTSS in the cancer population appeared higher during this period than what is generally observed in nonpandemic contexts (6%–9%).[17,24]

Our results suggest that PTSS decreased in patients with cancer during the first lockdown release (summer 2020), affecting 13.6% of patients. This is in line with a French oncologic survey that identified 14.7% of patients with cancer with moderate to severe PTSS during the same release period.[25] Our results are also consistent with data in the general population showing a decline in peritraumatic distress and anxiety from the early stages of lockdown to the release period.[7,26] We also observed that the rate of PTSS increased again at the second lockdown, suggesting a link between the psychological distress of individuals and the series of restrictions and release periods. Although no longitudinal data are available on PTSS changes over time during the COVID-19 pandemic in patients with cancer, this further increase in symptoms was recently reported in a UK representative population survey.[27] We hypothesize that COVID-19 leading to lockdowns was a factor of PTSS in addition to cancer, probably related to the distressing situation, life-threatening disease, modification of cancer treatments, and social isolation. However, we did not observe the same trend at the third lockdown, which could be explained by the advent of vaccination, less strict containment measures, and better understanding of COVID-19 infection, contributing to a potential resilience and decrease in fear of COVID-19, as observed in a German study.[28]

In our study, female sex, feeling socially isolated during the first lockdown, having fears of COVID-19 infection, and an increased self-reported use of psychotropic drugs were associated with PTSS. Female sex is a known risk factor for PTSD,[3] which has also been reported in the context of the COVID-19 pandemic in cancer and general populations.[7,13] Moreover, loneliness and worry about COVID-19 infection have been described as core features of the syndrome triggered by the pandemic.[29,30] Besides, patients with PTSS had poor QoL and more cognitive and insomnia complaints, all of which are known to be associated with PTSD.[3,17] In the context of the COVID-19 pandemic, sleep disturbances and impaired physical QoL have also been related to higher psychological distress.[31,32]

We identified 3 distinct trajectories of IES-R change over time. Although most patients had a stable low level of PTSS during the first year of the pandemic, almost one-fourth had moderate distress throughout the period, and, in particular, 17.6% showed worsened symptoms during the second lockdown. Mental health trajectories have already been investigated in the general population.[26,33] A 6-week Chinese study conducted at the beginning of the pandemic found that half of the participants were resilient, 22% had delayed PTSD, 19% had recovered PTSD, and 15% had chronic PTSD.[33] A UK longitudinal

national survey found that approximately three-fourths of individuals had consistently good mental health during the first 6 months of the pandemic, whereas the others had consistent or worsened psychological distress at a far higher level than before the pandemic.[26] Altogether, these results suggest that some psychological symptoms may be delayed in a substantial proportion of individuals, possibly because of the repetition of pandemic waves and associated social restrictions. We did not identify any specific factors associated with this delayed pattern of symptom onset, as compared with immediate PTSS onset, probably due to lack of power. However, considering a recent study assessing PTSD symptom trajectories, the delayed form may be associated with female sex and may be more frequent the later the age of the trauma exposure and the older the patients.[34] This could explain the high proportion of delayed PTSS in our study, whereas this trajectory is expected to be a minority in the literature.[35] Moreover, the delayed form could be associated with postevent stressors.[36] In the case of the pandemic, it could be the reexposure related to the different waves. Reassuringly, these delayed forms seem to be associated with more resilience and fewer psychological consequences.[34]

The COVIPACT study is the first longitudinal study with a long follow-up of 1 year to assess PTSS and QoL in patients with cancer during the COVID-19 pandemic using validated questionnaires at different periods of lockdowns. However, this study has limitations. We used the IES-R self-questionnaire, which measures PTSS but does not allow a medical diagnosis of PTSD. Moreover, mental health conditions such as anxiety and depression, which are commonly intertwined with PTSD, were not assessed in our study and this may have made it difficult to interpret the PTSS.[37,38] PTSD requires exposure to a specific traumatic event, and the question of whether the COVID-19 pandemic can be classified as a "sudden" and "catastrophic" trauma has been debated. For this reason, some authors have considered pandemic-induced PTSS as adjustment disorders.[39] In the absence of a control group, we could not evaluate whether patients with cancer had prevalence or evolution of PTSS similar to the general population. However, our results were consistent with prevalence estimates from a meta-analysis in the general population[5] and longitudinal trends over the repeated pandemic waves.[7,26,27] Female patients represented a high proportion of our population, which may have led to overestimating PTSS. Finally, the high attrition rate and the loss to follow-up rate are the main limitations of our study. Attrition may be explained by the inclusion method based on the nonopposition form. The loss to follow-up rate may be explained by the repetition of questionnaires over time. More patients who did not experience disease progression completed the questionnaires, which is why we adjusted for this important factor in longitudinal analysis. Although the clinical characteristics and baseline IES-R score were comparable between patients who completed follow-up assessments and those who completed baseline assessments, we cannot exclude the possibility that attrition may have biased the assessment of PTSS over time.

