



HAL
open science

Severity of self-reported symptoms and psychological burden 6-months after hospital admission for COVID-19

Philippine Eloy, Coralie Tardivon, Guillaume Martin-Blondel, Margaux Isnard, Paul Le Turnier, Marion Le Marechal, André Cabié, Odile Launay, Pierre Tattevin, Eric Senneville, et al.

► To cite this version:

Philippine Eloy, Coralie Tardivon, Guillaume Martin-Blondel, Margaux Isnard, Paul Le Turnier, et al.. Severity of self-reported symptoms and psychological burden 6-months after hospital admission for COVID-19: a prospective cohort study. *International Journal of Infectious Diseases*, 2021, 112, pp.247-253. 10.1016/j.ijid.2021.09.011 . hal-03369814

HAL Id: hal-03369814

<https://hal.science/hal-03369814>

Submitted on 5 Jan 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

1 **Severity of self-reported symptoms and psychological burden 6-months after hospital**
2 **admission for COVID-19: a prospective cohort study**

3 **Running title:** Severity of persistent symptoms 6 months after hospitalization for COVID-19

4
5 Philippine ELOY^{1,2}, Coralie TARDIVON^{1,2}, Guillaume MARTIN-BLONDEL³, Margaux
6 ISNARD⁴, Paul LE TURNIER⁵, Marion LE MARECHAL⁶, André CABIÉ⁷, Odile LAUNAY⁸,
7 Pierre TATTEVIN⁹, Eric SENNEVILLE¹⁰, Séverine ANSART¹¹, François GOEHRINGER¹²,
8 Catherine CHIROUZE¹³, Laurane BOUSSON², Cédric LAOUÉANAN^{1,2,14}, Manuel
9 ETIENNE¹⁵, Duc NGUYEN¹⁶, Jade GHOSN^{14,17}, Xavier DUVAL^{14,18} and the French COVID
10 cohort study and investigators groups*

11
12 ¹AP-HP, Hôpital Bichat, Département Epidémiologie Biostatistiques et Recherche Clinique, F-
13 75018 Paris, France

14 ²INSERM, Centre d'Investigations cliniques-Epidémiologie Clinique 1425, Hôpital Bichat, F-
15 75018 Paris, France

16 ³Service des Maladies Infectieuses et Tropicales, CHU de Toulouse

17 ⁴Service de Maladies Infectieuses et Médecine Interne, CH Métropole Savoie

18 ⁵Department of Infectious Diseases, Hotel-Dieu Hospital - INSERM CIC 1413, Nantes
19 University Hospital, Nantes, France

20 ⁶CHU Grenoble Rhône Alpes, Service de Maladies Infectieuses et Médecine Tropicale, F-
21 38000 Grenoble, France

22 ⁷Inserm CIC 1424, Université des Antilles EA 7524, Service de maladies infectieuses et
23 tropicales, CHU de Martinique, F-97200 Fort-de-France, France

24 ⁸Inserm CIC 1417, Faculté de Médecine Paris Descartes, Univ Paris, AP-HP, Hôpital Cochin,
25 Paris, France

26 ⁹Infectious Diseases and Intensive Care Unit, Pontchaillou University Hospital, University
27 Rennes-1, Rennes, France

28 ¹⁰Infectious Diseases Department, Gustave Dron Hospital, 59200 Tourcoing, France

29 ¹¹Tropical and Infection Diseases Unit, CHRU de Brest, F-29200 Brest, France

30 ¹²Service de Maladies Infectieuses et Tropicales, Centre Régional Universitaire de Nancy,
31 Hôpitaux de Brabois, Rue du Morvan, 54511 Vandoeuvre Lés Nancy, France

32 ¹³CHU Besançon, Service de Maladie Infectieuses et Tropicales, F-25000, Besançon, France

33 ¹⁴Université de Paris, INSERM, IAME UMR 1137, Paris, France

34 ¹⁵CHU Rouen, Service des Maladies Infectieuses et Tropicales, F-76000 Rouen, France

35 ¹⁶Department of Infectious and Tropical Diseases, CHU de Bordeaux, Bordeaux, France

36 ¹⁷AP-HP, Hôpital Bichat, Infectious and Tropical Diseases Department, Paris, France

37 ¹⁸AP-HP, Hôpital Bichat, Centre d'Investigation Clinique, Inserm CIC 1425, F-75018 Paris,
38 France

39 **Corresponding author:** Philippine ELOY

40 E-mail : philippine.eloy@aphp.fr

41 Phone number : +33 1 40 25 68 87

42 Postal address : AP-HP, Hôpital Bichat, Département Epidémiologie Biostatistiques et
43 Recherche Clinique, 46, rue Henri Huchard, 75018 Paris, France

44

45 *Membership of the French COVID cohort study and investigators groups is provided in the

46 Supplementary Material.

47 **Abstract**

48 **Objectives:** Few studies have reported clinical COVID-19 sequelae six months (M6) after
49 hospital discharge, but none has studied symptom severity.

50 **Methods:** Prevalence and severity of 7 symptoms were estimated until M6 using the self-
51 administered influenza severity scale in COVID-19 hospitalized patients enrolled in the French
52 COVID cohort. Factors associated with severity were assessed by logistic regression. Anxiety,
53 depression and health-related quality of life (HRQL) were also assessed.

