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Characteristics and outcomes of asthmatic outpatients with COVID-19 who receive home telesurveillance

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Dr. Beurnier reports personal fees from AstraZeneca, personal fees from Sanofi outside the submitted work. Pr. Humbert reports personal fees and non-financial support from GlaxoSmithKline, personal fees from Astrazeneca, personal fees from Novartis, personal fees from Sanofi, personal fees from Chiesi, outside the submitted work. The rest of the authors declare that they have no relevant conflicts of interest.

ABSTRACT

BACKGROUND: The prognosis of asthmatic outpatients with COVID-19 needs to be clarified. The objectives of this study were 1) to investigate the characteristics and outcomes of asthmatics receiving initial ambulatory care and home monitoring for COVID-19 with Covidom, a telesurveillance solution and 2) to compare the characteristics and outcomes between asthmatics and non-asthmatics.

METHODS: Inclusion criteria were age ≥ 18 years, suspected or confirmed COVID-19 diagnosis allowing initial ambulatory care, registration in Covidom between March 2020 and April 2021, completion of the initial medical questionnaire. We compared clinical characteristics and outcomes between asthmatics and non-asthmatics and we evaluated whether asthma was independently associated with clinical worsening (hospitalization or death) within 30 days follow-up using a multivariate logistic regression model.

RESULTS: 33,815 patients met the inclusion criteria. Asthma was reported in 4,276 (12.6%). The main comorbidities among asthmatics were obesity (23.1%), hypertension (12.7%) and diabetes (4.5%). As compared with non-asthmatics, asthmatics were more often female (70.0 vs 62.1%, p<0.001), of younger age (42.2 vs 43.8 years, p<0.001) and obese (23.1 vs 17.6%, p<0.001). The rate of hospitalization did not differ significantly (4.7 vs 4.2%, p=0.203) and no asthmatic patient died during follow-up (vs 25 non-asthmatics, 0.1%; p=0.109). In multivariate analysis, asthma was independently associated with higher risk of clinical worsening (OR=1.23 (1.04−1.44), p=0.013).

CONCLUSION: In a large French cohort of patients receiving initial ambulatory care and home monitoring for COVID-19, asthma was independently associated with higher risk of clinical worsening although no asthmatic patient died within the 30 days follow-up.

Key words: COVID-19, SARS-CoV-2, asthma, home monitoring

INTRODUCTION

Asthma is a chronic respiratory condition characterized by variable airflow obstruction, airway hyperresponsiveness and bronchial inflammation that results in a heavy burden for individuals and health services worldwide [1]. Exacerbations of asthma are potentially life-threatening events defined by an acute worsening of the disease, mostly due to viral infections. As coronaviruses are commonly detected in the airways of asthmatics, concerns have arisen about more frequent and/or more severe respiratory symptoms among asthmatics during the 2019 coronavirus disease (COVID-19) pandemic [2]. Surprisingly, the first observations from China reported a low prevalence of asthma among hospitalized patients [3] [4], which was further corroborated by multinational data [5] [6] [7]. In a French study conducted in the Greater Paris, asthmatics were not overrepresented among patients with COVID-19 who required hospitalization and the worse outcomes were observed mainly in patients with major comorbidities [5]. Another study in New York City concluded that asthma diagnosis was not associated with worse outcomes among hospitalized patients 65 years or younger with severe COVID-19, after controlling for age, obesity, or other high-risk comorbidities [8]. While many studies focused on patients with a severe form of the disease, the prognosis of asthmatics with mild COVID-19 receiving initial ambulatory care still needs to be clarified [2]. At the beginning of the outbreak in France, a telesurveillance solution dedicated to COVID-19 outpatients called Covidom was initially deployed in the Greater Paris. Covidom is the first and largest telesurveillance solution described for the home monitoring of COVID-19 cases [9] [10]. It allows close, but minimally invasive outpatient surveillance, using daily short questionnaires and algorithm-based alerts which trigger an adequate medical response. The objectives of this study were 1) to investigate the characteristics and outcomes of asthmatics receiving initial ambulatory care and home

monitoring for COVID-19 with Covidom and 2) to compare the characteristics and outcomes between asthmatics and non-asthmatics.

