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# Prevalence of Post-Acute COVID-19 Symptoms Twelve Months after Hospitalisation in Participants Retained in Follow-up: Analyses Stratified by Gender from a Large Prospective Cohort

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1 **Prevalence of post-acute COVID-19 symptoms twelve months after hospitalisation in**  
2 **participants retained in follow-up: analyses stratified by gender from a large prospective**  
3 **cohort**

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5  
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61 groups is provided in the Supplementary Material.

62

63 **Word count: abstract 272 words ; text 2597 words.**

**64 Abstract**

65

**66 Objectives**

67 Persistent post-acute COVID-19 symptom (PACS) have been reported up to 6-months (M6)  
68 after hospital discharge. Here we assessed, in the longitudinal prospective national French  
69 COVID cohort, symptoms that persisted 12-months (M12) after admission for COVID-19.

70

**71 Methods**

72 Hospitalized patients with a virologically-confirmed COVID-19 were enrolled. Follow-up was  
73 planned until M12 post-admission. Associations between persistence of  $\geq 3$  PACS at M12 and  
74 clinical characteristics at admission were assessed through logistic regression according to  
75 gender.

76

**77 Results**

78 We focused on participants enrolled between January 24<sup>th</sup> and July 15<sup>th</sup> 2020, in order to  
79 allow M12 follow-up. M12 data were available for 737 participants. Median age was 61  
80 years, 475 (64%) were men and 242/647 (37%) were admitted to ICU during the acute phase.  
81 At M12, 194/710 (27%) of participants had  $\geq 3$  persistent PACS, mostly fatigue, dyspnea and  
82 joint pain. Among those who had a professional occupation before the acute phase 91/339  
83 (27%) were still on sick leave at M12. Presence of  $\geq 3$  persistent PACS was associated with  
84 female gender, both anxiety and depression, impaired health-related quality of life (HRQL)  
85 and mMRC scale  $< 57$ . Compared to men, women more often reported presence of  $\geq 3$  persistent  
86 PACS (98/253, 39% vs 96/457, 21%), depression and anxiety (18/152, 12% vs 17/268, 6% and  
87 33/156, 21% vs 26/264, 10%, respectively), impaired physical HRQL (76/141, 54% vs  
88 120/261, 46%). Women had less often returned to work than men (77/116, 66% vs 171/223,  
89 77%).

90

**91 Conclusions**

92 A fourth of individuals admitted to hospital for COVID-19 still had  $\geq 3$  persistent PACS at M12  
93 post-discharge. Women reported more often  $\geq 3$  persistent PACS, suffered more from anxiety  
94 and depression, and had less often returned to work than men.

## 95 **Introduction**

96 Clinical presentation of SARS-CoV-2 infection ranges from asymptomatic cases to severe  
97 distress respiratory syndrome. When symptomatic, the acute phase commonly features cough,  
98 dyspnea, flu-like symptoms, myalgia, joint pain, gastro-intestinal symptoms and  
99 anosmia/ageusia (1). Several studies have reported the persistence of COVID-related symptoms  
100 following acute phase. In 2021, WHO has developed a clinical definition of post-COVID  
101 condition(2). According this definition, the proportion of patients experiencing at least one  
102 persistent post-acute COVID-19 symptom (PACS) reaches 66% at two months, 53% at  
103 four months and 32% at seven months post-infection in outpatients (3–5), and rises up to  
104 62 to 68% at six months post-infection in patients hospitalized during the acute phase (6,7).  
105 It was shown that ICU stay (with or without COVID-19) was associated with worse long-  
106 term outcome (8).  
107 Few data are available after 12 months post-infection with design heterogeneity (7,9–11).  
108 In the Chinese cohort with a 12-month follow-up as well as in the study performed in  
109 France with a six-month follow-up (6,7), female gender was associated with the persistence  
110 of PACS. Furthermore, it is known that, at the same age, women report poorer health than  
111 men in subjective health assessments, generally and in the COVID-19 specific setting (12–  
112 15).Therefore, to add relevant evidence to the current literature we report results stratified  
113 by gender from a large national multicentre cohort where COVID-19 patients were  
114 followed prospectively from hospital admission up to 12 months regardless development  
115 of PACS or not.