54 **Results:** At M6, among the 324 patients (median age 61 years, 63% men, 19% admitted to
55 intensive care during the acute phase), 187/324 (58%) reported at least one symptom mostly
56 fatigue (47%) and myalgia (23%). Symptom severity was scored, at most, mild in 125 (67%),
57 moderate in 44 (23%) and severe in 18 (10%). Female gender was the sole factor associated
58 with moderate/severe symptom reporting (OR = 1.98, 95%CI=1.13-3.47). Among the 225
59 patients with psychological assessment, 24 (11%) had anxiety, 18 (8%) depressive symptoms,
60 and their physical HRQL was significantly poorer than the general population (p=0.0005).

61 **Conclusion:** Even if 58% of patients reported ≥ 1 symptom at M6, less than 7% rated any
62 symptom as severe. Assessing symptoms severity could be helpful to identify patients requiring
63 appropriate medical care. Women may require special attention.

64 **Keywords :** COVID-19 - Sequelae – Persistent symptoms – Risk factors

65 **Abstract word count:** 200 words / **Text word count:** 2678 words

66 **Introduction**

67 Since the first cases of SARS-CoV-2 infection in December 2019, clinical presentation of
68 COVID-19 in its acute phase has been largely described (Docherty et al., 2020; Richardson et
69 al., 2020). However, long-term clinical sequelae of COVID-19 remains unclear. A few studies
70 reported persistent symptoms 2 to 4 months post discharge (Carfi et al., 2020; Garrigues et al.,
71 2020; Xiong et al., 2021). More recently, Huang et al. described the 6-months consequences
72 of COVID-19 and reported presence of fatigue or myalgia in 63% of patients in an inpatients
73 single-center cohort in China (Huang et al., 2021).

74 Here in a multicenter prospective cohort in France, we assessed self-reported symptoms 6
75 months after hospital admission for COVID-19, using the influenza severity scale and described
76 the evolution following diagnosis. We also assessed anxiety, depression and health-related
77 quality of life (HRQL) to measure the impact of these symptoms on patients' global health.

78

79 **Material and Methods**

80 *Study oversight*

81 The French COVID cohort (NCT04262921) is a national prospective multi-center cohort study
82 enrolling hospitalized patients with a RT-PCR virologically-confirmed COVID-19 in 80
83 hospitals in France since January 24, 2020 (Yazdanpanah and French COVID cohort
84 investigators and study group, 2021). Briefly, patients were followed-up from hospital
85 admission (D1) throughout hospitalization for COVID-19 and at discharge, 2 to 4 weeks after
86 discharge, month 3 (M3) and 6 (M6). The assessment of symptoms, anxiety, depression and
87 health-related quality of life using self-administered questionnaires were proposed to the
88 patients at each visit. All adult patients who fulfilled the self-administered symptoms

89 questionnaire at months 3 (M3) and 6 (M6) by March 22nd, 2021 were included in the present
90 analysis.

91 *Procedures*

92 The self-administered symptoms questionnaire recorded the presence and the severity of the 7
93 following symptoms: fatigue, myalgia, headache, cough, nasal obstruction, sore throat and
94 feverishness. All symptoms were rated by the patient using a four-point scale (0, none; 1, mild;
95 2, moderate; 3, severe) using a self-administered questionnaire previously used in influenza
96 infection (Duval et al., 2010; Hayden et al., 1997). For each date of evaluation, a total score
97 ranging from 0 to 21 was obtained by summing the points attributed for each symptom. Based
98 on the definition of symptom alleviation used in influenza, reporting of at least one moderate
99 or severe symptom was considered to reflect an abnormal state of health. Four additional
100 COVID-19 symptoms (joint pain, dyspnea, anosmia and ageusia) which were not included in
101 the influenza questionnaire were also collected by the practitioner (thereafter referred to as
102 “practitioner reported symptoms”) during M3 and M6 visits.

103 Anxiety and depression symptoms were assessed using the Hospital Anxiety and Depression
104 scale (HADS), subdivided in the HADS-Anxiety (HADS-A) and the HADS-Depression
105 (HADS-D) scales. Both scales contain 7 questions scored by the patients on a 4-point Likert
106 scale (0–3) with higher scores indicating more severe anxiety/depression. The items scores were
107 summed up separately for HADS-A and HADS-D, leading to two scores ranging between 0
108 and 21. Scores greater than or equal to 11 points indicated abnormal levels (Zigmond and
109 Snaith, 1983).

110 Health-related quality of life (HRQL) was assessed using the SF-12 Health Survey (Gandek et
111 al., 1998) including a Physical Component Summary (PCS) HRQL score and a Mental
112 Component Summary (MCS) HRQL score. These scores range from 0 to 100, with a high value

113 indicating good HRQL. A patient was defined as having an altered physical (or mental) HRQL
114 if his PCS (or MCS) was lower than the 25th percentile of the score distribution in the general
115 French population of the same age group and gender (Carrieri et al., 2003).

116 The self-administered questionnaires were collected using REDCap electronic data capture
117 tools (Harris et al., 2009) with a secured personal access given to each patient after hospital
118 discharge.