MATERIAL AND METHODS

Patients and study design

In this study we have included outpatients from the Greater Paris area, with suspected or confirmed COVID-19, that were given the opportunity to use the Covidom solution for home-monitoring of mild COVID-19 as initial outpatient management. As previously reported [9] [10], registration of patients in Covidom could be performed by any physician in case of suspected or confirmed COVID-19 after obtaining informed consent, in the context of initial outpatient management or after COVID-19-related hospitalization. Registration was completed by the patient through a dedicated link received via mobile message or email. Depending on their baseline risk evaluation, as defined by their treating physician, patients received 1 or 2 daily self-administrated monitoring questionnaires for 30 days after symptoms onset in order to assess respiratory rate, heart rate, temperature, and dyspnea as described elsewhere [9]. The answers could trigger alerts, that were handled in the Covidom regional control center, that led to various medical responses, including emergency medical services (EMS) intervention if required. Patients agreed to the potential use of their anonymized data for research purposes. This study was approved by the scientific and ethical committee of the Greater Paris University Hospitals (Assistance Publique-Hôpitaux de Paris) (IRB00011591). Eligible patients for this study were all those registered in Covidom after March 9st 2020, and with symptom onset before April 2nd 2021. Non-inclusion criteria were defined as follows: age < 18 years; non-confirmed registration; registration in Covidom at hospital discharge and non-completion of initial medical questionnaire.

Characteristics at diagnosis and outcomes

Age and gender were collected by the including physician. The following data were collected after inclusion by using a self-reported questionnaire: weight and height, declared chronic conditions or comorbidities using discrete questions (asthma, diabetes, hypertension, heart failure, chronic obstructive pulmonary disease, coronary artery disease, cancer under treatment, chronic renal disease) and initial symptoms. The following outcomes were investigated until 30 days after the onset of symptoms: alerts triggered (detailed as total events; alters leading to EMS call; number of alerts per patient and rate per daily questionnaire), hospitalization and death. Our primary outcome was clinical worsening, defined as hospitalization or death within 30 days after symptom onset. We used different approaches to assess this outcome as precisely as possible: 1) Patient answers to the follow-up questionnaires (15 and 30 days after symptom onset) 2) regional center reports after alerts management and the end of follow-up reasons in case of premature ending (patients or their relatives were called by the regional control center if they did not answer the daily questionnaires to check on their status). 3) Data on patients hospitalized from the Greater Paris University Hospitals (AP-HP) data warehouse (Entrepôt de données de santé [EDS] de l'AP-HP), which includes 39 university hospitals in the greater Paris area covering a large part of this area population (12 million inhabitants). Both hospitalization and death with 30 days after symptom onset, were analysed separately as secondary outcomes. The characteristics and outcomes of patients hospitalized in one of the AP-HP hospitals with accessible medical records on the AP-HP data warehouse were also investigated.

Statistical methods

Quantitative data were expressed as mean (standard deviation) or median (interquartile range (IQR)), with the IQR presented as first quartile to third quartile. Qualitative data were expressed as frequencies and percentages. Where there were missing data, the number of

patients with available information was provided for each variable. We compared patient characteristics, number of alerts and outcomes between asthmatics and non-asthmatics using t-tests or Mann–Whitney U-tests (if not normally distributed) for continuous variables and Chi-squared tests for discrete variables. Univariate followed by multivariate logistic regression models were used to identify whether asthma was independently associated with clinical worsening. Odds-ratios were adjusted on age, sex, current tobacco use and comorbidities: body mass index (BMI), hypertension, diabetes, heart failure, chronic obstructive pulmonary disease (COPD), coronary artery disease, cancer under treatment and chronic renal disease. These variables were considered as relevant to evaluate factors associated with clinical worsening, based on current literature. Alpha risk was set at 5% for all analyses.

RESULTS

Overall population

A flow-chart providing details on patient selection is presented in **Figure 1**. The number of patients registered in Covidom was 80,773. 19,264 patients (23.8%) were not included because they did not confirm their inscription and 17,257 (21.4%) because their medical history was not provided. 33,815 patients met the inclusion criteria, of which 4,276 (12.6%) reported being asthmatics. As compared with non-asthmatics, patients with asthma were younger (mean age 42.2 vs 43.8 years, $p<0.001$) and more likely female (70.0 vs 62.1%, $p<0.001$). The following comorbidities were more prevalent among asthmatics : obesity (23.1 vs 17.6%, $p<0.001$), chronic obstructive pulmonary disease (COPD) (5.1 vs 1.3%, $p<0.001$) and heart failure (2.4 vs 1.9%, $p=0.024$). A lower proportion of asthmatics were treated for cancer (0.8 vs 1.2%, $p=0.024$). Patients with asthma were more prone to experience respiratory symptoms, especially cough (68.2 vs 61.3%, $p<0.001$) and shortness of breath

(67.8 vs 44.7%, p<0.001). Chest pain and tightness were also more prevalent among asthmatics (**Table 1**).