116

## 117 **Patients and methods**

### 118 **Study oversight and data collection**

119 The design of this national multicentre prospective cohort (French COVID Cohort) has  
120 been described elsewhere (16). Briefly, hospitalized patients with a virologically confirmed  
121 COVID-19 were enrolled in the cohort (registered in clinicaltrials.gov NCT04262921); ethics  
122 approval was obtained from the French Ethic Committee CPP-Ile-de-France-VI (ID-RCB:  
123 2020-A00256-33). Patients were co-included in the European H2020 ORCHESTRA  
124 project.

125 Follow-up was planned with a physician's visit at month (M)3, M6 and M12 after hospital  
126 admission. Comorbidities were assessed according to the 4C Mortality Score (17).

127 We asked every center to check the French register of deceased persons  
128 (<https://arbre.app/en/insee>) in order to have the vital status (causes of death was not available)  
129 of those who did not attend follow-up visits.

130

### 131 **Study definitions and outcomes**

132 At each visit, the following ten COVID-19 symptoms were collected (fatigue, dyspnea at  
133 rest, joint pain, myalgia, headache, rhinorrhoea, cough, sore throat, ageusia and anosmia).

134 In addition, a physical exam and a 6-minute walking test (6MWT) were performed.

135 At M12 visit, a measure of the functional independence using the modified Rankin scale  
136 (mRS) (0 indicates no symptoms, 5 severe disability) and an assessment of muscle strength  
137 of each limb using the modified Medical Muscle Research council Scale (mMRC) (score  
138 from 0 to 60) were also performed (18). Patients were also interviewed on health-related  
139 quality of life (HRQL) with the 12-items Short Form Health Survey (SF-12) and on their  
140 psychological distress (Health Anxiety Depression Scale, HADS). For SF-12, an individual  
141 was defined as having an impaired physical (or mental) HRQL if his Physical (or Mental)  
142 Component Summary (was lower than the 25<sup>th</sup> percentile of the distribution in the general  
143 French population of the same age and gender. HADS is divided into anxiety (HADS-A)  
144 and depression subscale (HADS-D). Each HADS item was scored on a 4-point Likert scale  
145 with higher scores indicating more severe anxiety/depression. Scores  $\geq 11$  indicated  
146 abnormal levels.

147

### 148 **Statistical analysis**

149 All analyses were stratified by gender. Associations between presence of PACS at M12  
150 (defined by the presence of  $\geq 3$  of the ten COVID-19 symptoms) and baseline characteristics  
151 were assessed through bivariate logistic regressions. The final multivariate models were  
152 developed by starting with a model that included all covariates with  $< 10\%$  of missing  
153 values and  $p < 0.20$  and then excluding variables that did not improve the overall fit as  
154 measured by the  $-2\log$  likelihood ratio test.

155 Prevalence of symptoms are given with their 95% CI (exact Clopper-Pearson method). For  
156 patients who have both evaluation at M6 and M12, we compared the proportion of each  
157 symptom through McNemar paired tests. We compared the baseline characteristics between  
158 alive patients who attended the M12 visit to the eligible patients who did not (excluding  
159 deceased patients) using a chi-square test. We computed the observed proportion of  $\geq 3$  PACS  
160 and its 95% CI according to each combination of the risk factors found in the multivariate model

161 to impute patients without M12 visit. Finally, separately in women and men, as a sensitivity  
162 analysis, we obtained three estimations of the proportion of patients with  $\geq 3$  persistent PACS  
163 on the overall population of eligible patients for the M12 visit using three imputations: the mean  
164 proportion and proportions from the lower and the upper bound of the 95%CI. All tests were  
165 2-sided and analyses were performed with R software.

166

## 167 **Results**

168 We focused on participants enrolled between January 24<sup>th</sup> and July 15<sup>th</sup> 2020, in order to  
169 allow for a 12-month follow-up. Out of the 3426 participants enrolled during this period,  
170 391 died (11%) during initial hospitalization, 67 died (2%) between hospital discharge and  
171 M12. By September 2021, M12 data were available for 737 patients. The baseline and M12  
172 characteristics for the 737 patients (262 women and 475 men), are summarized in **Table 1**.

