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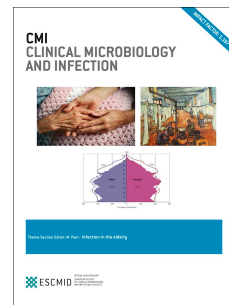
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Clinical characteristics and factors associated with hospital admission or death in 43,103 adult outpatients with COVID-19 managed with the Covidom telesurveillance solution: a prospective cohort study

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Key points: Clinical worsening was rare in this large cohort of outpatients with suspected or confirmed COVID-19 managed with Covidom. Male sex, older age and comorbidities such as chronic renal disease, active cancer, diabetes or obesity were independently associated with clinical worsening.

Word count : 2479

Abstract (249 words)

Objectives: Studies on coronavirus disease 2019 (COVID-19) have mainly focused on hospitalized patients or those with severe disease. We aim to assess the clinical characteristics, outcomes and factors associated with hospital admission or death in adult outpatients with COVID-19.

Methods: This is a prospective cohort of outpatients with suspected or confirmed COVID-19, registered in Covidom telesurveillance solution for home monitoring of patients with COVID-19 in the Greater Paris area, from March to August 2020. The primary outcome was clinical worsening, defined as hospitalization or death within 1 month after symptom onset.

Results: Among 43,103 patients, mean age was 42.9 years (SD=14.3); 93.0% (n=40,081) of patients were < 65 years old and 61.9% (n=26,688) were women. Of these 43,103 patients, 67.5% (n=29,104) completed a medical questionnaire on comorbidities and symptoms. The main reported comorbidities were asthma (12.8%; n=3,685), hypertension (12.3%; n=3,546) and diabetes (4.8%; n=1,385). A small proportion of all eligible patients (4.1% [95% CI: 3.9–4.2]; 1,751/43,103) experienced clinical worsening. The rate of hospitalisation was 4.0% (95% CI: 3.8–4.2; n=1,728) and 0.1% (95% CI: 0.1–0.2; n=64) died. Factors associated with clinical worsening were male sex, older age, obesity and comorbidities such as chronic renal disease or cancer under treatment. Probability of worsening was reduced with anosmia/ageusia.

Conclusions: Clinical worsening was rare among outpatients. Male sex, older age and comorbidities such as chronic renal disease, active cancers or obesity were independently associated with clinical worsening. However, our cohort may include patients younger and healthier than the general population.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection rapidly spread from a cluster of cases in China to a pandemic with more than 130 million cases and almost 3 million deaths worldwide[1,2].

Clinical characteristics of coronavirus disease 2019 (COVID-19) as well as factors associated with increased risk of poor outcome have been described[3–8]. Age, sex, hypertension, diabetes, cardiovascular disease, chronic respiratory disease, cancer and other chronic comorbidities such as obesity are associated with clinical worsening, treatment escalation and death[3–5,7–9]. These evaluations mainly focused on hospitalized patients[7,8]. However, more than 80% of patients initially present a mild form of the disease, some even being asymptomatic[10–13]. It was initially estimated that 10% to 15% of these patients would experience a more severe disease[14,15], but we currently lack precise estimates of the rate of clinical worsening in this population. Patients at risk of worsening must be quickly identified to adapt surveillance and propose prompt clinical management when the first signs of worsening occur. Only few studies have investigated the clinical features of outpatients with SARS-CoV-2 infection or the factors associated with hospital admission or death among these patients[16–18].

This study aimed to evaluate the rate of clinical worsening, defined as hospitalization or death, in adult COVID-19 outpatients managed with the Covidom telesurveillance solution, and to evaluate factors associated with clinical worsening.

METHODS

Study design and setting

This study is based on the Covidom cohort[19], an ongoing prospective cohort of patients in the greater Paris area using the Covidom telesurveillance solution. In summary, it is a Web application for home monitoring of patients with COVID-19 as part of initial outpatient management or at hospital discharge after a COVID-19–related hospitalization. Patients are registered in Covidom by a physician, at the end of a medical encounter for COVID-19-related symptoms, after a brief information and oral consent. After completing registration online, patients answer a medical questionnaire on comorbidities and symptoms, and they receive daily monitoring questionnaires for 30 days after symptom onset. The questionnaire answers can trigger alerts, managed in a single regional control center that can conduct a remote medical assessment, address the patient to a hospital or send mobile emergency services to patient home if necessary[19]. Patients are informed of the potential use of their anonymized data for research purposes. This study was approved by the Scientific and Ethical Committee of AP-HP (IRB00011591).

Participants

We included all adults ≥ 18 years with suspected or proven COVID-19 as evaluated by a physician, who completed registration, who were registered as outpatients, and who had a date of COVID-19 symptom onset earlier than August 11. We excluded patients included in Covidom at hospital discharge.

