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1 **Time to resolution of respiratory and systemic COVID-19 symptoms in community setting**

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30 **Abstract (242/250)**

31 **Objectives**

32 During the Coronavirus disease 2019 (COVID-19), symptom course among outpatients is not
33 well known. Our aim was to assess the time to resolution of respiratory and systemic
34 symptoms and their associated factors.

35 **Methods**

36 Cohort study including adult outpatients, managed with Covidom, a telesurveillance
37 solution, with RT-PCR confirmed diagnosis, from March 9th 2020 until February 23rd 2021.
38 Follow-up was 30 days after symptom onset.

39 **Results**

40 Among the 9,667 patients included, mean age was 43.2±14.0 years, and 67.5% were female
41 (n=6,522). Median body mass index (BMI) (IQR) was 25.0 kg/m² (22.1-28.8). Main
42 comorbidities were: hypertension (12.9%; n=1247), asthma (11.0%; n=1063), and diabetes
43 mellitus (5.5%; n=527). The most frequent symptom during follow-up was dyspnea (65.1%;
44 n=6,296), followed by tachypnea (49.9%; n=4,821), shivers (45.6%; n=4,410), and fever
45 (36.7%; n=3,550). Median time to resolution of systemic and respiratory symptoms were 3
46 days (95% CI: 2–4) and 7 days (95% CI: 6–8), respectively. Ultimately, 17.2% (95% CI:
47 15.7%–18.8%) still presented respiratory symptoms at day 30. Longer time to respiratory
48 symptom resolution was associated with older age, increased BMI, chronic obstructive
49 pulmonary disease (COPD), coronary artery disease, asthma, and heart failure. Regarding
50 systemic symptoms, coronary artery disease, asthma, age above 40 years, and elevated BMI
51 were associated with longer time to resolution.

52 **Conclusions**

53 Time to symptom resolution among outpatients with COVID-19 seemed shorter for systemic
54 than respiratory symptoms. Prolonged respiratory symptoms were common at day 30. Risk
55 factors associated with later resolution included age, cardiovascular and pulmonary
56 diseases.

57

58 **Key words:** COVID-19; symptom duration; dyspnea; sequelae; community setting;
59 telemedicine

60

61 **Introduction**

62 The clinical manifestations in COVID-19 patients range from asymptomatic to severe forms
63 requiring critical care, and the duration of symptoms can vary widely [1,2]. Most studies
64 described the clinical course of hospitalized severe cases [3–5]. However, most patients
65 present with milder forms of COVID-19 [6], and are therefore managed as outpatients. Data
66 on this population is scarce, but describing the symptom course of outpatients with COVID-
67 19 and factors associated with symptom duration may help provide adequate follow-up
68 [2,7–9].

69 Our study aimed to evaluate the time to resolution of COVID-19 respiratory and systemic
70 symptoms, and factors associated with a longer duration in a large cohort of outpatients.

71

72 **Material and methods**

73 This study included adult (≥ 18 years) patients, initially managed as outpatients, from March
74 9th 2020 to February 23rd 2021 by Covidom, a telesurveillance solution for home monitoring
75 of patients with COVID-19 in the greater Paris area [10]. Covidom outpatients were
76 registered by a physician after consulting for COVID-related symptoms and agreeing to the
77 monitoring. We included patients with a RT-PCR confirmed diagnosis, having answered at
78 least one monitoring questionnaire, and who provided medical background at inclusion.

79 Available data for each patient included age, gender, date of first symptoms, weight, height,
80 and comorbidities.

81 When included in Covidom, the patients completed, on a daily basis, one or two self-
82 administered questionnaires on symptoms until 30 days after symptoms onset. Self-reported
83 data were: respiratory rate (tachypnea defined as >20 breaths per minute), heart rate

84 (tachycardia defined as >100 beats per minute), temperature (fever and hypothermia
85 defined by temperature >38.5°C and <35.5°C, respectively), dyspnea (on a 1-to-5 modified
86 Borg scale [11], slight dyspnea defined by a rating ≥ 2 , and moderate dyspnea ≥ 3), oxygen
87 saturation (desaturation defined by <95%), dizziness, and shivers.