173

### 174 ***Global population***

175 At M12 visit, 194/710 (27%, 95%CI: 24-31%) participants had  $\geq 3$  persistent PACS. Fatigue  
176 (327/705, 46%, 95%CI: 43-50%), dyspnea (235/704, 33%, 95%CI: 30-37%) and joint pain  
177 (146/703, 21%, 95%CI: 17-24%) were the 3 most frequently reported symptoms  
178 individually or in combination. Women reported myalgia frequently in addition to latter 3  
179 symptoms (**eFigure 1**). Pulmonary auscultation was reported as “normal” in 507/634  
180 patients (87%, 95%CI: 83-89%). In those with abnormal pulmonary auscultation, persistent  
181 crackles were reported in 19/74 (26%) and wheezing in 10/74 (14%) cases, respectively.  
182 The median percentage of predicted value of the 6MWT was 88% (IQR: 74;100) for the  
183 163 patients who did this test. Of note, this was lower in the 61 patients who reported  
184 dyspnea compared to those who did not (85% [IQR: 71;99] vs. 95% [IQR: 76;101],  
185  $p=0.04$ ). When focusing on dyspnea at rest, persistent dyspnea at M12 was reported in 187/578  
186 (32%) of the subset of individuals with no pulmonary chronic condition. Globally, the  
187 presence of  $\geq 3$  persistent PACS was associated with female gender (data not shown because  
188 all analysis were presented by gender), both anxiety and depression, impaired HRQL  
189 (physical and mental), mRS  $\geq 2$  (**Supplementary Table 1**). Anxiety at M12 was associated  
190 with female gender (OR=2.46, 95%CI: 1.41-4.32), not getting back to work (OR=2.72,  
191 95%CI: 1.17-6.27) and dyspnea (OR=3.49, 95%CI: 1.98-6.27) (**Supplementary Table 2**).  
192 Six hundred and sixty-three patients attended both M6 and M12 visits. Between the two  
193 visits, there was no global evolution of the frequency of the ten PACS except for



194 rhinorrhoea and cough that were more often reported at M12 in women only (**Figure 1**).  
195 Some patients reported an onset of symptoms at M12 compared to M6: 95/339 (28%,  
196 95%CI: 33-46%) patients who did not have fatigue at M6 reported fatigue at M12, 101/425  
197 (24%, 95%CI: 20-28%) for dyspnea and 81/490 (17%, 95%CI: 13-20%) for joint pain.

198

### 199 ***Results according to gender***

200 Compared to men, women more often reported the presence of  $\geq 3$  persistent PACS (98/253,  
201 39%, 95%CI: 33-45% vs. 96/455, 21%, 95%CI: 17-25%), depression and anxiety  
202 (respectively, 18/152, 12%, 95%CI: 7-18% vs. 17/268, 6%, 95%CI: 4-10% and 33/156,  
203 21%, 95%CI: 15-28% vs. 26/264, 10%, 95%CI: 7-14%), an altered physical HRQL  
204 (76/141, 54% vs. 120/261, 46%, 95%CI: 40-52%), and a mRS  $\geq 2$  (respectively, 45/170,  
205 26%, 95%CI: 20-34% vs. 59/310, 19%, 95%CI: 15-24%). For those who previously had  
206 an occupation, women were more often on sick leave than men (39/116, 34%, 95%CI: 25-  
207 43% vs. 52/223, 23%, 95%CI: 18-29%).

208 In women, factors associated with the presence of  $\geq 3$  persistent PACS at M12 were age  $< 65$   
209 years (aOR=1.8, 95%CI: 1.0-3.2) and having  $\geq 3$  symptoms at admission during the acute  
210 phase (aOR=2.2, 95%CI: 1.3-3.9). For men, only hospitalization in ICU and use of oxygen  
211 during the acute phase were significant factors (respectively OR=3.1, 95%CI: 1.4-7.9 and  
212 OR=2.7, 95%CI: 1.2-7.0) (**Table 2**).

213 The observed proportions of  $\geq 3$  persistent PACS at M12 for each of the combinations of  
214 risk factors are reported in **efigure 2**. In women, these proportions ranged between 22%  
215 with no risk factor (age  $\geq 65$  years,  $< 3$  symptoms at admission) to 53% in those with both  
216 risk factors. In men, these proportions ranged between 10% with no risk factor (no oxygen,  
217 no invasive ventilation, no ICU stay) to 23% in those with both risk factors.

218

### 219 ***Comparison between eligible participants who attended M12 visit and those who did not,*** 220 ***and sensitivity analysis on all eligible participants***

221 Comparing the 737 patients who attended the M12 visit to the 2231 eligible patients who did  
222 not, significant differences were found for admitted/transferred to ICU. Patients who attended  
223 the M12 visit had been more often admitted/transferred to ICU (242/654, 37% versus 581/1937,  
224 30%;  $p < 0.001$ ) (**Table 3**).