Conclusions

Overall, we identified approximately one-fourth of patients with cancer with persistent PTSS over the first year of the COVID-19 pandemic. We hypothesize that lockdown periods could explain an increase in PTSS, and the approach to it must be particularly thoughtful in view of its potential psychological consequences, especially in PTSD at-risk populations such as patients with cancer. Long-term follow-up studies should shed light on the consequences of such psychological distress, especially in the field of oncology, where distress is correlated with poor adherence to treatment and survival.[40] COVIPACT 2 (ClinicalTrials.gov identifier: NCT04747249), a study including the patients of COVIPACT with a moderate to severe level of PTSS, is underway to evaluate the benefit of psychological interventions to reduce them.

Acknowledgments

We acknowledge the Northwest Data Center (CTD-CNO) for managing the data. It is supported by grants from the French League Against Cancer (LNC) and the French National Cancer Institute (INCa). We thank the clinical research associates Chantal Rieux, Bérénice Legrand, Clotilde Pupin, Delphine Bridelance, and Loréna Masseline for data collection, as well as Bérengère de Gourmont for support with data entry. We acknowledge Ray Cooke for copyediting the manuscript. We also thank all patients who agreed to participate. The National Clinical Research Platform for Quality of Life in Oncology is labeled by the LNC.

Submitted March 11, 2022; final revision received July 15, 2022; accepted for publication October 11, 2022. Published online Februry 22, 2023.
Author contributions: *Conceptualization:* Clarisse, Joly. *Formal analysis:* Lefèvre-Arbogast, Lequesne. *Funding acquisition:* Clarisse. *Investigation:* Bastien, Gernier, Binarelli, Lange, Fernette, Tron, Richard, Quilan. *Methodology:* Lefèvre-Arbogast, Lequesne, Clarisse. *Project administration:* Grellard, Richard, Leconte. *Resources:* Rigal, Morel, Leheurteur, Faveyrial, Joly. *Supervision:* Griffon, Pépin, Clarisse, Joly. *Writing–original draft:* Bastien, Lefèvre-Arbogast, Lequesne, Clarisse, Joly. *Writing–review and editing:* All authors.

Data availability: The data that support the findings of this study are available upon reasonable request from the corresponding author.

Disclosures: The authors have disclosed that they have not received any financial consideration from any person or organization to support the preparation, analysis, results, or discussion of this article.

Funding: This work was supported by a research grant from Fondation ARC (COVID202001320) and financial support from the GEFLUC Normandie (Les Entreprises Contre le Cancer/Campaigns Against Cancer, Rouen-Normandie).

Disclaimer: The funders had no role in the design of the study; the collection, analysis, and interpretation of the data; the writing of the manuscript; and the decision to submit the manuscript for publication.

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Supplemental online content for:

Posttraumatic Stress Symptoms in Patients With Cancer During the COVID-19 Pandemic: A One-Year Longitudinal Study