88 Two main groups of symptoms were defined:

- 89 - Systemic symptoms: fever or hypothermia, dizziness, tachycardia, shivers.
- 90 - Respiratory symptoms: dyspnea, tachypnea, low oxygen saturation.

91 Kaplan-Meier estimators were used to evaluate time to resolution of symptoms. Patients
92 were considered at risk from the date of first symptom onset (declared at inclusion) until the
93 last occurrence of each symptom in daily questionnaires. Regarding symptom groups,
94 patients were considered at risk until the last day of any symptom occurrence of the group.
95 Patients were censored at the end of their follow-up (30 days or earlier in case of premature
96 ending). Factors independently associated with longer time to resolution of systemic and
97 respiratory symptoms were evaluated separately on complete cases using multivariate Cox
98 models and inversed hazard ratios as the event of interest was initially resolution of
99 symptoms. Alpha risk was set at 5%.

100 Patients provided electronic consent for the Covidom telesurveillance program and were
101 informed of the use of their anonymized data for research. This study was approved by the
102 scientific and ethical committee of APHP (IRB00011591).

103

104 **Results**

105 Among the 62,993 patients included in the Covidom cohort as outpatients, 15,086 (23.9%)
106 had a COVID-19 RT-PCR confirmed diagnosis, 14,965 (23.8%) were adult patients, 11,984

107 (19.0%) answered at least one monitoring questionnaire, and 9,667 (15.3%) provided
108 medical background at inclusion and thus were included in this study (patients
109 characteristics presented in Table S1 in Supplementary appendix).

110 Mean age was 43.2 years old (SD 14.0) and 67.5% were female (n=6,522). Median body mass
111 index (BMI) (IQR) was 25.0 kg/m² (22.1-28.8). Main comorbidities were hypertension (12.9%;
112 n=1247), asthma (11.0%; n=1,063), and diabetes mellitus (5.5%; n=527). Other comorbidities
113 were reported by less than 1.5% of patients. Weight (and BMI) was missing for 121 patients,
114 and gender for 18 patients.

115 The last answer to a daily questionnaire occurred at a median time of 28 days after symptom
116 onset (IQR 17–30 days), with a median Covidom monitoring duration of 19 days (IQR 11–24
117 days). There were 65.1% of patients (n=7,805) missing at least one daily monitoring
118 questionnaire, and the median number of skipped questionnaires per patient was 2 (IQR
119 0–5).

120 The most common symptom was dyspnea in 65.1% of patients (n=6,296), with 2,802
121 patients (29.0%) rating their dyspnea as moderate or higher. Tachypnea, shivers, and fever
122 were reported by 49.9% (n=4,821), 45.6% (n=4,410), and 36.7% (n=3,550) of patients,
123 respectively. A total of 2,590 (26.8%) patients reported tachycardia, 1,197 (12.4%) reported
124 dizziness, and 582 (25.1%) of 2,319 patients with an oximeter reported desaturation at least
125 once.

126 Considering time to symptom resolution (Figure 1), the longest symptoms were desaturation
127 with a median (95% Confidence Interval (CI)) of 10 days (8–12), and slight dyspnea with 9
128 days (7–10). Median time to resolution of moderate dyspnea was 4 days (2–5). Symptoms
129 with shorter time to resolution included shivers, tachypnea and tachycardia, with median

130 durations (95% CI) respectively of 1 day (1–2), 2 days (1–2) and 2 days (1–2). The probability
131 of slight dyspnea lasting until 30 days after first symptoms onset was 18.3% (95% CI
132 16.6%–20.0%), while the systemic symptom with highest probability at day 30 was dizziness
133 with 1.1% (0.5%–2.2%).

134 Age above 30 years (hazard ratios (HR) 1.27 [95%CI 1.16–1.38]), 40 years (1.50 [1.37–1.65]),
135 50 years (1.68 [1.53–1.85]), and 60 years (1.64[1.45–1.84]), as well as increased BMI (both
136 obesity and overweight, 1.13 [1.15–1.21] and 1.18 [1.09–1.28], respectively), chronic
137 obstructive pulmonary disease (COPD) (2.00 [1.41–2.83]), coronary artery disease (1.55
138 [1.14–2.11]), asthma (1.43 [1.30–1.58]), heart failure (1.42 [1.08–1.86]), and hypertension
139 (1.12 [1.01–1.23]) were associated with longer time to resolution of respiratory symptoms
140 (Figure 2). No variable appeared associated with a shorter time to resolution.