225 In the sensitivity analysis, we obtained three estimations of the proportion of  $\geq 3$  persistent  
226 PACS among all eligible patients for the M12 visit. In women, the mean proportion was  
227 39% (95%CI: 36-41), the imputed proportion from the lower bound of the 95%CI was



228 33%, and the imputed proportion from the upper bound of the 95%CI was 46%. In men,  
229 these proportions were 21% (95%CI: 19-23), 17% and 25%, respectively.

230

## 231 **Discussion**

232 Epidemiology and natural history of PACS are poorly understood. PACS subtypes are  
233 widely distributed and cover exercise intolerance, pain syndromes, cognition, mood and  
234 sleep disorders, and dysautonomia (19). In this large national prospective cohort of patients  
235 hospitalized for confirmed COVID-19 during the acute phase, with 12-month follow-up  
236 after hospital discharge, a fourth of the participants reported the presence of  $\geq 3$  persistent  
237 PACS. The prevalence of PACS in our cohort is probably overestimated given the high  
238 proportion of participants not retained in follow-up, and given the fact that those still  
239 attending follow-up visits might be more prone to complain from PACS than those who  
240 did not attend. In addition, there was no change between M6 and M12 globally but in a  
241 same individual, some symptoms that were not reported at M6 could arise at M12. As these  
242 signs are very unspecific, it is disputable whether they are linked with COVID-19. For  
243 example, the 28% of people with fatigue at M12 among those who did not at M6 may not be  
244 related to acute infection one-year-ago. Furthermore, 20% of participants stated that they had  
245 not regained full independence at M12. These symptoms had disabling consequences since  
246 a fourth of those who had a professional occupation before COVID-19 was still on sick  
247 leave at M12.

248 It has been previously shown that women reported symptoms more frequently than men,  
249 generally and in the COVID-19 setting (12–15), therefore, we chose to stratify our analyses  
250 according to gender. Indeed, factors associated with the presence of PACS at M12 were  
251 different according to gender. In men, admission/transfer to ICU and oxygen therapy were  
252 associated with the presence of  $\geq 3$  PACS at M12, suggesting a potential role of the initial  
253 severity of the disease in the persistence of symptoms. This could also suggest a role of the  
254 antiviral adaptive response, or of the innate immune response. However, in women, the  
255 persistence of  $\geq 3$  PACS at M12 was associated with having  $\geq 3$  symptoms at admission and  
256 with younger age. Also, women reported more often anxiety and depression than men.  
257 Recently, it has been shown that cognitive complaints at one month after a hospitalization for  
258 COVID-19 were associated with psychological distress, independently of objective  
259 neuropsychological status (20). We show that women are more likely to present to health care  
260 clinics with symptoms post discharge. Increase presentation is associated with severity of initial

261 presentation and the presence of anxiety which may be associated with increased health seeking  
262 behavior at M12 in this population. Our results at M6 were in keeping with those reported in a  
263 Chinese cohort of hospitalized COVID-19 patients; however, the proportion of individuals with  
264  $\geq 1$  symptom and the proportion of those still on sick leave at M12 were lower in the Chinese  
265 cohort than in ours (7). Of note, median age in the Chinese cohort was 59 years versus 61 in  
266 ours, and the proportion of women was higher in the Chinese cohort (47%) than in ours (34%).  
267 In addition, if 88% of participants were indeed back to work at M12 visit in the Chinese cohort,  
268 it is important to emphasize that 24% did not return to pre-COVID-19 level of work (7).

269 Interestingly, our results favorably compared with those reported in Dutch ICU patients at M12  
270 post admission (8).

271 The proportion of patients still complaining from PACS at M6 post COVID-19 (6) was  
272 higher than that reported in matched patients who had influenza (21). The pathophysiology  
273 underlying these persistent or fluctuant PACS long after the acute phase is still unknown.  
274 Chronic inflammation, initial cytokine storm, residual virus in lungs post recovery,  
275 activation of the complement system, microthrombi and macrothrombi formation have  
276 been suggested as potential causes for these persistent symptoms (22,23). In our series,  
277 21% of participants had a mRS  $\geq 2$ , and the percentage of predicted value of the 6MWT  
278 was lower in the 61 patients who reported dyspnea compared to those who did not. CRP,  
279 however, was low in all participants, but this marker might not be a good marker of  
280 prolonged/chronic inflammation. Also, no samples for identification of residual viral  
281 persistence were obtained. Indeed, a few studies reported detection of viral proteins and  
282 RNA in various tissues, by *in situ* methods, months after infection (24,25). Chronic distress  
283 can also be associated with chronic inflammation (26).