Outcomes

The rate of clinical worsening did not differ between asthmatics and non-asthmatics (4.7 vs 4.3%, p=0.235). The rate of hospitalization was similar (4.7 vs 4.2%, p=0.203). No death was reported at 30 days among asthmatics (vs 25 deaths or 0.1% among non-asthmatics, p=0.109) (**Table 2**). Asthmatics were more prone to trigger at least one Covidom alert (90 vs 85%, p<0.001) and the proportion of alerts leading to emergency service call was higher among asthmatics (1.5 vs 0.8%, p<0.001). In multivariate analysis, asthma was independently associated with clinical worsening (OR=1.23 [1.04-1.44], p=0.013) (**Table 3**). Among patients with available and positive RT-PCR (n=12,212; 36,1%), asthma was also independently associated with clinical worsening (OR=1.29 [1.06−1.56], p=0.012).

Characteristics and outcomes of asthmatics requiring hospitalization during follow-up

Medical records were accessible for 61 (31%) of the 200 hospitalized asthmatics. In this subset of patients, the mean (SD) age was 49.5 (16.2) years with a predominance of female (62.3%). Obesity was the most prevalent comorbidity (33.3%), followed by hypertension (21.3%), diabetes (6.6%) and heart failure (6.6%). SARS-CoV-2 pneumonia was documented in 30 cases (49%) and was mostly associated with mild-to-moderate radiological extension (83%). Three patients (8%) were admitted in a critical care unit. None of them died. Of note, one patient was diagnosed with an asthma exacerbation. She was a 46 years-old female with positive RT-PCR and no comorbidity, previously treated for mild asthma with salbutamol as needed. She was admitted in hospital for dyspnea, cough and wheezing 4 days after the onset of symptoms. No pneumonia was found on the chest CT-scan and she was successfully

treated with nebulization of bronchodilators. No systemic corticosteroids were administrated and she was quickly discharged from hospital at day 2. One patient was treated with biologic for severe asthma (omalizumab). She was a 50 years-old female without comorbidity admitted in hospital due to worsening of diarrhea and vomiting without any respiratory distress. She was discharged from hospital at day 2.

DISCUSSION

In a large French cohort of patients from the Greater Paris area receiving initial ambulatory care and home monitoring with a telesurveillance solution for COVID-19, asthma was independently associated with clinical worsening, but no asthmatic died after a 30 days follow-up.

Asthmatic patients accounted for 12.8% of this cohort total population, whereas the prevalence of asthma in France has been recently reported at 6.4% [11]. Although it might reflect a higher risk of SARS-CoV-2 infection among asthmatics, several factors must be taken into consideration when interpreting this finding. Firstly, we found an overrepresentation of women in the entire cohort (which is consistent with better health-care programs adherence in women, as previously described [12]); since asthma is more frequently diagnosed in adult women [13], this unbalanced sex ratio may contribute to overestimate its prevalence. Likewise, we can assume that asthmatics were more prone to accept registration on a home-monitoring telesurveillance solution than patients without respiratory comorbidity [14][14]. Consistent with our results, the study from Chhiba et al. found that 14% of 1,526 COVID-19 outpatients were asthmatics; the mortality rate was low in these patients and did not differ significantly from the non-asthmatics [15].

In the present study, asthma was independently associated with clinical worsening which was not found in a previous study describing factors associated with clinical worsening among COVID-19 outpatients managed with the Covidom telesurveillance solution [10]. In the present work we included more patients and reached statistical significance which could be clinically relevant, but could also have enhanced some bias. Indeed, in the context of real-life settings we cannot exclude overdiagnosis of asthma, as already reported in industrialized countries [14] and among obese patients [16]. As defined in the GINA report [17], the diagnosis of asthma should be based on both history of variable respiratory symptoms and evidence of airflow limitation. In this large cohort, we were not able to verify that those criteria were obtained for each individual and self-reported comorbidities might have resulted in misdiagnoses (i.e, misclassification of asthma by respondants). We can also hypothesize that asthmatics are also more likely to report symptoms, which may precipitate hospitalization. Given the real-life settings of our study, COVID-19 was clinically-diagnosed by a physician, regardless to the positivity of RT-PCR. Despite the fact that COVID-19 was a major cause of viral symptoms in the Greater Paris area during the study period (march 2020 – april 2021), diagnostic errors cannot be excluded. Notably, similar results were obtained in the subset of patients with available and positive RT-PCR. Other conditions associated with COVID-19-related clinical worsening can masquerade as asthma (such as cardiac insufficiency or COPD) [17], which would impact our main outcome. In the study of Choi et al., asthma was not an independent risk factor for the clinical outcomes of COVID-19 after adjustment [7]. Other authors emphasized the prognostic impact of asthma control during the previous year in COVID-19 patients, reporting an increase in COVID-19-related mortality in asthmatics who experienced an exacerbation within one year [18] [19]. As highlighted elsewhere, chronic use of systemic corticosteroids is an independent risk factor for worst

COVID-19 severity and all-cause mortality in asthmatic patients infected with SARS-CoV-2 [20]. Of note, we did not observe any death in our study of 4,276 asthmatics with COVID-19.