141 For systemic symptoms, coronary artery disease (1.53 [1.18–1.98]), as well as age above 40
142 years (1.12 [1.02–1.22], 1.16 [1.06–1.26] and 1.20 [1.08–1.34] respectively for ages >40, >50
143 and >60) and increased BMI (1.09 [1.03–1.16] for BMI >25kg/m², 1.10 [1.03–1.18] for BMI
144 >30kg/m²) were associated with longer time to resolution (Figure 2). Male sex was
145 associated with shorter time to resolution (0.92 [0.87–0.97]). Complete analysis results are
146 presented in Table S2 in Supplementary appendix.

147 Lastly, the number and proportion of patients per monitoring question, answer, and day are
148 described in Figure S1 in Supplementary appendix.

149

150 **Discussion**

151 Our study provides important inputs regarding time to resolution of respiratory and systemic
152 symptoms over one month in ambulatory patients, which can help direct care [5,12–14].

153 Median time to resolution of symptoms was up to 10 days with wide variability, and 18.3%
154 of slight dizziness symptoms still present at end of follow-up. Systemic symptoms were
155 slightly less frequent than respiratory symptoms, and had shorter time to resolution. Factors
156 associated with prolonged symptoms included age over 30, elevated BMI, and cardiovascular
157 and pulmonary diseases.

158 The strength of our study includes the size of the cohort and the standardized questionnaire
159 during the entire 30-day follow-up. Several studies showed, among hospitalized patients,
160 that fever, cough, dyspnea, and gastrointestinal symptoms were the main clinical
161 manifestations of COVID-19 [15]. In our cohort that included only non-hospitalized patients,
162 those symptoms had a lower prevalence.

163 Our results corroborate that COVID-19 may cause prolonged symptoms, even among
164 outpatients with mild disease [2], or in patients with or without few comorbidities.

165 **Limits**

166 Our study relies on patients' self-reporting, resulting in possible recall bias. Furthermore, we
167 focused on general and respiratory symptoms and did not evaluate the duration of other
168 symptoms like smell and taste alteration. Secondarily, non-respondents might have differed
169 from respondents regarding their clinical course. Finally, our models do not take into
170 account each symptom's onset delay, only the date until which each symptom lasts, starting
171 from the onset of the first symptom. This describes the course of symptoms relative to the
172 illness globally, but different factors may affect symptom onset delay and symptom
173 duration.

174

175 **Conclusion**

176 Time to symptom resolution in outpatients with COVID-19 varies widely with shorter
177 systemic symptoms and longer respiratory symptoms. Prolonged respiratory symptoms,
178 especially dyspnea, were common at day 30. Factors associated with later resolution were
179 age over 30, elevated BMI, cardiovascular and pulmonary diseases.

180

181 **Transparency declaration**

182 The authors declare that they have no conflicts of interest. All authors have full control of all
183 primary data and they agree to allow review of their data upon request.

184

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189

190 **Authors' contributions**

191 ADi, LJ, ADe, XL, and YY conceptualized the study. ADi, LJ, ADe, CD, HM, and YY collected,
192 analysed and interpreted the data. LH conducted the statistical analysis. ADi, LJ, ADe, CD, and
193 YY wrote the first draft of the manuscript. All authors revised the manuscript and approved
194 the final version. ADi had full access to all of the data in the study and takes responsibility for
195 the integrity of the data and the accuracy of the data analysis.