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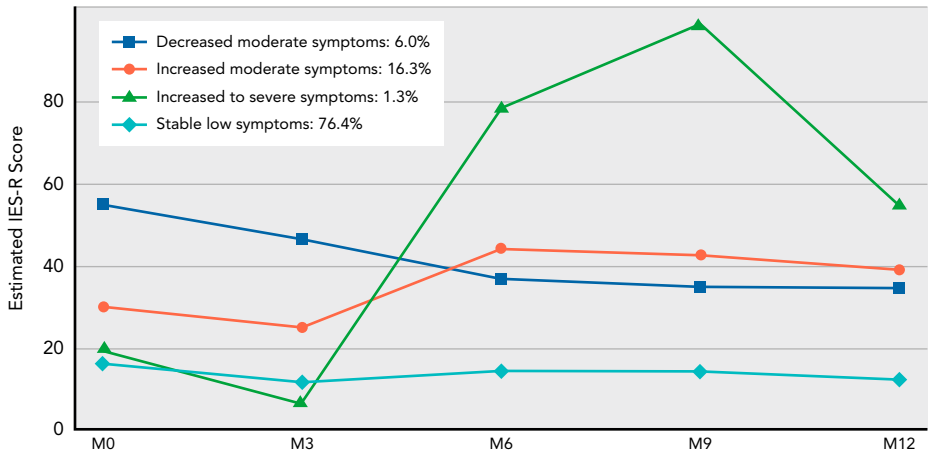
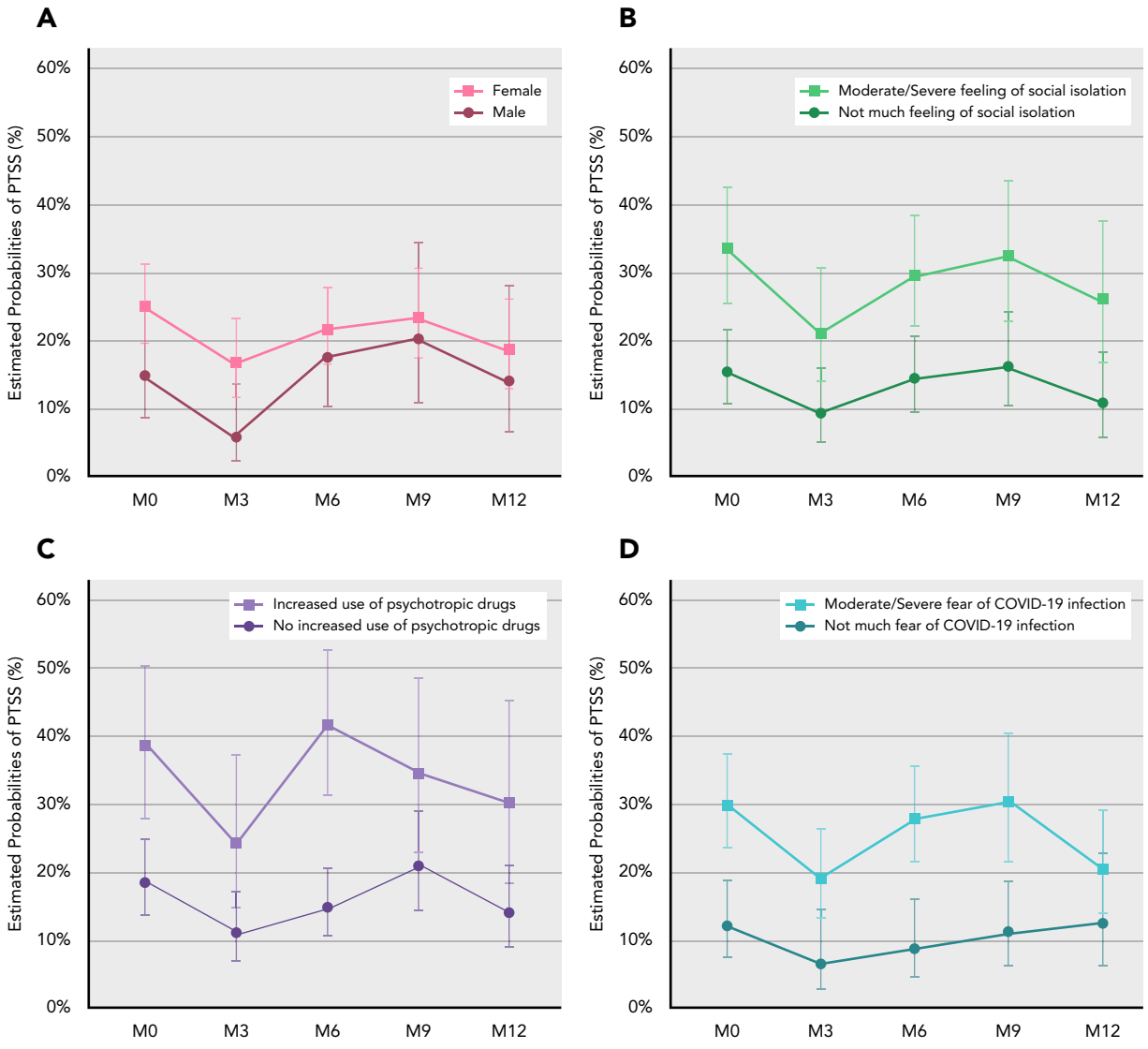
J Natl Compr Canc Netw 2023;21(3):265–272.e7