284 Our study had several limitations. First, the severity of PACS was not assessed. Indeed, in  
285 our cohort at M6, when focusing on self-reported symptoms (and not symptoms reported  
286 by the physician), the proportion of reported symptoms was roughly the same but most  
287 symptoms were grade 1 (27). Second, is the potential bias in patients who attended M12  
288 follow-up, such patients being more prone to be more symptomatic and thus, continue to  
289 seek medical care, than those who have completely recovered. Indeed, patients who did not  
290 attend the M12 visit had been less admitted/transferred to ICU than those who did attend,  
291 these characteristics being less frequently associated with persistent PACS far from the  
292 acute episode. This limitation might explain in part the differences between our results and  
293 those of the Chinese cohort in which the number of participants attending M6 and M12  
294 visits was similar, whereas the number of those attending M12 visit in our cohort was not

295 only lower than expected regarding the total number of eligible patients, but also lower  
296 than those who attended M6 visit. We performed a sensitivity analysis by computing the  
297 observed proportion of  $\geq 3$  PACS at M12 according to each combination of the risk factors found  
298 in the multivariate model to impute patients without M12 visit. However, this approach, which  
299 takes into account the differences on the distribution of risk factors, assumes that there is  
300 no specific selection bias, i.e., it assumes that patients without visit behave as those with a  
301 visit according to the combination of risk factors. Of note, scheduling follow-up hospital  
302 visits in this time of saturation of the healthcare system was challenging. Third, we did not  
303 have the health status (HRQL, anxiety and depression) of patients before acute infection.  
304 Finally, the impact of vaccines, treatment and less virulent strains (such as Omicron  
305 variant) is unknown.

306 In conclusion, longitudinal follow-up of individuals with severe COVID-19 is warranted  
307 to precisely determine the nature and frequency of persistent PACS, with self-reported  
308 online or telephone assessments to reduce the number of patients lost to follow-up, with  
309 additional questionnaires to address somatic symptom disorders, and to better understand  
310 the pathophysiology underlying this long-term persistence.

**311 Conflict of Interest**

312 Authors report no conflict of interest except JG who reports personal fees from Merck, grants  
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326 **Author Contributions:** Dr Laouéan had full access to all of the data in the study and take  
327 responsibility for the integrity of the data and the accuracy of the data analysis.

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

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

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413

Journal Pre-proof



414 **Table 1.** Characteristics at hospital admission and clinical symptoms at 12 months follow-up  
 415 of 737 patients enrolled in the French COVID cohort