Alerts were more often triggered by asthmatics, however only a few led to EMS call. We found that asthmatics were more prone to experience respiratory symptoms such as cough and shortness of breath. Symptoms of asthma exacerbation may overlap with those of COVID-19 and the distinction between those two clinical presentations might be difficult. Thus, the proportion of alerts related to asthma worsening remains uncertain. We can speculate it was low and some respiratory discomfort might be due to anxiety and dysfunctional breathing disorders, that are notably more frequent in asthmatic women [21] and prevalent among post-COVID-19 patients [22] [23] [24] [25] [26][26]. In a subset of 61 patients with accessible medical records, we found that SARS-CoV-2 pneumonia was the main cause for hospitalization. Only three patients (5%) required admission in an intensive care unit and the only patient diagnosed with an asthma exacerbation had quick recovery. Moreover, we did not find an overrepresentation of severe asthmatics treated with biologics. The presence of other comorbidities such as obesity is probably a crucial element that determine the prognostic of asthmatic patients infected with SARS-COV-2 [5] [27] [28]. Findings also suggest that the risk of SARS-CoV-2 infection and disease severity depends on asthma phenotype, and may be reduced by Th2-high inflammation [29]. Several hypotheses have been proposed to explain the limited impact of asthma on COVID-19-related outcomes: lower bronchial expression of ACE2 viral receptor in asthmatics, protective role of bronchial mucus, advantageous immune profile, better compliance with medical recommendations during the COVID-19 pandemics (social distancing, hand washing, use of mask…) [30]. There is also moderate evidence for a protective role of inhaled corticosteroids [31], which was not analyzed in our study because this information was not systematically collected. In addition, we can hypothesize that a

careful telesurveillance with the Covidom solution had beneficial effects on asthma control, as previously described with other home-monitoring devices [32]. The Covidom solution does not allow a self-monitoring of lung function using a mobile spirometry at home, as previously described by others [33]. This might be a relevant option, as long as enhanced coaching and education by video and telemedicine can be provided [34].

In conclusion, asthma appeared independently associated with clinical worsening in outpatients receiving ambulatory care for COVID-19 using the Covidom telesurveillance solution for home-monitoring, but no death was reported among asthmatics. These results may reflect an increased risk of COVID-19-related clinical worsening among asthmatics, but we cannot exclude underlying epidemiologic biases inherent to this particular population in our convenience sample (i.e, patients who were more likely to be ascertained and over-interpret symptoms). Further research is needed to investigate the potential benefits of home-monitoring among asthmatic patients during the COVID-19 pandemic.

AUTHORS' CONTRIBUTION

AB (guarantor) was involved in the study conception, data analysis, interpretation of results and drafting the manuscript. YY, ADe, LJ were involved in the study conception, data extraction, data analysis, interpretation of results and drafting the manuscript. ADi, ED, FXL and PJ were involved in the Covidom solution development, interpretation of results and critically revising the manuscript. MH was involved in the study conception, data analysis, interpretation of results and critically revising the manuscript.

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Table 1. Clinical characteristics of patients with or without asthma (n=33,815)

Patient characteristics	Asthmatics (n=4,276)	Non asthmatics (n=29,539)	p value
Age (years), mean (SD)	42.2 (13.7)	43.8 (14.2)	<0.001
45 < Age ≤ 65 (%)	1,394 (32.6)	10,729 (36.3)	
BMI (kg/m²), median (IQR), n=33,347	25.3 (22.3-29.4)	24.8 (22.0-28.3)	<0.001
Female gender (%), n=33,774	2,989 (70.0)	18,312 (62.1)	<0.001
Comorbid conditions			
Overweight (BMI 25–30 kg/m²), n=33,347	1,210 (28.6)	8,704 (29.9)	
Obesity (BMI>30kg/m²), n=33,347	979 (23.1)	5,124 (17.6)	<0.001
Hypertension	541 (12.7)	3,591 (12.2)	0.369
Diabetes	193 (4.5)	1,494 (5.1)	0.136
Heart failure	102 (2.4)	551 (1.9)	0.024
Chronic obstructive pulmonary disease	217 (5.1)	378 (1.3)	<0.001
Coronary artery disease	72 (1.7)	393 (1.3)	0.074
Cancer under treatment	34 (0.8)	355 (1.2)	0.024
Chronic renal disease	61 (1.4)	325 (1.1)	0.072
Respiratory symptoms			
Cough	2,916 (68.2)	18,120 (61.3)	<0.001
Shortness of breath	2,898 (67.8)	13,205 (44.7)	<0.001
Chest pain	1,371 (32.1)	7,043 (23.8)	<0.001
Chest tightness	1,491 (34.9)	7,215 (24.4)	<0.001
General symptoms			
Fatigue	3,758 (87.9)	25,368 (85.9)	<0.001
Fever	2,062 (48.2)	14,405 (48.8)	0.517
Shivers	2,439 (57.0)	15,808 (53.5)	<0.001
Myalgia	2,505 (58.6)	15,932 (53.9)	<0.001
Gastrointestinal symptoms			
Anorexia	1,695 (39.6)	11,387 (38.5)	0.176
Nausea/vomiting	1,210 (28.3)	6,838 (23.1)	<0.001
Diarrhea	1,655 (38.7)	10,175 (34.4)	<0.001
Neurological symptoms			
Anosmia	1,300 (30.4)	9,924 (33.6)	<0.001
Ageusia	1,326 (31.0)	9,700 (32.8)	0.018
Cutaneous symptoms			
Rash	507 (11.9)	2,614 (8.8)	<0.001
Chilblains	88 (2.1)	530 (1.8)	0.253
Conjunctivitis	392 (9.2)	2,021 (6.8)	<0.001