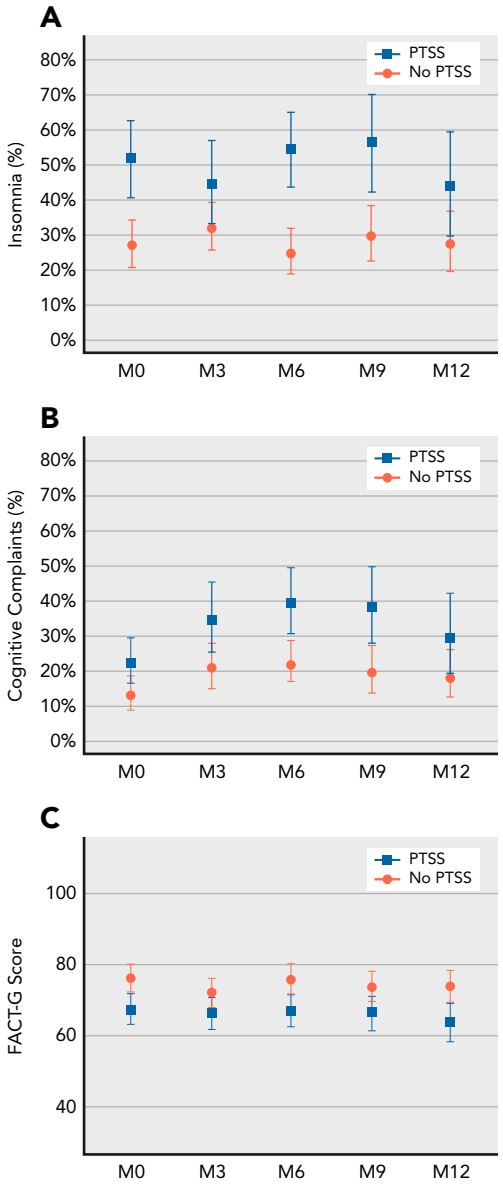


eFigure 1. Four trajectory classes of IES-R change over time. Distinct trajectories of IES-R were identified using latent class mixed models, which account for heterogeneity in patterns of change. The optimal number of latent classes from 2 to 6 was chosen according to the Bayesian information criterion. The latent class model that provided best statistical fit identified 4 trajectory groups. The smallest trajectory class, shown in green (n=5) was combined a posteriori with the trajectory class shown in orange (n=63) as the "Increased moderate IES-R" group.
Abbreviations: IES-R, Impact of Event Scale–Revised; M0, first French lockdown (April–May 2020); M3, first French lockdown release (July–August 2020); M6, second French lockdown (October–November 2020); M9, second French lockdown release (January–February 2021); M12, third French lockdown (April–May 2021).



eFigure 2. Trajectories of PTSS during the COVID-19 pandemic by characteristics of patients with cancer assessed at first lockdown in the French COVIPACT study (N=386). Estimates and 95% confidence intervals are from separate logistic mixed models on PTSS (defined as IES-R score ≥33), with discrete time and random patient effect and including as independent fixed factor: **(A)** patient sex, **(B)** feeling of social isolation, **(C)** increased use of psychotropic drugs, and **(D)** fear of COVID-19 infection during first COVID-19 lockdown in France.