Characteristics	Missing	All N=737	Women N=262	Men N=475
<b>At hospital admission</b>				
Age - Median [IQR] – years	0	61 [52; 70]	60 [51; 70]	61 [52; 70]
Age <65 years - no/total no (%)	0	437/737 (59)	155/262 (59)	282/475 (59)
Comorbidities - no/total no (%)				
Chronic cardiac disease (not hypertension)	58	108/679 (16)	31/248 (12)	77/431 (18)
Hypertension	72	258/665 (39)	86/243 (35)	172/422 (41)
Chronic kidney disease	55	55/682 (8)	11/248 (4)	44/434 (10)
Malignant neoplasm	57	46/680 (7)	15/248 (6)	31/432 (7)
Moderate or severe liver disease	70	7/667 (1)	1/244 (0)	6/423 (1)
Obesity (clinician definition)	71	139/666 (21)	63/240 (26)	76/426 (18)
Chronic pulmonary disease (not asthma)	55	78/682 (11)	22/248 (9)	56/434 (13)
Diabetes (type 1 and 2)	67	129/670 (19)	43/245 (18)	86/425 (20)
No of comorbidities - no/total no (%) <sup>a</sup>				
0		188/683 (28)	72/249 (29)	116/434 (27)
1		202/683 (30)	78/249 (31)	124/434 (29)
≥2		293/683 (43)	99/249 (40)	194/434 (45)
Symptoms - no/total no (%) <sup>b</sup>				
None	82	39/655 (6)	19/241 (8)	20/414 (5)
1-2		250/655 (38)	86/241 (36)	164/414 (40)
≥3		366/655 (56)	136/241 (56)	230/414 (56)
<b>Management during hospitalisation</b>				
ICU during acute phase	90	242/647 (37)	63/234 (27)	179/412 (43)
Oxygen therapy - no/total no (%)	105	482/632 (76)	165/234 (71)	317/398 (80)
Non-invasive ventilation (e.g. BIPAP, CPAP) - no/total no (%)	115	126/622 (20)	43/233 (18)	83/389 (21)
Pharmacological treatment during acute COVID-19 - no/total no (%)				
Antiviral agent	104	178/633 (28)	56/234 (24)	122/399 (31)
Hydroxychloroquine	129	106/608 (17)	37/222 (17)	69/386 (18)
Immunomodulator (for example anti-IL6)	146	17/591 (3)	2/219 (1)	15/372 (4)
Corticosteroids	98	142/639 (22)	48/238 (20)	94/401 (23)
Length of hospital stay - Median [IQR] - d	77	9 [5; 17]	8 [5; 13]	11 [6; 19]
<b>M12 follow-up after discharge</b>				
Days from symptom onset to M12 visit - Median [IQR] – d	55	391 [374; 419]	391 [374; 415]	392 [373; 420]
Days from discharge to M12 visit - Median [IQR] – d	56	370 [352; 398]	371 [355; 395]	368 [350; 400]
Six-minute walk test (6MWT) done at M12 visit - no/total no (%)	195	264/542 (49)	75/189 (40)	187/351 (53)
Distance walked in % - Median [IQR]	570	88 [74; 100]	85 [75; 100]	94 [74; 100]

Medical Research Council Scale <48 at M12 visit - no/total no (%)	253	8/484 (2)	3/168 (2)	5/316 (2)
Simplified Modified Rankin Scale at M12 visit - no/total no (%)	257			
0 - No symptoms		242/480 (50)	76/170 (45)	166/310 (54)
1 - No significant disability		134/480 (28)	49/170 (29)	85/310 (27)
2 - Slight disability		79/480 (16)	34/170 (20)	45/310 (15)
3 - Moderate disability		22/480 (5)	10/170 (6)	12/310 (4)
4 - Moderately severe disability		2/480 (0)	1/170 (1)	1/310 (0)
5 - Severe disability		1/480 (0)	0/170 (0)	1/310 (0)
HADS - no/total no (%)	317			
Anxiety score $\geq 11$		59/420 (14)	33/156 (21)	26/264 (10)
Depression score $\geq 11$		35/420 (8)	18/152 (12)	17/268 (6)
SF-12 - no/total no (%)	335			
Impaired physical HRQL		196/402 (49)	76/141 (54)	120/261 (46)
Impaired mental HRQL		126/402 (31)	45/141 (32)	81/261 (31)
If applicable, back to work at M12 - no/total no (%)	398	248/339 (73)	77/116 (66)	171/223 (77)
CRP at M12 visit - Median [IQR] – mg/L	323	3 [1; 4]	3 [2; 7]	2 [1; 4]
Persistent PACS 12 months after hospital admission - no/total no (%) <sup>b</sup>	27			
None		236/710 (33)	62/253 (25)	174/457(38)
1-2		280/710 (39)	93/253 (37)	187/457 (41)
$\geq 3$		194/710 (27)	98/253 (39)	96/457 (21)

416 <sup>a</sup> Comorbidities were defined using the Charlson comorbidity index, with the addition of clinician-  
417 defined obesity.

418 <sup>b</sup> Number of symptoms among: fatigue, dyspnea, joint pain, myalgia, headache, rhinorrhoea, cough,  
419 sore throat, ageusia and anosmia.