119 *Statistical analyses*

120 Categorical variables were summarized as counts (percentage) and frequency distributions were
121 compared with the Chi-square, the Fisher exact or the McNemar for paired samples tests as
122 appropriate. Continuous variables were expressed as median [interquartile range (IQR)] unless
123 otherwise specified and compared with the Mann-Whitney U test. Prevalence of symptoms are
124 given with their 95% confidence interval, estimated by using the exact Clopper-Pearson
125 method.

126 To assess the representativeness of the population of patients who fulfilled the questionnaire,
127 demographic characteristics, comorbidities and clinical data at hospital admission were
128 compared between patients who fulfilled or not the 7-symptoms questionnaire at M3 and M6
129 using logistic multivariate regression models. The latter were adjusted on age, sex and ethnic
130 group, in order to assess for confounding variables.

131 Associations between having at least one moderate or severe symptom at M6 and baseline
132 characteristics were assessed through univariate logistic regressions. All Variables were putted
133 in the multivariate models. Variable selection was then performed by starting with a model that
134 included all covariates and then excluding those that did not improve the overall fit as measured
135 by the likelihood ratio test (LRT). A P-value cut-off point of .05 was used as stopping rule for
136 this backward manual selection. Two-way interactions between risk factors kept in the

137 multivariate analysis (including “ICU during the acute phase”) were tested. No imputation
138 strategy was applied for missing data. Any case that has a missing value was discarded from
139 the analysis.

140 All tests were 2-sided and p-values $<.05$ were considered significant. All statistical analyses
141 were performed using R version 4.0.2.

142 *Ethics and regulatory issues*

143 The study was conducted with the understanding and the consent of each participant or its
144 surrogate. The French Ethics Committee (CPP-Ile-de-France VI, ID RCB: 2020-A00256-33)
145 has approved the study protocol.

146

147 **Results**

148 *Patient characteristics*

149 Of 3,497 French COVID cohort adult participants enrolled between January 24th and September
150 22nd, 2020, in order to allow for a six-month follow-up, 392 died during initial hospitalization
151 and 45 between hospital discharge and M6. Out of the 3,060 patients alive at M6, 324 patients
152 fulfilled the 7-symptoms questionnaire at M3 and M6 and represented the study population
153 (Figure S1). The median time interval between hospital admission and M6 assessment was 185
154 [182-191] days.

155 The main demographic comorbidities and characteristics at admission of these 324 patients are
156 presented in Table 1. The median age was 61 years [52-69], and 205 (63%) were men. The most
157 common comorbidities were hypertension (n=110, 35%), chronic pulmonary disease (n=56,
158 18%), chronic cardiac disease (n=57, 18%), obesity (n=53, 17%) and diabetes (n=48, 15%).
159 Fifty-four patients (19%) were admitted to intensive care unit (ICU) at any time during
160 hospitalization.

161 As compared to the 2,736 patients who did not complete the 7-symptoms questionnaire at M3
162 and M6, the 324 patients were younger, less likely to have diabetes, chronic kidney disease at
163 admission, or to have been hospitalized in ICU (Table S1).

164 *Symptoms at M6*

165 At Month 6, 187 (58%) of the 324 patients who completed the self-administered questionnaire
166 reported at least one persistent symptom: 80 (25%) reported one symptom, 48 (15%) two and
167 59 (18%) ≥ 3 symptoms. A total 7-symptoms score ≥ 3 was found in 73 (22.5%, 95% CI =
168 [18.1% ; 27.5%]) patients. Among these 187 patients, median [IQR] total 7-symptoms score
169 was 2 [1-3].

170 Among the 7 self-reported symptoms, the most frequent was fatigue (n=151, 47%) which was
171 scored as mild in 103 (68%), moderate in 32 (21%) and severe in 16 (11%) (Figure 1). Myalgia
172 was the second most frequent symptom (n=74, 23%) which was scored as mild in 46 (62%),
173 moderate in 22 (30%) and severe in 6 (8%) patients. Either of the 2 symptoms was reported in
174 160 (49%) patients. Among the 187 patients with at least 1 symptom, the severity of the reported
175 symptoms was scored at most mild in two thirds (n=125, 67%), moderate in 44 (23%) and
176 severe in 18 (10%).

177 Reporting of a moderate or severe symptom at M6 was only associated with female gender (OR
178 = 1.98, 95% CI = 1.13 - 3.47) in multivariate analysis after variable selection, while age (OR =
179 0.94, 95% CI = 0.52 - 1.65), hospitalization in ICU (OR = 0.67, 95% CI = 0.28 - 1.44), or
180 having ≥ 2 comorbidities (OR=1.13, 95% CI = 0.62 – 2.03) were not (Table S2).

181 Among the 324 analyzed patients, 301 (93%) had practitioner examination available at M6: the
182 practitioner reported joint pain in 53 (18%), dyspnea in 64 (21%), anosmia in 24 (8%), and
183 ageusia in 21 (7%) patients.

184 *HADS and HRQL at M6*

185 HADS and SF-12 Health survey were completed in 225/324 (69%) patients at M6. Median
186 HADS-Anxiety score was 4.0 [3.0; 7.0]; 24 (11%) patients had a HADS-Anxiety score above
187 or equal to 11. Median HADS-Depression score was 2.0 [1.0; 5.0]; 18 (8%) patients had a
188 HADS-Depression above or equal to 11.