Data

We collected patient characteristics recorded by the including physicians: means of inclusion (general practitioners [GP], hospital, emergency medical services medical dispatcher [EMS]), age, sex, date of first symptoms, postal code, and risk profile (low or high risk). Patient were considered at high risk if they had cardiovascular disease, diabetes, chronic lung disease, immunodeficiency, were in the third trimester of pregnancy or over 65 years old. The remaining characteristics were recorded in the self-reported medical questionnaire, generally completed at inclusion:

- Weight and height, from which we calculated body mass index (BMI)
- Comorbidities
- Current tobacco use
- Symptoms
- Diagnosis: whether the infection has been confirmed by a molecular test (RT-PCR).

The diagnosis information was collected from the including physicians, self-reported medical questionnaires and cross-checked with the biological databases of the AP-HP hospital network. AP-HP is a network of 39 university hospitals in the greater Paris area covering a large part of this area's population (12 million inhabitants). We considered that a patient was positive if a positive test was self-reported or available in the biological databases during the 30 days follow up.

By using data from the French Institute for Statistics and Economic Studies (INSEE) overlaid with the patient's area of residence, we also collected the local median income as a proxy of the patient's socioeconomic status[20].

Outcomes

Our primary outcome was clinical worsening, defined as hospitalization or death within 1 month after symptom onset. We used 3 complementary approaches to evaluate this outcome:

1) Patient responses to follow-up questionnaires sent 15 and 30 days after symptom onset that asked patients whether they had been hospitalized during follow-up. 2) Responses reported by the regional control center to the different types of alerts and the end of follow-up reasons in case of premature ending (the regional control center called back all patients who did not answer the daily questionnaires or their relatives to check their status). 3) Data on patients hospitalized from the AP-HP warehouse (Entrepôt de données de santé [EDS] de l'AP-HP). We evaluated hospitalization and death within 1 month after symptom onset, separately, as secondary outcomes.

Statistical analyses

We describe patient characteristics with frequencies (percentages) for categorical variables and mean (standard deviation) or median (quartile 1-quartile 3) for continuous variables. We used hierarchical clustering to identify clusters of symptoms based on the Jaccard index. We described the characteristics of all eligible patients, those with a completed medical questionnaire (overall and by PCR status: positive, negative, untested). We evaluated the primary outcome in these populations. Then, we used univariable logistic regression models followed by a multivariable logistic regression model including all relevant variables based on clinical likelihood and literature to evaluate factors associated with clinical worsening among patients with a completed medical questionnaire and a positive PCR test. Two sets of highly correlated symptoms (anosmia and ageusia, and fatigue, shivers and myalgia) were regrouped to avoid collinearity. We conducted three sensitivity analyses for the multivariable model to evaluate the consistency of results: 1) analysis based on all patients with a medical questionnaire regardless of the RT-PCR result, 2) analysis based on all eligible patients, 3) analysis with inverse probability weighting to adjust for patients not answering the medical

questionnaire. The propensity score is defined as the probability of answering given characteristics recorded at registration. Alpha risk was set at 5% for all analyses.

RESULTS

From March 9, 2020 to August 11, 2020, 63,273 patients with a suspected or confirmed COVID-19 were registered in Covidom by more than 3800 physicians. Of these, 51,971 (82.1%) had confirmed registration and 43,103 (68.1%) met our inclusion criteria (Figure 1). A total of 29,104 patients (67.5%) completed the medical questionnaire on comorbidities and symptoms. Regarding follow-up, 71% of patients (n=20,647) had a follow-up of at least 29 days. Among patients with a shorter follow-up, 167 were hospitalized or deceased (median follow-up: 14 days, Q1-Q3: 9–20), 3296 patients (11.3%) chose to interrupt follow-up early (20 days, Q1-Q3: 16–24) while 4988 (17.1%) stopped responding without formally ending follow-up (23 days, Q1-Q3: 18–26).

Patient general characteristics

Mean age was 42.9 years (SD 14.3), with 93.0% of patients < 65 years old (n=40,081), and 61.9% were women (n=26,688). The median time from symptom onset to registration was 4 days (Q1-Q3: 2–8 days). General characteristics of patients having completed the medical questionnaire did not appear different (Table 1). Among those patients, median BMI was 24.8 kg/m² (Q1-Q3: 22.1–28.4), with 30.2% (n=8568) being overweight and 18.3% (n=5,195) obese. Current tobacco use was reported by 5,103 (17.7%) patients. Main comorbidities were asthma, hypertension and diabetes reported by 12.8% (n=3,685), 12.3% (n=3,546) and 4.8% (n=1,385) of patients, respectively.

