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# Management of severe asthma during the first lockdown phase of SARS-CoV-2 pandemic: Tips for facing the second wave

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ABSTRACT

SARS-CoV-2 pandemic has contributed to implement telemedicine, allowing clinicians to follow the patient remotely, therefore minimizing the risk of any exposure to positive COVID-19 patients. We summarize the approaches adopted to treat and monitor severe asthmatic patients during the lockdown phase of the pandemic. Our experience supports the strategy that every effort should be made to minimize patient contact with the health-care system, planning a pathway that allows patients to receive appropriate medical care and continue the biological therapies, thus preventing the loss of disease control and acute severe exacerbations.

## 1. Introduction

The new coronavirus outbreak (SARS-CoV-2) [1] is characterized by high contagiousness and mainly causes respiratory tract infections [2]; thus, it has become necessary to design new approaches to reorganize health resources and to guarantee social distancing in order to limit the spread of the virus. Outpatient clinics have also been rearranged with the purpose of maintaining the follow-up of patients with chronic respiratory diseases. Most of the outpatient visits have been transformed into "virtual visits" in which the patient is followed through electronic means [3]. The current emergency situation has therefore contributed to implement telemedicine, allowing clinicians to follow the patient remotely, minimizing the risk of any exposure to positive COVID-19 patients related to in-person healthcare visits in hospital facilities [4]. Telemedicine has proven to be particularly useful in the management of patients with chronic diseases such as asthma that need continuous monitoring. Romano et al. [5] showed that the use of telemedicine to follow-up asthmatics patients led to a reduction of respiratory symptoms and improve quality of life. Another study compared telemedicine with face-to-face visits and showed equal disease control suggesting that telemedicine can be considered as a valid alternative [6] for a home-monitoring healthcare system.

Patients with severe asthma are with an increased risk of serious and frequent exacerbations, hospital admissions, therefore the pharmacological treatment of asthma needs to be carefully chosen and frequently reassessed [7,8]. The impact of COVID-19 pandemic implied the determination of a global new approach to guide clinicians in the management of severe asthma; The use of oral corticosteroids (OCS), when needed, is strongly supported to minimize the risk of severe attacks or exacerbations; the importance of an asthma home-monitoring system that is focused on symptoms control and adherence to treatment has been suggested, highlighting that biologic therapies should be maintained in order to limit the need for OCS [9,10]. Nonetheless, a relevant problem is the differential diagnosis between acute asthma exacerbations and COVID-19. The clinical scenario in which SARS-CoV-2 infection occurs is indeed dominated by dry cough and dyspnea, symptoms also attributable to asthma. The presence of additional symptoms such as fever, ageusia, anosmia, and diarrhea, supported by the epidemiological link, may guide physicians to the diagnosis of COVID-19 [2].

We narratively summarize our experience of monitoring severe asthmatic patients during the lockdown phase of the pandemic. Strategies and approaches adopted to treat and monitor severe asthmatic patients who were regularly followed at the outpatient clinic for severe asthma of the University Hospital of Palermo, Italy, during the lockdown period of the pandemic and their effects on disease control and quality of life are described.

## 2. Materials and methods

In accordance with current guidelines [11], all patients kept their inhalation therapy unchanged. As stated by Wang [12], the risk of

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**Abbreviations**

OCS oral corticosteroids
ICSinhaled corticosteroid
PSPpatient supported program
ACQ-6 Asthma Control Questionnaire
ACTAsthma Control Test
AQLQ Asthma Quality of Life Questionnaire
EMDelectronic monitoring devices
PL pre lockdown
DL during lockdown

exacerbation is higher whether it is associated with inhaled corticosteroid (ICS) discontinuation. On the other hand, nebulization is an aerosol-generating medical procedure that can increase the risk of aerosolization of SARS-CoV-2. A metered-dose inhaler with a valved-holding chamber or a dry powder inhaler were therefore preferred over nebulizers to reduce the risk of aerosol spread of virus particles for healthcare workers and caregivers.