189 Median Physical HRQL score was 50.2 [42.2 – 53.9]; 79 (35%, 95% CI [29 - 42%]) of the
190 patients had physical HRQL lower than the 25th percentile of the distribution of the score in the
191 general French population (p=0.0005); 66% of patients with a 7-symptoms score ≥ 3 at M6 has
192 also an impaired physical HRQL.

193 Median mental HRQL was 51.2 [42.3 – 55.8]; 59 (26%, 95% CI [21 - 32%]) of patients had a
194 mental HRQL lower than the 25th percentile of the distribution of the score in the general French
195 population, which was not statistically different (p=0.7).

196

197 *Global burden of the disease at Month 6*

198 The combinations of 7-symptoms score ≥ 3 , anxiety, depression, and impaired physical and
199 mental HRQL at M6 are presented in Figure S2; 116/225 (52%) patients presented at least one
200 modality among total 7-symptoms score ≥ 3 , HADS-Anxiety score ≥ 11 , HADS-Depression
201 score ≥ 11 , impaired physical HRQL and impaired mental HRQL. Most frequent modality and
202 combinations were impaired physical HRQL, total 7-symptoms score ≥ 3 , and combination of
203 impaired physical HRQL with total 7-symptoms score ≥ 3 . Twenty-eight of the 135 (21%)
204 patients who had professional activities before admission had not returned to work at M6.

205 *M6 evaluation as compared to previous evaluations*

206 The proportions of patients who self-reported symptoms regardless of their severity at D1,
207 discharge, 2 to 4 weeks after discharge, M3 and M6 are shown in Figure 2a. Self-reporting of
208 each symptom was not significantly different between M3 and M6. Similar results were
209 obtained in a sensitivity analysis excluding patients who were admitted to ICU at any time
210 during hospitalization (Figure S3). Reporting of each symptom according to its severity at M3
211 and M6 are represented Figure 1.

212 Evolution of 7-symptoms total score over time is shown in Figure 2b. Of note, median 7-
213 symptoms score in patients with at least one symptom at M6 was 9 [5 – 11], 3 [1 -6], 2 [1 – 5],
214 2 [1 – 3], 2 [1 – 4] at D1, discharge, 2 to 4 weeks after discharge, M3 and M6, respectively
215 (Figure S4).

216 Proportion of patients with a total 7-symptoms score ≥ 3 was not significantly different between
217 M3 (24% [19-29%]) and M6 (23% [18-28%]) (p=0.8). Rates of practitioner-reported
218 symptoms, anxiety, depression and physical and mental HRQL remained also stable between
219 M3 and M6 (Table 2).

220

221 **Discussion**

222 To our knowledge, this is the first study assessing the severity of persistent symptoms 6 months
223 after hospital admission for COVID-19 and their evolution since admission. In our population,
224 56% of patients still reported at least one symptom at M6, but less than 7% rated any symptom
225 as severe. Except for female gender, we did not identify any other factor linked to high burden
226 of symptoms at M6 that could prompt specific follow-up management options, and thus
227 improve patients' outcome.

228 The French COVID cohort was launched at the very beginning of COVID-19 pandemic when
229 the first cases were identified in France and recruited patients in all types of French hospitals,
230 throughout France including overseas territories. The database extraction date of March 22,
231 2021 made it possible to assess the health status of patients included between January 24, 2020
232 and September 22, 2020. The younger age of the population who responded to the questionnaire
233 compared to those who did not, was probably explained by a greater propensity of younger
234 people to complete a questionnaire on the WEB. The lower age of the respondents was logically
235 associated with a lower proportion of comorbidity and of ICU admission.

236 The proportion of patients (approximately one out of two) who reported at least one symptom
237 at M6 using the 7-symptom influenza questionnaire was high, with most common reported
238 symptoms being fatigue and myalgia; this is consistent with previous studies on mid-term
239 follow up of SARS-CoV-2 (Carfi et al., 2020; Garrigues et al., 2020; Huang et al., 2021; Xiong
240 et al., 2021) or long term follow-up of other SARS survivors (Lam et al., 2009; Lee et al., 2007;
241 Tansey et al., 2007), although the range of values was wide. This large range of reported
242 symptoms could be due to differences in the characteristics of patients included in the cohort
243 or filling the forms, such as the age, the proportions of women or of patients with comorbidities
244 (Huang et al., 2021).

245 Since we did not know patients' symptoms before they experienced COVID, we were not able
246 to assess to what extent, the M6 reported symptoms were related to the COVID episode or to a
247 pre-existing condition. For this reason, and taking into account the experience of self-
248 questionnaire performed in influenza, we assessed the severity of the symptoms and defined
249 symptom alleviation as seven symptoms were scored absent or only mild (Duval et al., 2010;
250 Hayden et al., 1997). This led to a fifth of the patients being considered to have a poor M6
251 clinical outcome. Beyond the proportion attributable to the COVID that cannot be precisely
252 estimated, on one hand, the association between a score higher than three and a poor physical

253 quality of life, and on the other hand, the significantly higher proportion of subjects with an
254 impaired physical quality of life compared to a control population argue for the COVID's
255 responsibility for the symptoms reported by patients. This is all the more to be taken into
256 account as the persistence of symptoms as well as the alteration in quality of life at M3 and M6
257 did not suggest a rapid improvement and invites to extend the patient follow-up beyond M6.
258 Considering the persistence of altered quality of life between M3 and M6, especially regarding
259 mental health, supportive cares should be taken as early as 3 months after hospitalization in
260 patients who need it.