The most common symptoms were fatigue (n=25,014; 85.9%), cough (n=18,014; 61.9%), shivers (n=15,706; 54.0%), myalgia (n=15,721; 54.0%), shortness of breath (n=14,358; 49.3%), and fever (n=14,124; 48.5%). Almost one third of patients reported anosmia (n=9,109; 31.3%) or ageusia (n=9,170; 31.5%). Clusters of symptoms are reported in the supplementary Figure 1, showing a cluster with anosmia and ageusia symptoms, one with chest pain and chest oppression and a larger cluster with general symptoms as fever, fatigue, shivers, and myalgia associated with cough. In total, 45.7% (n=12,601) patients had available RT-PCR results, 58.1% (n=7320) being positive. Characteristics stratified by RT-PCR status are reported in Table 1. Age, sex ratio, comorbidities and symptoms did not appear different from the complete cohort, while RT-PCR positive patients appeared to be included in hospitals more often, and reported anosmia or ageusia more frequently (Table 1).

Clinical worsening

A small proportion of all eligible patients (4.1%; 95% CI: 3.9–4.2; 1,751/43,103) experienced clinical worsening. At 1 month after symptom onset, 4.0% (95% CI: 3.8–4.2; n=1,728) required hospitalisation and 0.1% died (95% CI: 0.1–0.2; n=64). Among the patients with a positive RT-PCR, 9.0% (95% CI: 8.3–9.7; 659/7320) experienced clinical worsening, 9.0% (95% CI: 8.3–9.7; n=659) required hospitalisation and 0.04% died (95% CI: 0.01–0.09; n=3) (Table 2). Patient characteristics by clinical outcome and by RT-PCR status are reported in the Supplementary Table 1. Independent factors associated with clinical worsening are reported in Figure 2 and Table 3. Both age >65 years and obesity were independent predictors of worsening: OR 4.05 (95% CI: 2.94-5.58) and 1.57 (95% CI: 1.25-1.97). Male sex was also associated with worsening (OR 2.08; 95% CI: 1.74-2.50), as was chronic renal disease (OR 2.59; 95% CI: 1.42–4.73) and cancer under treatment (OR 2.11; 95% CI: 1.20–3.72).

Temperature, shortness of breath, and anorexia were associated with worsening, but patients appeared less prone to worsening if they presented anosmia or ageusia (OR 0.69; 95% CI: 0.57–0.84). Current tobacco use appeared associated with a lower risk of worsening (OR 0.68; 95% CI: 0.48–0.96).

The sensitivity analyses were consistent for factors associated with clinical worsening (Supplementary Table 2/Supplementary Figure 2).

DISCUSSION

In this study, we describe the characteristics, outcomes and factors associated with disease worsening in a large population of adult outpatients with suspected or confirmed COVID-19 with mild symptoms, and followed by the Covidom telesurveillance program. Only a small proportion of these patients experienced hospitalisation or death, and the mortality rate was 0.1% (95% CI: 0.1–0.2). Male sex, older age and comorbidities as chronic renal disease, active cancer or obesity were independently associated with clinical worsening.

Covidom represents the largest telesurveillance program deployed in the context of COVID-19 and a unique source of epidemiological data on the outpatients with COVID-19, who represent most cases but are the least studied. Most of the literature focused on hospitalized patients or those with severe COVID-19 disease and reported a higher rate of clinical worsening with 5% to 36.1% of patients needing admission in intensive care units, and an overall mortality ranging from 2,3% to 26.2%[4,7,8,14,21]. In a study describing outpatients, 6% of patients needed hospital referral after remote assessment by an emergency physician but they did not distinguish patients addressed to the hospital for a consultation and those who were hospitalized[16]. The Chinese Center for Disease Control and Prevention initially

estimated that 10% to 15% of patients with mild disease will worsen, with a final case-fatality rate of 2.3% [14]. However, most of these patients were likely hospitalized because immediate admission of all potential COVID-19 patients was recommended to control the pandemic in mainland China [22]. Therefore, our cohort gives a unique insight into the evolution of outpatients with mild COVID-19 symptoms.

Factors independently associated with clinical worsening were comparable to those identified in hospitalised patients [7–9]. Age is a well-known risk factor that could be explained by the possible stronger host innate responses to virus infection than in younger adults or by age-dependent defects in T- and B-cell function [23]. Obesity seem to worsen the effect of COVID-19; high BMI was significantly correlated with young age in COVID-19 patients requiring intensive care due to reduced respiratory function or susceptibility to trigger hyperinflammation [3,9,24]. As others, we found a lower rate of worsening among patients who reported being current smokers [25,26], but further studies are needed to explore these results.