Qualitative data are expressed as frequency (% of total). In case of variable with missing data, the number of patients with available information is specified. BMI: body mass index; IQR: interquartile range presented as first quartile (Q1) – third quartile (Q3); SD : standard deviation.

Table 2. Outcomes of patients with or without asthma (n=33,815)

Outcomes	Asthmatics	Non asthmatics	p value
Worsening (hospitalization or death, %)	200 (4.7)	1,261 (4.3)	0.235
Hospitalization (%)	200 (4.7)	1,253 (4.2)	0.203
Death (%)	0 (0.0)	25 (0.1)	0.109
At least 1 COVIDOM Alert (%)	3,849 (90.0)	25,095 (85.0)	<0.001
Alert leading to emergency service call (%)	65 (1.5)	249 (0.8)	<0.001
Number of alerts per patient, median (IQR), n=28,944	5.0 (2.0-11.0)	4.0 (2.0-9.0)	<0.001
Rate of alerts per follow-up, median (IQR), n=28,944	0.4 (0.1-0.8)	0.3 (0.1-0.7)	<0.001

Qualitative data are expressed as frequency (% of total). In case of variable with missing data, the number of patients with available information is specified. IQR: interquartile range presented as first quartile (Q1) – third quartile (Q3).

Table 3. Association between asthma and clinical worsening

Multivariate analysis	OR (95% CI)	p-value
Unadjusted	1.10 (0.94−1.28)	0.235
Adjusted on age, sex, current tobacco use and comorbidities	1.23 (1.04−1.44)	0.013

Comorbidities are BMI, hypertension, diabetes, heart failure, COPD, coronary artery disease, cancer under treatment, and chronic renal disease. Age and BMI as 3 categories (18−45 years, 46−65 years, > 65 years and < 25 kg/m², 25−30 kg/m², > 30 kg/m²).

REFERENCES

1. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir. Med.* 2020; 8: 585–596.

2. Hartmann-Boyce J, Gunnell J, Drake J, Otunla A, Suklan J, Schofield E, Kinton J, Inada-Kim M, Hobbs FDR, Dennison P. Asthma and COVID-19: review of evidence on risks and management considerations. *BMJ Evid.-Based Med.* [Internet] Royal Society of Medicine; 2020 [cited 2021 Jan 3]; Available from: https://ebm.bmj.com/content/early/2020/09/02/bmjebm-2020-111506.

3. Zhang J, Dong X, Cao Y, Yuan Y, Yang Y, Yan Y, Akdis CA, Gao Y. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy* 2020; 75: 1730–1741.

4. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, Shi J, Zhou M, Wu B, Yang Z, Zhang C, Yue J, Zhang Z, Renz H, Liu X, Xie J, Xie M, Zhao J. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J. Allergy Clin. Immunol.* Elsevier; 2020; 146: 110–118.

5. Beurnier A, Jutant E-M, Jevnikar M, Boucly A, Pichon J, Preda M, Frank M, Laurent J, Richard C, Monnet X, Duranteau J, Harrois A, Chaumais M-C, Bellin M-F, Noël N, Bulifon S, Jaïs X, Parent F, Seferian A, Savale L, Sitbon O, Montani D, Humbert M. Characteristics and outcomes of asthmatic patients with COVID-19 pneumonia who require hospitalisation. *Eur. Respir. J.* [Internet] European Respiratory Society; 2020 [cited 2020 Dec 29]; Available from: https://erj.ersjournals.com/content/early/2020/07/23/13993003.01875-2020.