261 Female gender was found to be the sole risk factor of persistence of moderate or severe
262 symptom, consistently with previous studies in SARS-CoV-2 survivors (Ghosn et al., 2021;
263 Huang et al., 2021; Xiong et al., 2021), whereas women are prone to develop less severe acute
264 COVID than men (Richardson et al., 2020; Yazdanpanah and French COVID cohort
265 investigators and study group, 2021; Zhou et al., 2020). The pathophysiology mechanisms
266 underlying this finding remain to be explored. Neither ICU admission, nor reporting of
267 moderate or severe symptoms at admission which could be considered as a proxy of the disease
268 severity at admission, were associated with poor clinical outcome at M6.

269 This study has several limitations. First, M3 and M6 self-administered questionnaires were not
270 completed by all survivors. On one hand, as the population was younger and therefore less
271 prone to have been admitted to ICU during hospitalization, our study might underestimate the
272 proportion of COVID-19 survivors with poor clinical outcome at M6 post-hospitalization
273 (Huang et al., 2021). On the other hand, one cannot ruled out that the propensity to complete a
274 questionnaire is higher among those with symptoms than those without. Second, M6 assessment
275 took place between end of July, 2020 and March, 2021, a semester during which the health
276 situation in France deteriorated with an alternation of curfews and lockdown measures, thus
277 promoting an anxiety-provoking climate. Differences in the patients' characteristics of those

278 evaluated and those not, specific health care facilities bottleneck at the time of follow-up,
279 improvement of support of care strategies over the outbreak and evolution of virus
280 characteristics did not allow us to impede extrapolation of our results to all survivors of
281 COVID-19. Third, the 7-symptoms questionnaire was previously used to assess symptom
282 alleviation in acute phase of influenza disease, but not long-term sequelae. However, when
283 focusing on patients with a total score above or equal to 3 at M6, the same number of patients
284 had a poor outcome and the determinants remained the same.

285 Identifying patients needing specific care after COVID-19 could be beneficial in terms of public
286 health. The use of a simple web-based questionnaire with a scale of severity could be helpful
287 to identify patients requiring appropriate medical care including psychological support within
288 months following recovery, especially since close follow-up of all COVID-19 survivors after
289 hospital discharge seems difficult to achieve in the context of successive epidemic waves and
290 congestion in health-care facilities.

291 In conclusion, persistence of symptoms in more than half of the patients and impaired
292 physical health-related quality of life at M6 promotes long-term follow-up beyond six months
293 following recovery.

294 **Acknowledgment**

295 **Sources of funding:** This work was supported by the REACTing (REsearch & ACTION
296 emergING infectious diseases) consortium and by a grant of the French Ministry of Health
297 (PHRC n°20-0424).

298 **Group Information:** The members of the French COVID cohort study and investigators
299 groups are provided in Supplementary Material.

300 **Additional Information:** The study included a scientific advisory board composed of Dominique
301 COSTAGLIOLA, Astrid VABRET, Hervé RAOUL and Laurence WEISS.

302

303 **Ethics and regulatory issues**

304 The study was conducted with the understanding and the consent of each participant or its
305 surrogate. The French Ethics Committee (CPP-Ile-de-France VI, ID RCB: 2020-A00256-33)
306 has approved the study protocol.

307

308 **References**

309 Carfi A, Bernabei R, Landi F, for the Gemelli Against COVID-19 Post-Acute Care Study
310 Group. Persistent Symptoms in Patients After Acute COVID-19. *JAMA* 2020;324:603.
311 <https://doi.org/10.1001/jama.2020.12603>.

312

313 Carrieri P, Spire B, Duran S, Katlama C, Peyramond D, François C, et al. Health-Related
314 Quality of Life After 1 Year of Highly Active Antiretroviral Therapy: *JAIDS J Acquir Immune*
315 *Defic Syndr* 2003;32:38–47. <https://doi.org/10.1097/00126334-200301010-00006>.

316

317 Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of
318 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation
319 Protocol: prospective observational cohort study. *BMJ* 2020;369:m1985.
320 <https://doi.org/10.1136/bmj.m1985>.

321

322 Duval X, van der Werf S, Blanchon T, Mosnier A, Bouscambert-Duchamp M, Tibi A, et al.
323 Efficacy of oseltamivir-zanamivir combination compared to each monotherapy for seasonal
324 influenza: a randomized placebo-controlled trial. *PLoS Med* 2010;7:e1000362.
325 <https://doi.org/10.1371/journal.pmed.1000362>.

326

327 Gandek B, Ware JE, Aaronson NK, Alonso J, Apolone G, Bjorner J, et al. Tests of Data Quality,
328 Scaling Assumptions, and Reliability of the SF-36 in Eleven Countries. *J Clin Epidemiol*
329 1998;51:1149–58. [https://doi.org/10.1016/S0895-4356\(98\)00106-1](https://doi.org/10.1016/S0895-4356(98)00106-1).

330

331 Garrigues E, Janvier P, Kherabi Y, Le Bot A, Hamon A, Gouze H, et al. Post-discharge
332 persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J*
333 *Infect* 2020;81:e4–6. <https://doi.org/10.1016/j.jinf.2020.08.029>.