Our study has some limitations. Our population is not representative of all outpatients with COVID-19. Only those with initially mild symptoms and a smartphone, tablet or computer, at ease with these recent technologies and accepting the telesurveillance program were included. Digital readiness of older adults has often been described as one of the causes of their lower engagement with electronic health or with mobile device-based monitoring. This could possibly explain that only 7.0% of the patients included in our study were over 65-years old. The low rate of clinical worsening should be understood in the context of this younger population. In addition, our data concern only patients included in the greater Paris area, which is a high-density area and a major epicenter during the outbreak. Our population is based on suspected or confirmed cases of COVID-19 following the definition of French public health authorities. Many patients were initially not tested in France because RT-PCR

tests were mostly reserved for the most severe patients or those with comorbidities. In the region of the study, 41,539 positive RT-PCR have been reported by public health authorities, while over the same time period 40,076 COVID-19 hospitalizations were reported. These numbers highlight the lack of RT-PCR tests availability, in France, at this time[27]. In our study, among tested patients, 58.1% had positive results, which seems slightly lower than expected RT-PCR false negative rates, given that up to 33% of patients hospitalized with acute respiratory symptoms and typical radiological findings tested negative at least once on respiratory specimens, and RT-PCR false negative rates could represent as much as 29%, depending on the assay used[28,29]. We cannot exclude that some of these patients did not have COVID-19. However, we believe that eliminating a possible SARS-CoV2 infection in a population of patients presenting symptoms compatible with COVID-19 (i.e with a high pre-test probability), in a region with a high infection incidence, and in a context of lack of PCR test availability, on the basis of a negative naso-pharyngeal RT-PCR would possibly lead to underestimating the pandemic burden. We therefore believe that it is important to also consider the patients that were not tested in the first wave but who had a suspected COVID-19 infection according to the assessing physician, to capture the overall picture of the disease and its evolution. Most data were self-reported by patients, with a potential risk of misclassification, recall bias or social desirability bias, but these data were previously shown to be reliable[30]. Not all patients completed the medical questionnaire because it was not initially available. Nevertheless, characteristics were not different and results were consistent in sensitivity analyses. The fact that the patients in our cohort have benefited from an initial medical evaluation could lead to a selection bias towards a healthier, better cared for, population. Finally, ethnicity was not recorded in Covidom, in accordance with French legislation.

In conclusion, the rate of clinical worsening in adult outpatients with COVID-19 was lower than expected, about 4%, with a mortality rate of 0.1%. Male sex, older age and comorbidities such as chronic renal disease, active cancer and obesity were independently associated with worsening. As countries face a third wave of the COVID-19 pandemic, our results give a unique insight into the outcomes of patients with mild symptomatology.

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DECLARATIONS

Ethics approval : This study received the ethical approval of the ethics committee of APHP (IRB00011591).

Availability of data and materials: The datasets generated and analysed during the current study are not publicly available due to restrictions by the French data protection authority. But all reasonable request should be addressed to the corresponding author.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Table 1. Demographic characteristics, comorbidities and symptoms of all eligible patients and in the cohort of patients having filled the medical questionnaire by type of PCR results (positive, negative, untested)

	<i>All eligible patients N= 43,103</i>	<i>Eligible patients with a completed medical questionnaire N= 29,104</i>	<i>Medical questionnaire and Positive PCR N=7320</i>	<i>Medical questionnaire and Negative PCR N=5281</i>	<i>Medical questionnaire and No PCR result N=16,503</i>
<i>General characteristics</i>					
Age, mean (SD)	42.9 ±14.3	43.0 ±14.0	43.0 ±13.9	43.1 ±14.3	42.9 ±13.9
Women	26668 (61.9%)	18329 (63.0%)	5006 (68.5%)	3440 (65.2%)	9883 (59.9%)
Male	16385 (38.1%)	10743 (37.0%)	2301 (31.5%)	1835 (34.8%)	6607 (40.1%)
<i>Time to registration in Covidom</i>					
After symptom onset, days, median (Q1-Q3)	4.0 (2.0-8.0)	4.0 (2.0-7.0)	5.0 (3.0-8.0)	4.0 (2.0-7.0)	4.0 (2.0-7.0)
After physician referral, days, median (Q1-Q3)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	0.0 (0.0-0.0)
<i>High risk profile</i>	17160 (39.8%)	11521 (39.6%)	2710 (37.0%)	2406 (45.6%)	6405 (38.8%)
<i>Mode of inclusion</i>					
GP	23087 (53.6%)	16115 (55.4%)	1781 (24.3%)	2921 (55.3%)	11413 (69.2%)
Hospital	11977 (27.8%)	8053 (27.7%)	4475 (61.1%)	1763 (33.4%)	1815 (11.0%)
EMS	8039 (18.7%)	4936 (17.0%)	1064 (14.5%)	597 (11.3%)	3275 (19.8%)
<i>Socio-economic indicators</i>					
District median income in euros, median (Q1-Q3)	24110.0 (20320.0-27990.0)	24110.0 (20320.0-27990.0)	23160.0 (19720.0-27700.0)	24110.0 (20320.0-28180.0)	24110.0 (20320.0-28180.0)