Abbreviations: IES-R, Impact of Event Scale–Revised; M0, first French lockdown (April–May 2020); M3, first French lockdown release (July–August 2020); M6, second French lockdown (October–November 2020); M9, second French lockdown release (January–February 2021); M12, third French lockdown (April–May 2021); PTSS, posttraumatic stress symptom.



eFigure 3. Changes in **(A)** insomnia, **(B)** cognitive complaints, and **(C)** QoL (FACT-G) by PTSS during the COVID-19 pandemic in patients with cancer in the French COVIPACT study. Estimates are from logistic and linear mixed models adjusted for baseline age, sex, study center, and cancer progression at M6. Curves are plotted for an average study participant profile (a female patient from the François Baclesse center aged <70 years who did not experience disease progression at M6). PTSS are defined at each time as IES-R score ≥33. Insomnia is defined as ISI score ≥15. Cognitive complaints are defined as FACT-Cog PCI score ≥ age-dependent cutoff (59 for patients aged <50 years, 47 for patients aged 50–69 years, 41 for patients aged >70 years). QoL is measured using the total score of the FACT-G, with higher scores indicating better QoL.

Abbreviations: FACT-Cog, Functional Assessment of Cancer Therapy–Cognitive Function; IES-R, Impact of Event Scale–Revised; ISI, Insomnia Severity Index; M0, first French lockdown (April–May 2020); M3, first French lockdown release (July–August 2020); M6, second French lockdown (October–November 2020); M9, second French lockdown release (January–February 2021); M12, third French lockdown (April–May 2021); PCI, perceived cognitive impairment; PTSS, posttraumatic stress symptoms; QoL, quality of life.

eTable 1. Fit of Latent Class Models Identifying Distinct Trajectory Classes of IES-R Evolution

Model With n Classes	loglik	AIC	BIC	SABIC	Entropy	Class 1 N	Class 2 N	Class 3 N	Class 4 N	Class 5 N	Class 6 N
1	−6,044.58	12,103.16	12,130.85	12,108.64	1	386					
2	−5,972.70	11,971.39	12,022.82	11,981.57	0.8959	358	28				
3	−5,945.90	11,929.80	12,004.96	11,944.68	0.8672	21	327	38			
4	−5,912.71	11,875.43	**11,974.32**[a]	11,895.00	0.8521	23	63	5	295		
5	−5,900.56	11,863.11	11,985.74	11,887.38	0.8648	36	298	34	5	13	
6	−5,893.40	11,860.80	12,007.16	11,889.77	0.5964	9	0	15	14	280	68

Abbreviations: AIC, Akaike information Criterion; BIC, Bayesian Information Criterion; IES-R, Impact of Event Scale–Revised; SABIC, sample-size-adjusted BIC.
[a]Selection model based on minimum BIC.

eTable 2. Clinical Characteristics of Patients at Baseline and Retained in and Excluded From the Longitudinal Analysis

	Sample Available at Baseline n (%)	Sample Retained in Longitudinal Analysis n (%)	*P* Value[a]	Sample Excluded From Longitudinal Analysis n (%)
Total, n	565	386		179
Age, median (min–max), y	63 (24–87)	63 (28–87)	.67	64 (24–84)
Age			1.00	
<70 y	419 (74%)	287 (74%)		132 (74%)
≥70 y	146 (26%)	99 (26%)		47 (26%)
Sex			.32	
Male	155 (27%)	94 (24%)		61 (34%)
Female	410 (73%)	292 (76%)		118 (66%)
Study center			.041	
François Baclesse center	465 (82%)	296 (77%)		169 (94%)
Henri Becquerel center	100 (18%)	90 (23%)		10 (6%)
ECOG performance status			.69	
0 or 1	531 (94%)	366 (95%)		165 (92%)
>1	34 (6%)	20 (5%)		14 (8%)
Months since diagnosis, median (min–max)	15 (0.48–410)	14 (0.67–410)	.96	18 (0.48–290)
Type of cancer			.072	
Breast	252 (45%)	193 (50%)		59 (33%)
Digestive	94 (17%)	44 (11%)		50 (28%)
Lung, head and neck	109 (19%)	64 (17%)		45 (25%)
Urologic and gynecologic	85 (15%)	71 (18%)		14 (8%)
Other solid and hematologic	25 (4%)	14 (4%)		11 (6%)
Metastatic cancer			.24	
Yes	329 (59%)	204 (54%)		125 (70%)
No	226 (41%)	173 (46%)		53 (30%)
Not applicable/missing	10	9		1
History of anxiety and depression			.94	
Yes	46 (8%)	32 (8%)		14 (8%)
No	519 (92%)	354 (92%)		165 (92%)
Adapted cancer treatment or care during first lockdown			.41	
Yes	149 (26%)	112 (29%)		37 (21%)
No	416 (74%)	274 (71%)		142 (79%)