334

335 Ghosn J, Piroth L, Epaulard O, Le Turnier P, Mentré F, Bachelet D, et al. Persistent COVID-
336 19 symptoms are highly prevalent 6 months after hospitalization: results from a large
337 prospective cohort. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis*
338 2021;27:1041.e1-1041.e4. <https://doi.org/10.1016/j.cmi.2021.03.012>.

339

340 Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data
341 capture (REDCap)—A metadata-driven methodology and workflow process for providing
342 translational research informatics support. *J Biomed Inform* 2009;42:377–81.
343 <https://doi.org/10.1016/j.jbi.2008.08.010>.

344

345 Hayden FG, Osterhaus ADME, Treanor JJ, Fleming DM, Aoki FY, Nicholson KG, et al.
346 Efficacy and Safety of the Neuraminidase Inhibitor Zanamivir in the Treatment of
347 Influenzavirus Infections. *N Engl J Med* 1997;337:874–80.
348 <https://doi.org/10.1056/NEJM199709253371302>.

349

350 Huang C, Huang L, Wang Yeming, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-
351 19 in patients discharged from hospital: a cohort study. *Lancet Lond Engl* 2021;397:220–32.
352 [https://doi.org/10.1016/S0140-6736\(20\)32656-8](https://doi.org/10.1016/S0140-6736(20)32656-8).
353

354 Lam MH-B, Wing Y-K, Yu MW-M, Leung C-M, Ma RCW, Kong APS, et al. Mental
355 morbidities and chronic fatigue in severe acute respiratory syndrome survivors: long-term
356 follow-up. *Arch Intern Med* 2009;169:2142–7.
357 <https://doi.org/10.1001/archinternmed.2009.384>.
358

359 Lee AM, Wong JGWS, McAlonan GM, Cheung V, Cheung C, Sham PC, et al. Stress and
360 psychological distress among SARS survivors 1 year after the outbreak. *Can J Psychiatry Rev*
361 *Can Psychiatr* 2007;52:233–40. <https://doi.org/10.1177/070674370705200405>.
362

363 Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al.
364 Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized
365 With COVID-19 in the New York City Area. *JAMA* 2020;323:2052.
366 <https://doi.org/10.1001/jama.2020.6775>.
367

368 Tansey CM, Louie M, Loeb M, Gold WL, Muller MP, de Jager J, et al. One-year outcomes and
369 health care utilization in survivors of severe acute respiratory syndrome. *Arch Intern Med*
370 2007;167:1312–20. <https://doi.org/10.1001/archinte.167.12.1312>.
371

372 Xiong Q, Xu M, Li J, Liu Y, Zhang J, Xu Y, et al. Clinical sequelae of COVID-19 survivors in
373 Wuhan, China: a single-centre longitudinal study. *Clin Microbiol Infect* 2021;27:89–95.
374 <https://doi.org/10.1016/j.cmi.2020.09.023>.
375

376 Yazdanpanah Y, French COVID cohort investigators and study group. Impact on disease
377 mortality of clinical, biological, and virological characteristics at hospital admission and
378 overtime in COVID-19 patients. *J Med Virol* 2021;93:2149–59.
379 <https://doi.org/10.1002/jmv.26601>.
380

381 Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality
382 of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*
383 2020;395:1054–62. [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3).
384

385 Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*
386 1983;67:361–70. <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>.

Figure legends

Figure 1: Frequency and severity of self-reported symptoms in patients from the French COVID cohort at 3 and 6 months (M3 and M6) after hospital admission.

Figure 2: Evolution of 7-symptoms over time in patients from the French COVID cohort.

Table 1: Baseline characteristics in patients of the French COVID cohort who fully completed the 7-symptoms questionnaire 6 months after diagnostic confirmation.

Table 2: Practitioner-reported symptoms, Hospital Anxiety and Depression scale (HADS), and Health-related quality of life (HRQL) at 3 and 6 months (M3 and M6) after hospital admission.