<i>Risk factors</i>	Lowest income districts (Q1)	11718 (27.5%)	7759 (27.0%)	2286 (31.7%)	1357 (26.0%)	4116 (25.3%)	
	Median income districts (Q2-Q3)	20313 (47.8%)	13862 (48.3%)	3317 (46.0%)	2535 (48.6%)	8010 (49.2%)	
	Highest income districts (Q4)	10505 (24.7%)	7103 (24.7%)	1610 (22.3%)	1322 (25.4%)	4171 (25.6%)	
	18 ≤ Age ≤ 45	25455 (59.1%)	17049 (58.6%)	4160 (56.9%)	3096 (58.6%)	9793 (59.4%)	
	45 < Age ≤ 65	14626 (33.9%)	10204 (35.1%)	2774 (37.9%)	1806 (34.2%)	5624 (34.1%)	
	Age > 65	3016 (7.0%)	1845 (6.3%)	383 (5.2%)	379 (7.2%)	1083 (6.6%)	
	BMI, median (Q1-Q3)		24.8 (22.1-28.4)	25.3 (22.4-29.1)	24.7 (21.9-28.4)	24.7 (22.0-28.2)	
	Healthy weight (BMI ≤ 25 kg/m²)		14621 (51.5%)	3424 (47.9%)	2700 (53.0%)	8497 (52.6%)	
	Overweight (BMI 25–30 kg/m²)		8568 (30.2%)	2185 (30.6%)	1451 (28.5%)	4932 (30.5%)	
	Obesity (BMI > 30 kg/m²)		5195 (18.3%)	1532 (21.5%)	942 (18.5%)	2721 (16.8%)	
<i>Main comorbidities</i>	Current tobacco use		5103 (17.7%)	790 (10.9%)	1163 (22.5%)	3150 (19.2%)	
	Asthma		3685 (12.8%)	814 (11.2%)	824 (16.0%)	2047 (12.5%)	
	Hypertension		3546 (12.3%)	978 (13.5%)	706 (13.7%)	1862 (11.4%)	
	Diabetes		1385 (4.8%)	402 (5.6%)	286 (5.5%)	697 (4.2%)	
	Heart failure		557 (1.9%)	118 (1.6%)	138 (2.7%)	301 (1.8%)	
	Chronic obstructive pulmonary disease		517 (1.8%)	87 (1.2%)	147 (2.8%)	283 (1.7%)	
	Coronary artery disease		399 (1.4%)	77 (1.1%)	97 (1.9%)	225 (1.4%)	
	Cancer under treatment		322 (1.1%)	92 (1.3%)	106 (2.1%)	124 (0.8%)	
	Chronic renal disease		312 (1.1%)	66 (0.9%)	69 (1.3%)	177 (1.1%)	
	Multiple comorbidities (> 1)		1881 (6.5%)	465 (6.4%)	459 (8.9%)	957 (5.8%)	
	None of the reported comorbidities		20468 (71.1%)	5180 (71.6%)	3378 (65.5%)	11910 (72.6%)	
	<i>Symptoms</i>						

<i>General symptoms</i>				
Fatigue	25014 (85.9%)	6592 (90.1%)	4330 (82.0%)	14092 (85.4%)
Temperature \geq 38.5 degrees	14124 (48.5%)	4130 (56.4%)	2160 (40.9%)	7834 (47.5%)
Shivers	15706 (54.0%)	4162 (56.9%)	2570 (48.7%)	8974 (54.4%)
Myalgia	15721 (54.0%)	4443 (60.7%)	2574 (48.7%)	8704 (52.7%)
Fatigue, shivers, or myalgia	26258 (90.2%)	6819 (93.2%)	4582 (86.8%)	14857 (90.0%)
<i>Respiratory symptoms</i>				
Cough	18014 (61.9%)	4910 (67.1%)	2816 (53.3%)	10288 (62.3%)
Shortness of breath	14358 (49.3%)	3470 (47.4%)	2606 (49.3%)	8282 (50.2%)
Chest pain	7643 (26.4%)	1587 (21.8%)	1433 (27.5%)	4623 (28.1%)
Chest oppression	7913 (27.2%)	1713 (23.4%)	1479 (28.0%)	4721 (28.6%)
<i>Gastrointestinal symptoms</i>				
Anorexia	11216 (38.5%)	3528 (48.2%)	1616 (30.6%)	6072 (36.8%)
Nausea/vomiting	6478 (22.3%)	1771 (24.2%)	1292 (24.5%)	3415 (20.7%)
Diarrhea	10483 (36.0%)	2742 (37.5%)	1848 (35.0%)	5893 (35.7%)
<i>Neurological symptoms</i>				
Anosmia	9109 (31.3%)	4039 (55.2%)	644 (12.2%)	4426 (26.8%)
Ageusia	9170 (31.5%)	3859 (52.7%)	760 (14.4%)	4551 (27.6%)
<i>Cutaneous symptoms</i>				
Rash	2851 (9.8%)	721 (9.8%)	499 (9.4%)	1631 (9.9%)
Chilblains	580 (2.0%)	128 (1.8%)	111 (2.1%)	341 (2.1%)
Conjunctivitis	2222 (7.6%)	530 (7.2%)	408 (7.7%)	1284 (7.8%)
<i>Diagnosis confirmation</i>				
PCR Untested	14983 (54.3%)	0 (0.0%)	0 (0.0%)	14983 (100.0%)
PCR Negative	5281 (19.1%)	0 (0.0%)	5281 (100.0%)	0 (0.0%)
PCR Positive	7320 (26.5%)	7320 (100.0%)	0 (0.0%)	0 (0.0%)

EMS, emergency medical service; GP, general practitioner; BMI, body mass index

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Table 2. Patient outcomes in all eligible patients and in the cohort of patients having filled the medical questionnaire by type of PCR results (positive, negative, untested).