[a]*P* values are from Wilcoxon Mann-Whitney and chi-square tests for continuous and categorical variables, respectively, to compare sample available at baseline to sample retained in longitudinal analysis.

eTable 3. Multivariable Analysis of Posttraumatic Stress Symptoms (N=357 in Complete Case Analysis)

	Association at Baseline		Association With Change Over Follow-up				
	β_{M0} (OR)	*P* Value	β_{M3}	β_{M6}	β_{M9}	β_{M12}	*P* Value
Sex		.005					
Male	Ref						
Female	0.87 (2.40)						
Feeling of social isolation during first lockdown		.008					
No/Not much	Ref						
Moderate/Severe	0.62 (1.86)						
Fear of COVID-19 infection		<.001					
No/Not much	Ref						
Moderate/Severe	1.25 (3.48)						
Increased use of psychotropic drugs during first lockdown		<.001					
No	Ref						
Yes	0.87 (2.40)						
Current occupation status		.13					.080
In activity	Ref						
Retired	0.65 (1.92)		−0.21	0.10	−0.13	1.41	
Not active	0.10 (1.10)		−0.11	0.85	0.80	1.69	
Adapted cancer treatment or care during first lockdown		.17					.006
No	Ref						
Yes	0.42 (1.52)		−0.85	0.04	−1.00	0.39	

Multivariable logistic mixed model including factors associated with baseline PTSS or change with *P*<.10 in univariable analysis and adjusted for study center and progressive disease at M6.

If the factor was associated with PTSD at baseline but not with PTSD change at *P*<.10, only the association at baseline was included. In this case, the factor is associated at baseline and consistently over the follow-up (ie, with same trajectory of change).

If the factor was associated with PTSD change at *P*<.10 but not baseline PTSS, both the association with change and the association at baseline were included in the model. In this case, there is no association/difference at baseline, but there are different trajectories of change over follow-up according to this factor.

If the factor was associated with both baseline PTSS and PTSD change at *P*<.10, both the association at baseline and the association with change were included in the model. In this case, there is an association/difference at baseline, and there are different trajectories of change over follow-up (ie, the baseline association either decrease [and possibly disappear] or increase over follow-up).

β_{M0} refers to the association between the factor and PTSD at baseline.

$\beta_{M0} + \beta_{MX}$ refers to the association between the factor and PTSD at month MX (X=3, 6, 9, or 12). High absolute value of β_{MX} indicates difference in association between M0 and MX, with increased association if β_{MX} and β_{MX} are in the same direction, and reduced association if they are in opposite direction (and no difference of association when β_{MX} is close to zero).

Abbreviations: M0, first French lockdown (April–May 2020); M3, first French lockdown release (July–August 2020); M6, second French lockdown (October–November 2020); M9, second French lockdown release (January–February 2021); M12, third French lockdown (April–May 2021); OR, odds ratio; PTSD, posttraumatic stress disorder; PTSS, posttraumatic stress symptoms.

eTable 4. Multivariable Associations Between Patient Characteristics and PTSS Trajectory Class

	RRR (95% CI) Class 2 vs 1 (Increased Moderate IES-R vs Stable Low IES-R)	RRR (95% CI) Class 3 vs 1 (Decreased Moderate IES-R vs Stable Low IES-R)	*P* Value
Feeling of social isolation during first lockdown			.0192
No/Not much	Ref	Ref	
Moderate/Severe	2.17 (1.19–3.95)	2.11 (0.79–5.62)	
Fear of COVID-19 infection during first lockdown			<.001
No/Not much	Ref	Ref	
Moderate/Severe	2.94 (1.41–6.14)	11.78 (1.53–91)	
Increased use of psychotropic drugs during first lockdown			.0129
No	Ref	Ref	
Yes	1.74 (0.93–3.26)	3.62 (1.41–9.27)	

RRR and 95% confidence intervals are from multivariable multinomial logistic regression adjusted for study center and progressive disease at M6 and including factors with $P<.10$ in univariate analysis.
Abbreviations: IES-R, Impact of Event Scale–Revised; M6, second French lockdown (October–November 2020); PTSS, posttraumatic stress symptom; RRR, relative risk ratio.