6. Caminati M, Vultaggio A, Matucci A, Senna G, Almerigogna F, Bagnasco D, Chieco-Bianchi F, Cosini F, Girelli D, Guarnieri G, Menzella F, Micheletto C, Olivieri O, Passalacqua G, Pini L, Rossi O, Vianello A, Vivarelli E, Crisafulli E. Asthma in a large COVID-19 cohort: Prevalence, features, and determinants of COVID-19 disease severity. *Respir. Med.* [Internet] Elsevier; 2021 [cited 2021 Jan 3]; 176Available from: https://www.resmedjournal.com/article/S0954-6111(20)30401-7/abstract.

7. Choi YJ, Park J-Y, Lee HS, Suh J, Song JY, Byun MK, Cho JH, Kim HJ, Lee J-H, Park J-W, Park HJ. Effect of Asthma and Asthma Medication on the Prognosis of Patients with COVID-19. *Eur. Respir. J.* [Internet] European Respiratory Society; 2020 [cited 2020 Dec 29]; Available from: https://erj.ersjournals.com/content/early/2020/09/17/13993003.02226-2020.

8. Lovinsky-Desir S, Deshpande DR, De A, Murray L, Stingone JA, Chan A, Patel N, Rai N, DiMango E, Milner J, Kattan M. Asthma among hospitalized patients with COVID-19 and related outcomes. *J. Allergy Clin. Immunol.* Elsevier; 2020; 146: 1027-1034.e4.

9. Yordanov Y, Dechartres A, Lescure X, Apra C, Villie P, Marchand-Arvier J, Debuc E, Dinh A, Jourdain P. Covidom, a Telesurveillance Solution for Home Monitoring Patients

With COVID-19. *J. Med. Internet Res.* [Internet] 2020 [cited 2021 Jan 3]; 22Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7644373/.

10. Yordanov Y, Dinh A, Bleibtreu A, Mensch A, Lescure F-X, Debuc E, Jourdain P, Jaulmes L, Dechartres A. Clinical characteristics and factors associated with hospital admission or death in 43 103 adult outpatients with coronavirus disease 2019 managed with the Covidom telesurveillance solution: a prospective cohort study. *Clin. Microbiol. Infect.* Elsevier; 2021; 27: 1158–1166.

11. Raherison-Semjen C, Izadifar A, Russier M, Rolland C, Aubert J-P, Sellami R, Leynaud D, Fabry-Vendrand C, Didier A. Late Breaking Abstract - Asthma prevalence and management in adults in France in 2018: ASTHMAPOP survey. *Eur. Respir. J.* [Internet] European Respiratory Society; 2018 [cited 2021 Jan 10]; 52Available from: https://erj.ersjournals.com/content/52/suppl_62/OA292.

12. Deeks A, Lombard C, Michelmore J, Teede H. The effects of gender and age on health related behaviors. *BMC Public Health* 2009; 9: 213.

13. Leynaert B, Sunyer J, Garcia-Esteban R, Svanes C, Jarvis D, Cerveri I, Dratva J, Gislason T, Heinrich J, Janson C, Kuenzli N, Marco R de, Omenaas E, Raherison C, Real FG, Wjst M, Zemp E, Zureik M, Burney PGJ, Anto JM, Neukirch F. Gender differences in prevalence, diagnosis and incidence of allergic and non-allergic asthma: a population-based cohort. *Thorax* BMJ Publishing Group Ltd; 2012; 67: 625–631.

14. Luks VP, Vandemheen KL, Aaron SD. Confirmation of asthma in an era of overdiagnosis. *Eur. Respir. J.* European Respiratory Society; 2010; 36: 255–260.

15. Chhiba KD, Patel GB, Vu THT, Chen MM, Guo A, Kudlaty E, Mai Q, Yeh C, Muhammad LN, Harris KE, Bochner BS, Grammer LC, Greenberger PA, Kalhan R, Kuang FL, Saltoun CA, Schleimer RP, Stevens WW, Peters AT. Prevalence and characterization of asthma in hospitalized and nonhospitalized patients with COVID-19. *J. Allergy Clin. Immunol.* 2020; 146: 307-314.e4.

16. Aaron SD, Vandemheen KL, Boulet L-P, McIvor RA, FitzGerald JM, Hernandez P, Lemiere C, Sharma S, Field SK, Alvarez GG, Dales RE, Doucette S, Fergusson D. Overdiagnosis of asthma in obese and nonobese adults. *CMAJ* CMAJ; 2008; 179: 1121–1131.

17. GINA-Main-Report-2021-V2-WMS.pdf [Internet]. [cited 2021 Oct 18].Available from: https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf.

18. Lee SC, Son KJ, Han CH, Jung JY, Park SC. Impact of comorbid asthma on severity of coronavirus disease (COVID-19). *Sci. Rep.* Nature Publishing Group; 2020; 10: 21805.

19. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, Curtis HJ, Mehrkar A, Evans D, Inglesby P, Cockburn J, McDonald HI, MacKenna B, Tomlinson L, Douglas IJ, Rentsch CT, Mathur R, Wong AYS, Grieve R, Harrison D, Forbes H, Schultze A, Croker R, Parry J, Hester F, Harper S, Perera R, Evans SJW, Smeeth L, Goldacre B. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* Nature Publishing Group; 2020; 584: 430–436.

20. Adir Y, Humbert M, Saliba W. COVID-19 risk and outcomes in adult asthmatic patients treated with biologics or systemic corticosteroids: Nationwide real-world evidence. *J. Allergy Clin. Immunol.* 2021; 148: 361-367.e13.

21. Thomas M, McKinley RK, Freeman E, Foy C, Price D. The prevalence of dysfunctional breathing in adults in the community with and without asthma. *Prim. Care Respir. J. J. Gen. Pract. Airw. Group* 2005; 14: 78–82.

22. Motiejunaite J, Balagny P, Arnoult F, Mangin L, Bancal C, Vidal-Petiot E, Flamant M, Jondeau G, Cohen-Solal A, d'Ortho M-P, Frija-Masson J. Hyperventilation as one of the mechanisms of persistent dyspnoea in SARS-CoV-2 survivors. *Eur. Respir. J.* [Internet] European Respiratory Society; 2021 [cited 2021 Oct 18]; 58Available from: https://erj.ersjournals.com/content/58/2/2101578.

23. Aparisi Á, Ybarra-Falcón C, García-Gómez M, Tobar J, Iglesias-Echeverría C, Jaurrieta-Largo S, Ladrón R, Uribarri A, Catalá P, Hinojosa W, Marcos-Mangas M, Fernández-Prieto L, Sedano-Gutiérrez R, Cusacovich I, Andaluz-Ojeda D, de Vega-Sánchez B, Recio-Platero A, Sanz-Patiño E, Calvo D, Baladrón C, Carrasco-Moraleja M, Disdier-Vicente C, Amat-Santos IJ, San Román JA. Exercise Ventilatory Inefficiency in Post-COVID-19 Syndrome: Insights from a Prospective Evaluation. *J. Clin. Med.* 2021; 10: 2591.

24. Motiejunaite J, Balagny P, Arnoult F, Mangin L, Bancal C, d'Ortho M-P, Frija-Masson J. Hyperventilation: A Possible Explanation for Long-Lasting Exercise Intolerance in Mild COVID-19 Survivors? *Front. Physiol.* 2020; 11: 614590.

25. Taverne J, Salvator H, Leboulch C, Barizien N, Ballester M, Imhaus E, Chabi-Charvillat M-L, Boulin A, Goyard C, Chabrol A, Catherinot E, Givel C, Couderc L-J, Tcherakian C. High incidence of hyperventilation syndrome after COVID-19. *J. Thorac. Dis.* [Internet] AME Publishing Company; 2021 [cited 2021 Sep 8]; 13Available from: https://jtd.amegroups.com/article/view/52497.

26. George PM, Barratt SL, Condliffe R, Desai SR, Devaraj A, Forrest I, Gibbons MA, Hart N, Jenkins RG, McAuley DF, Patel BV, Thwaite E, Spencer LG. Respiratory follow-up of patients with COVID-19 pneumonia. *Thorax* BMJ Publishing Group Ltd; 2020; 75: 1009–1016.

27. Wang Y, Ao G, Qi X, Ma M. The relationship between severe or dead COVID-19 and asthma: A meta-analysis. *Clin. Exp. Allergy* [Internet] [cited 2020 Dec 29]; n/aAvailable from: https://onlinelibrary.wiley.com/doi/abs/10.1111/cea.13773.

28. Antonicelli L, Tontini C, Manzotti G, Ronchi L, Vaghi A, Bini F, Scartabellati A, Menzella F, Michele FD, Musarra A, Micheletto C, Bilò MB. Severe asthma in adults does not significantly affect the outcome of COVID-19 disease: Results from the Italian Severe Asthma Registry. *Allergy* [Internet] [cited 2020 Dec 29]; n/aAvailable from: https://onlinelibrary.wiley.com/doi/abs/10.1111/all.14558.

29. Adir Y, Saliba W, Beurnier A, Humbert M. Asthma and COVID-19: an update. *Eur. Respir. Rev.* [Internet] European Respiratory Society; 2021 [cited 2022 Jan 6]; 30Available from: https://err.ersjournals.com/content/30/162/210152.

30. Farne H, Singanayagam A. Why asthma might surprisingly protect against poor outcomes in COVID-19. *Eur. Respir. J.* [Internet] European Respiratory Society; 2020 [cited 2020 Dec 29]; Available from: https://erj.ersjournals.com/content/early/2020/10/29/13993003.03045-2020.