	<i>All eligible patients N=43,103</i>	<i>Eligible patients with a completed medical questionnaire N=29,104</i>	<i>Medical questionnaire and Positive PCR N=7320</i>	<i>Medical questionnaire and Negative PCR N=5281</i>	<i>Medical questionnaire and No PCR result N=16,503</i>	
Clinical worsening	1751 (4.1%; 95% CI 3.9–4.2)	1124 (3.9%; 95% CI 3.6–4.1)	659 (9.0%; 95% CI 8.3–9.7)	239 (4.5%; 95% CI 4.0–5.1)	226 (1.4%; 95% CI 1.2–1.5)	
Patient outcome*	Hospitalized	1728 (4.0%; 95% CI 3.8–4.2)	1121 (3.9%; 95% CI 3.6–4.1)	659 (9.0%; 95% CI 8.3–9.7)	239 (4.5%; 95% CI 4.0–5.1)	223 (1.4%; 95% CI 1.2–1.5)
	Deceased	64 (0.1%; 95% CI 0.1–0.2)	6 (0.02%; 95% CI 0.00–0.04)	3 (0.04%; 95% CI - 0.01–0.09)	0 (0.00%; 95% CI 0.00–0.00)	3 (0.02%; 95% CI - 0.00–0.04)

*The sum of the categories can exceed the total number of patients having experienced a clinical worsening as some were included in more than one category
95% CI, 95% confidence interval

Table 3. Univariable and multivariable analyses of factors associated with clinical worsening, for the cohort of Covidom patients with a positive RT-PCR (n=7320).

	Univariable OR (95% CI)	Multivariable OR (95% CI)
General characteristics		
<i>Female (ref)</i>	0.43 (0.37–0.51)	1 (1 – 1)
<i>Male</i>	2.32 (1.97–2.72)	2.08 (1.74–2.50)
High risk profile	2.55 (2.17–3.00)	1.56 (1.29–1.90)
Mode of inclusion		
<i>EMS</i>	0.99 (0.82–1.19)	2.39 (1.88–3.03)
<i>GP (ref)</i>	0.46 (0.40–0.55)	1 (1 – 1)
<i>Hospital</i>	3.18 (2.66–3.80)	0.98 (0.79–1.22)
Socio-economic indicators		
<i>Lowest income districts (Q1)</i>	1.25 (1.06–1.48)	1.16 (0.95–1.42)
<i>Median income districts (Q2-Q3, ref)</i>	0.79 (0.67–0.93)	1 (1 – 1)
<i>Highest income districts (Q4)</i>	1.05 (0.87–1.27)	1.07 (0.85–1.34)
Risk factors		
<i>18 ≤ Age ≤ 45 (ref)</i>	0.42 (0.35–0.49)	1 (1 – 1)
<i>45 < Age ≤ 65</i>	1.48 (1.26–1.73)	1.46 (1.20–1.78)
<i>Age > 65</i>	4.42 (3.48–5.63)	4.05 (2.94–5.58)
<i>Normal weight (BMI ≤ 25 kg/m², ref)</i>	0.51 (0.43–0.61)	1 (1 – 1)
<i>Overweight (BMI 25–30 kg/m²)</i>	1.45 (1.22–1.71)	1.39 (1.13–1.71)
<i>Obesity (BMI > 30 kg/m²)</i>	1.53 (1.28–1.83)	1.57 (1.25–1.97)