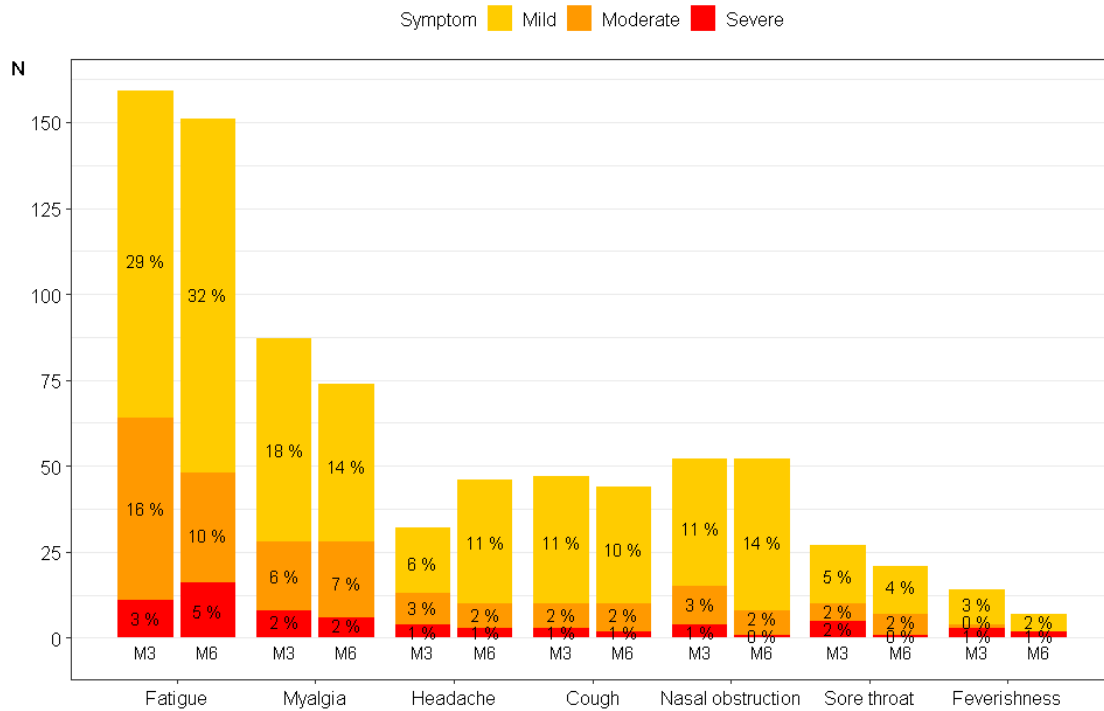


Figure 1: Frequency and severity of self-reported symptoms in patients from the French COVID cohort at 3 and 6 months (M3 and M6) after hospital admission.

Barplot representing each symptom severity for the N = 324 patients who fully completed their 7-symptoms questionnaire at 3 and 6 months after diagnostic confirmation. The score for each symptom is given on a four-degree scale going from 0 to 3 (i.e. none, mild, moderate, severe). The corresponding percentages are given in each colored bar. Of note, patients presenting no symptom at all are not represented on this graph.

Figure 2a.

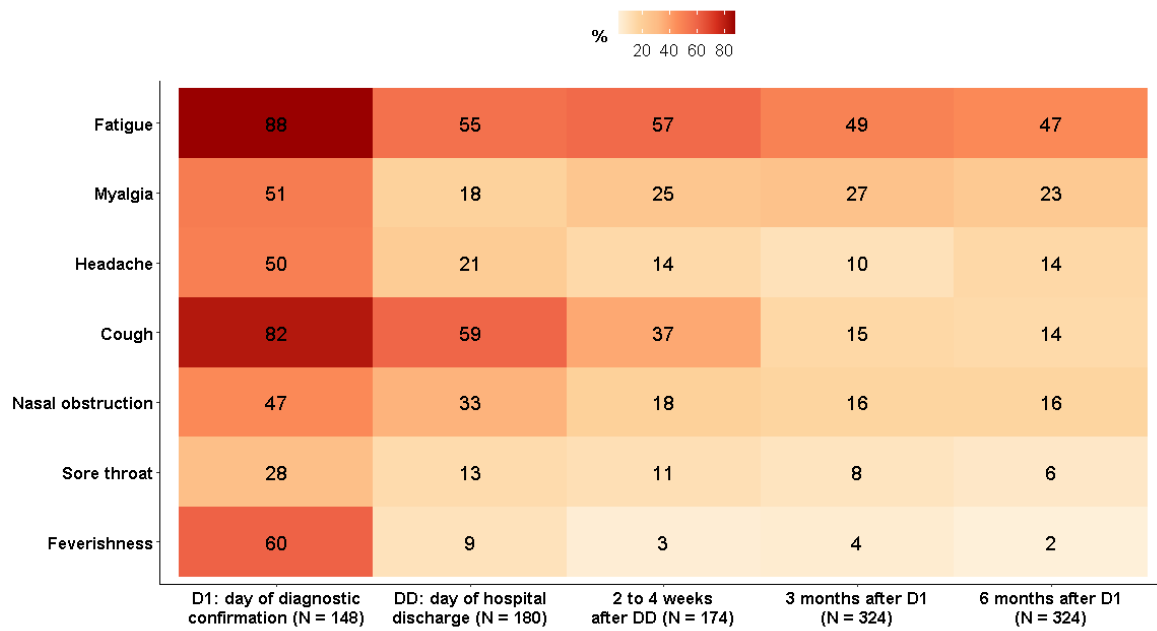


Figure 2b.