31. Griesel M, Wagner C, Mikolajewska A, Stegemann M, Fichtner F, Metzendorf M-I, Nair AA, Daniel J, Fischer A-L, Skoetz N. Inhaled corticosteroids for the treatment of COVID-19. *Cochrane Database Syst. Rev.* [Internet] John Wiley & Sons, Ltd; 2022 [cited 2022 Jul 7]; Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD015125/full/es.

32. Ryan D, Pinnock H, Lee AJ, Tarassenko L, Pagliari C, Sheikh A, Price D. The CYMPLA trial. Mobile phone-based structured intervention to achieve asthma control in patients with uncontrolled persistent asthma: a pragmatic randomised controlled trial. *Prim. Care Respir. J. J. Gen. Pract. Airw. Group* 2009; 18: 343–345.

33. Kupczyk M, Hofman A, Kołtowski Ł, Kuna P, Łukaszyk M, Buczyłko K, Bodzenta-Łukaszyk A, Nastałek P, Soliński M, Dąbrowiecki P. Home self-monitoring in patients with asthma using a mobile spirometry system. *J. Asthma* Taylor & Francis; 2021; 58: 505–511.

34. Wilson KC, Kaminsky DA, Michaud G, Sharma S, Nici L, Folz RJ, Barjaktarevic I, Bhakta NR, Cheng G, Chupp GL, Cole A, Dixon AE, Finigan JH, Graham B, Hallstrand TS, Haynes J, Hankinson J, MacIntyre N, Mandel J, McCarthy K, McCormack M, Patil SP, Rosenfeld M, Senitko M, Sethi S, Swenson ER, Stanojevic S, Teodorescu M, Weiner DJ, Wiener RS, et al. Restoring Pulmonary and Sleep Services as the COVID-19 Pandemic Lessens. From an Association of Pulmonary, Critical Care, and Sleep Division Directors and American Thoracic Society–coordinated Task Force. *Ann. Am. Thorac. Soc.* American Thoracic Society - AJRCCM; 2020; 17: 1343–1351.

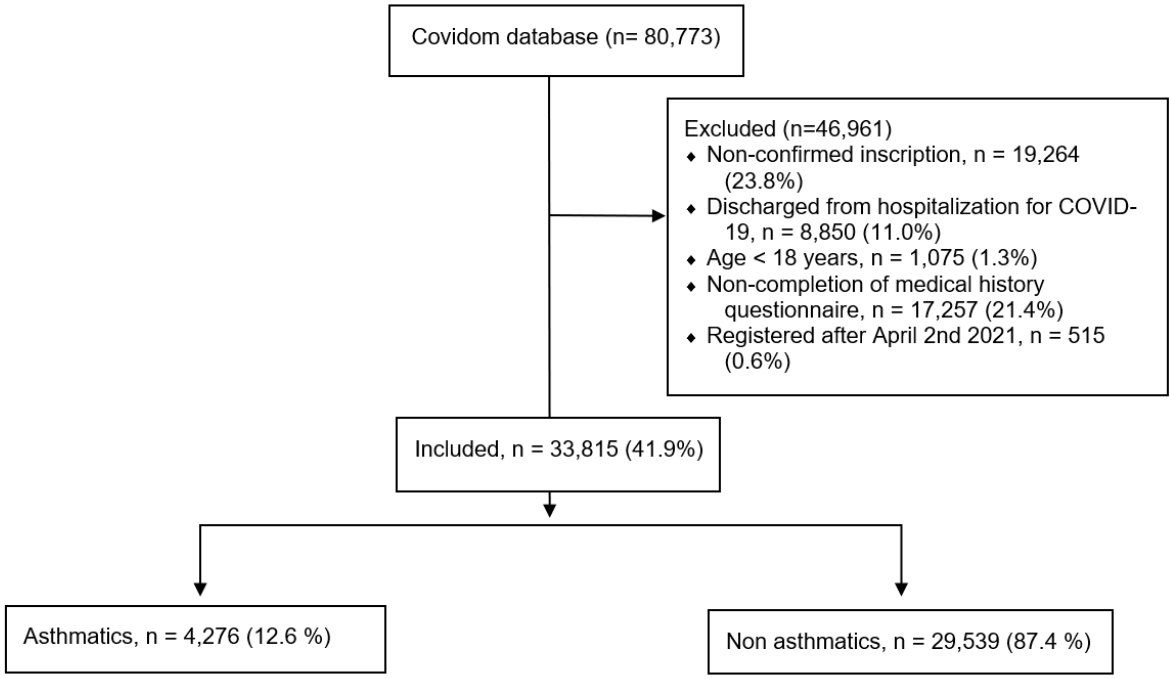

Figure 1. Selection of patients from the Covidom database.