Main comorbidities	Current tobacco use	0.48 (0.34–0.67)	0.67 (0.47–0.95)
	Asthma	1.32 (1.04–1.67)	0.96 (0.74–1.24)
	Hypertension	1.76 (1.44–2.16)	0.77 (0.61–0.99)
	Diabetes	2.49 (1.91–3.25)	1.20 (0.88–1.64)
	Heart failure	2.10 (1.29–3.42)	0.73 (0.41–1.30)
	Chronic obstructive pulmonary disease	1.47 (0.78–2.79)	0.64 (0.32–1.28)
	Coronary artery disease	2.08 (1.14–3.79)	1.18 (0.61–2.30)
	Cancer under treatment	2.87 (1.74–4.74)	2.11 (1.20–3.72)
	Chronic renal disease	4.51 (2.65–7.67)	2.59 (1.42–4.73)
Symptoms			
<i>General</i>			
	Temperature \geq 38.5 degrees	1.97 (1.66–2.35)	1.31 (1.07–1.60)
	Fatigue, shivers, or myalgia	1.22 (0.87–1.72)	0.69 (0.47–1.02)
<i>Respiratory</i>			
	Cough	1.55 (1.29–1.86)	1.05 (0.85–1.29)
	Shortness of breath	2.35 (1.99–2.79)	2.21 (1.81–2.70)
	Chest pain	1.50 (1.25–1.79)	1.19 (0.96–1.46)
	Chest oppression	1.26 (1.05–1.51)	1.03 (0.83–1.28)
<i>Gastrointestinal</i>			
	Anorexia	1.68 (1.43–1.98)	1.43 (1.17–1.75)
	Nausea/vomiting	1.41 (1.18–1.68)	1.18 (0.96–1.46)
	Diarrhea	1.57 (1.33–1.84)	1.15 (0.95–1.39)
<i>Neurological symptoms</i>			
	Anosmia or ageusia	0.63 (0.54–0.74)	0.69 (0.57–0.84)
<i>Cutaneous symptoms</i>			
	Rash	1.04 (0.80–1.36)	1.05 (0.78–1.40)
	Chilblains	1.35 (0.78–2.32)	1.02 (0.55–1.86)

Conjunctivitis	0.88 (0.64–1.22)	0.81 (0.58–1.15)
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EMS, emergency medical service; BMI, body mass index; GP, general practitioner; OR, odds ratio; 95% CI, 95% confidence interval

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Figure 1. Flow chart of patients registered in Covidom from March 9 to August 11, 2020 and included in the study.