196

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249

250 **Figure legends**

Figure 1: Time to resolution of respiratory and systemic symptoms (in days) modeled using Kaplan-Meier estimators

251 **Figure 2:** Risk factors associated with longer time to resolution of clinical symptoms

252

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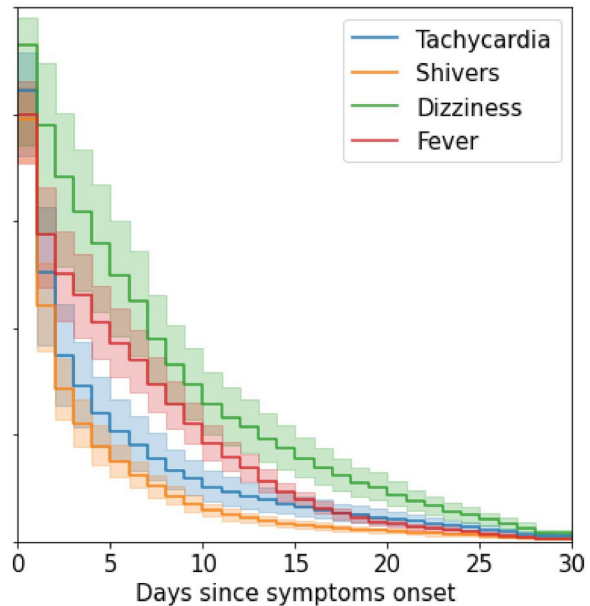
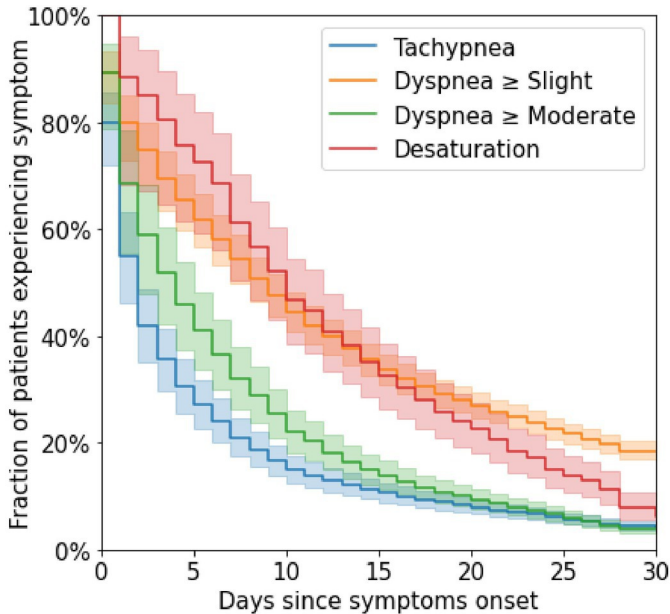
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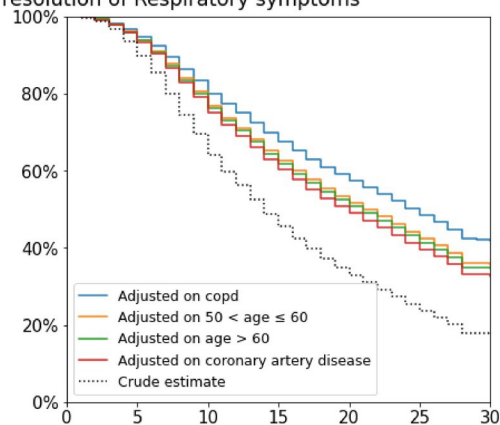
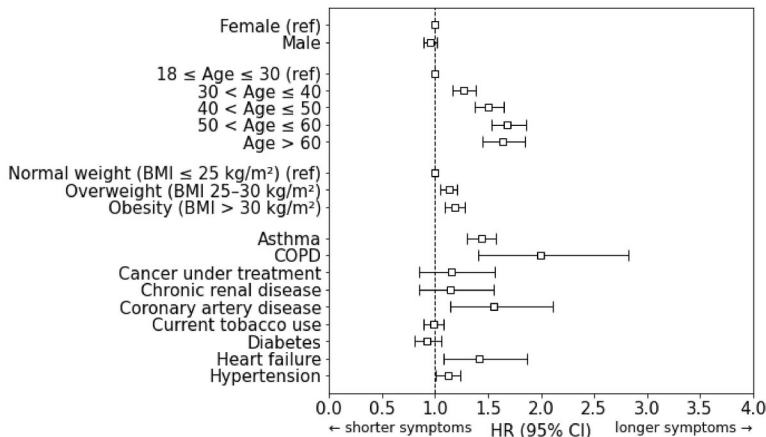
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Kaplan-Meier modelisation of time to symptom resolution



Factors associated with time to resolution of Respiratory symptoms



Factors associated with time to resolution of Systemic symptoms