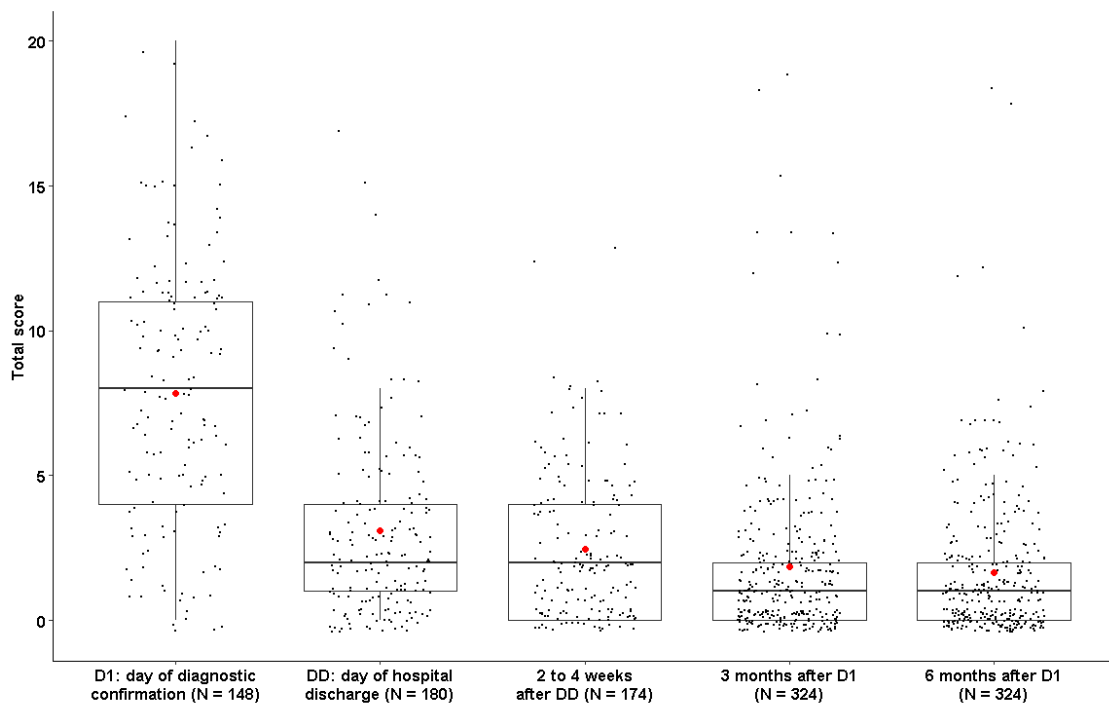


Figure 2: Evolution of 7-symptoms over time in patients from the French COVID cohort.

a. Heatmap of the 7 self-reported symptoms. For a given symptom at a given time-point, the box is colored according to the proportion of patients reporting this symptom, and the percentage is displayed in each box. P-values of McNemar test for paired samples comparing proportions of patients reporting symptoms at 3 and 6 months (M3 and M6) after hospital admission are: Fatigue, $p=0.5$; Myalgia, $p=0.2$; Headache, $p=0.06$; Cough, $p=0.8$; Nasal obstruction, $p=1$; Sore throat, $p=0.3$; Feverishness, $p=0.2$. **b.** Boxplots of the total score obtained by adding the scores for each of the 7 self-reported symptoms. The score for each symptom is given on a four-degree scale going from 0 to 3, the total score is thus comprised between 0 and 21. The red dots represent the mean values.

Table 1: Baseline characteristics in patients of the French COVID cohort who fully completed the 7-symptoms questionnaire 6 months after diagnostic confirmation.

Category	n/ntot (%) N = 324
Male Sex	205/324 (63)
Ethnic group	
White	212/264 (80)
Black	25/264 (10)
Arab	19/264 (7)
Asian	4/264 (2)
Other	4/264 (2)
Age	
Adult (18-64)	200/324 (62)
Elders (>64)	124/324 (38)
Smoking history	
Current smoker	19/265 (7)
Never smoked	171/265 (64)
Former smoker	75/265 (28)
Health worker	31/306 (10)
Intensive care unit	
At any time	54/286 (19)
At admission	33/302 (11)
Comorbidities	
Diabetes	48/311 (15)
Hypertension	110/311 (35)
Obesity	53/304 (17)
Chronic cardiac disease	57/311 (18)
Chronic pulmonary disease	56/311 (18)
Chronic kidney disease	16/311 (5)
Moderate or severe chronic liver disease	3/311 (1)
Mild chronic liver disease	4/311 (1)
Chronic neurological disorder	20/311 (6)
Malignant neoplasm	20/310 (6)
Chronic haematologic disease	16/311 (5)
AIDS/HIV	1/311 (0.3)
Dementia	1/311 (0.3)
Rheumatologic disorder	16/311 (5)

Category	n/ntot (%) N = 324
Number of comorbidities*	
0	99/311 (32)
1	94/311 (30)
2 or more	118/311 (38)

* Comorbidities were defined using the Charlson comorbidity index, with the addition of clinician-defined obesity.

Table 2: Practitioner-reported symptoms, Hospital Anxiety and Depression scale (HADS), and Health-related quality of life (HRQL) at 3 and 6 months (M3 and M6) after hospital admission.

	M3	M6
Practitioner-reported symptoms N=301		
Joint pain	51 (17%)	53 (18%)
Dyspnea	73 (24%)	64 (21%)
Anosmia	24 (8%)	24 (8%)
Ageusia	25 (8%)	21 (7%)
At least 1 among above symptom	122 (41%)	111 (37%)
HADS N= 225		
HADS-A ≥ 11	26 (12%)	24 (11%)
HADS-D ≥ 11	18 (8%)	18 (8%)
SF-12 N=225		
Impaired physical HRQL	95 (42%)	79 (35%)
Impaired mental HRQL	62 (28%)	59 (26%)

Note: HADS is divided into an anxiety (HADS-A) and depression (HADS-D) subscale. Each HADS item was scored on a 4-point Likert scale (0–3) with higher scores indicating more severe anxiety/depression. The items scores were summed up separately for HADS-A and HADS-D, leading to two scores ranging between 0 and 21. Scores between 11–21 points indicated abnormal levels. SF-12: an individual was defined as having an impaired physical (or mental) health-related quality of life if his Physical Component Summary (or Mental Component Summary) was lower than the 25th percentile of the distribution of the score in the general French population of the same age group and gender.