420 **Table 2.** Univariate and multivariate association analyses with 3 or more symptoms at M12 visit separately in women and in men

	Missing	<3 symptoms at M12	≥3 symptoms at M12	Bivariate analysis <sup>a</sup>		Multivariate analysis <sup>b</sup>		
				OR [95% CI]	p-value	aOR [95% CI]	p-value	
<b>Women</b>	Age <65 years, n (%)	0	83 (54%)	67 (68%)	1.87 [1.11; 3.21]	0.020	1.79 [1.03; 3.15]	0.042
	≥3 symptoms at admission, n (%)	19	69 (49%)	64 (69%)	2.30 [1.34; 4.02]	0.003	2.21 [1.28; 3.89]	0.005
	≥2 comorbidities, n (%)	11	54 (37%)	41 (43%)	1.31 [0.77; 2.22]	0.32		
	Antiviral agent, n (%)	26	37 (27%)	17 (19%)	0.63 [0.32; 1.19]	0.16		
	Corticosteroids, n (%)	22	28 (20%)	18 (20%)	0.99 [0.50; 1.90]	0.97		
	ICU/non invasive ventilation/oxygen	31						
	No		34 (25%)	26 (30%)	1 reference			
	Oxygen only (no ICU, no ventilation)		58 (43%)	33 (38%)	0.74 [0.38; 1.45]	0.38		
	ICU or non invasive ventilation		42 (31%)	29 (33%)	0.90 [0.45; 1.81]	0.77		
<b>Men</b>	Age <65 years, n (%)	0	213 (59%)	58 (60%)	1.06 [0.67; 1.69]	0.80		
	≥3 symptoms at admission, n (%)	56	170 (54%)	51 (60%)	1.27 [0.78; 2.08]	0.34		
	≥2 comorbidities, n (%)	37	144 (44%)	40 (46%)	1.11 [0.69; 1.78]	0.68		
	Antiviral agent, n (%)	73	84 (28%)	31 (37%)	1.46 [0.87; 2.41]	0.15		
	Corticosteroids, n (%)	71	64 (21%)	23 (27%)	1.39 [0.79; 2.40]	0.24		
	ICU/non invasive ventilation/oxygen	70						
	No		63 (21%)	7 (9%)	1 reference		1 reference	
	Oxygen only (no ICU, no ventilation)		98 (32%)	30 (37%)	2.77 [1.25; 7.03]	0.019	2.70 [1.17; 7.02]	0.028
	ICU or non invasive ventilation		143 (47%)	44 (54%)	2.76 [1.20; 7.16]	0.024	3.08 [1.38; 7.85]	0.010

421 OR: odds ratio; aOR: adjusted odds ratio; CI: confidence interval

422 <sup>a</sup> Women: n=253, 155 with <3 symptoms at M12 and 98 with ≥3 symptoms at M12. Men: n=457, 361 with <3 symptoms at M12 and 96 with ≥3 symptoms at M12423 <sup>b</sup> Women: n=234, 141 with <3 symptoms at M12 and 93 with ≥3 symptoms at M12. Men: n=385, 304 with <3 symptoms at M12 and 81 with ≥3 symptoms at M12

424 **Table 3.** Comparison between patients included in the analyses and patients not deceased who  
 425 did not attend M12 visit  
 426

	Included in the analyses (N=737)	Not included in the analyses (N=2231)	p-value*
Age ≥ 65 years	300 (41%)	973 (44%)	0.12
Female gender	262 (36%)	852 (39%)	0.13
≥ 3 symptoms at admission	366 (56%)	1116 (57%)	0.65
Intensive care unit during acute phase	<b>242 (37%)</b>	<b>581 (30%)</b>	<b>&lt;0.001</b>
≥ 2 comorbidities	293 (43%)	947 (45%)	0.24

\* chi-square test

427

428 **Figure legends**

429 **Figure 1:** COVID-19 related symptoms during the acute phase and during follow-up visits of  
430 patients with M6 and M12 visits for women (n=235) and for men (n=428) enrolled in the French  
431 COVID cohort

432

433 **Note: McNemar paired tests (M6 vs M12) for each symptom among women and men:**

434 Women: fatigue (p=1, N=213), dyspnea (p=0.11, N=215), joint pain (p=0.11, N=215), myalgia (p=0.37,  
435 N=209), cough (p=0.007, N=211), headache (p=1, N=206), rhinorrhoea (p=0.026, N=210), ageusia  
436 (p=0.45, N=205), anosmia (p=0.40, N=205), sore throat (p=0.40, N=209).

437 Men: fatigue (p=0.31, N=385), dyspnea (p=0.29, N=385), joint pain (p=0.22, N=381), myalgia (p=1,  
438 N=381), cough (p=0.55, N=384), headache (p=0.090, N=382), rhinorrhoea (p=0.093, N=379), ageusia  
439 (p=0.82, N=383), anosmia (p=0.65, N=382), sore throat (p=0.45, N=384).