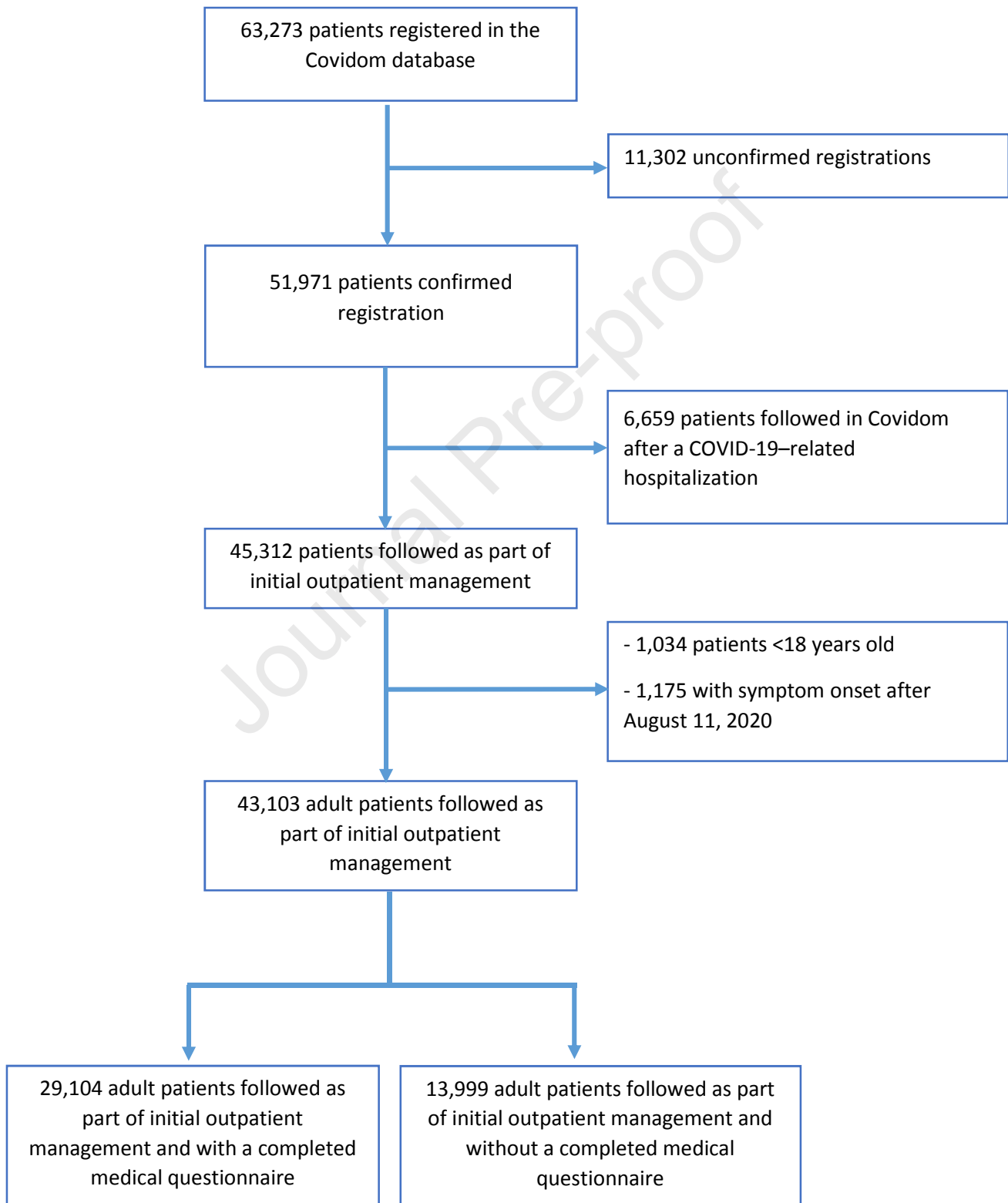
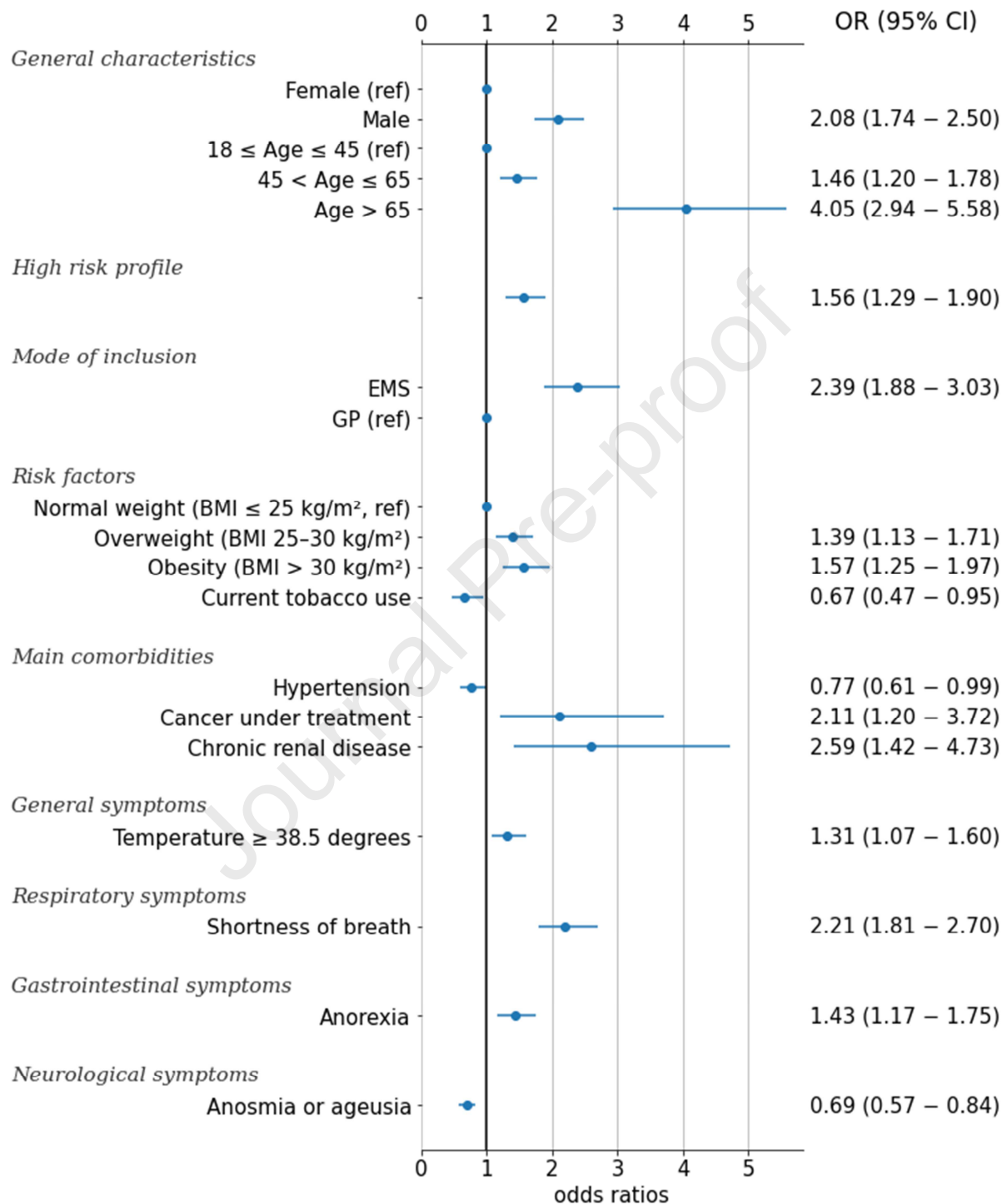


Figure 2. Independent factors associated with clinical worsening from a multivariate logistic regression model for the cohort of Covidom patients with a positive RT-PCR (n=7320).



EMS, emergency medical services; GP, general practitioner; BMI, body mass index; OR, odds ratio; 95% CI, 95% confidence interval