Patients under biologic drugs were advised to continue the administration of medications. With the aim to reduce contacts and to avoid any withdrawal of biological treatment, patients supported programs (PSP) were implemented and home delivery of medications were activated. Patients treated with Benralizumab and Dupilumab were trained to self-administer. Since stress, fear and anxiety can trigger asthma attacks, we tried help patients to feel more in control and preserve mental health, suggesting to have good quality information and reliable sources about COVID-19 and to avoid rumors and speculations that could increase their concerns. Emotional and psychological support provided by the Health Ministry and civil protection department, available every day accessible 16 h/die by phone or online and free of charge was recommended for more frail subjects. A special care was dedicated to older patients, since it has been demonstrated that biologics are safe in this population [13].

**Table 1**
**Characteristics of study subjects.** * ACT pre, ACQ pre and AQLQ pre, registered when patients started a new biological treatment. PL: pre lockdown; DL: during lockdown.

| N. | Sex | Age | Drug | Administration | ACT $_{PL}$ | ACT$_{DL}$ | ACQ $_{PL}$ | ACQ $_{DL}$ | AQLQ $_{PL}$ | AQLQ $_{DL}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| **1*** | F | 58 | Benralizumab | Home | 20 | 25 | 2.50 | 0.00 | 2.12 | 6.28 |
| **2*** | M | 68 | Benralizumab | Home | 12 | 24 | 3.16 | 0.33 | 3.53 | 6.03 |
| **3** | F | 56 | Benralizumab | Home | 11 | 10 | 3.0 | 2.6 | 3.96 | 3.50 |
| **4** | M | 62 | Benralizumab | Home | 22 | 21 | 0.33 | 0.66 | 5.25 | 6.03 |
| **5** | F | 72 | Benralizumab | Home | 11 | 19 | 2.33 | 1.66 | 6.0 | 5.28 |
| **6** | F | 48 | Benralizumab | Hospital | 15 | 8 | 1.50 | 5.16 | 3.75 | 1.87 |
| **7** | F | 19 | Benralizumab | Home | 15 | 14 | 2.16 | 2.60 | 5.18 | 4.46 |
| **8** | F | 71 | Benralizumab | Home | 13 | 15 | 3.16 | 3.16 | 2.18 | 2.18 |
| **9** | M | 43 | Benralizumab | Home | 12 | 20 | 2.83 | 0.83 | 4.43 | 2.67 |
| **10** | F | 52 | Benralizumab | Home | 5 | 5 | 4.85 | 4.85 | 1.87 | 1.87 |
| **11** | F | 60 | Benralizumab | Home | 22 | 22 | 1.66 | 1.66 | 3.53 | 4.53 |
| **12*** | F | 58 | Benralizumab | Home | 21 | 24 | 2.5 | 0.33 | 4.46 | 6.09 |
| **13** | F | 59 | Benralizumab | Home | 20 | 21 | 1.5 | 1.5 | 4.53 | 4.53 |
| **14** | F | 40 | Benralizumab | Home | 12 | 14 | 2.16 | 3.33 | 3.12 | 3.12 |
| **15** | F | 42 | Benralizumab | Home | 10 | 9 | 3.66 | 3.16 | 3.06 | 3.25 |
| **16** | F | 52 | Benralizumab | Hospital | 10 | 11 | 2.67 | 2.00 | 3.53 | 4.53 |
| **17** | M | 44 | Benralizumab | Home | 20 | 22 | 1.30 | 0.66 | 4.87 | 5.34 |
| **18** | M | 49 | Benralizumab | Home | 25 | 25 | 0.00 | 0.00 | 6.78 | 6.78 |
| **19** | M | 55 | Benralizumab | Home | 20 | 14 | 0.83 | 2.33 | 6.28 | 4.09 |
| **20** | M | 52 | Benralizumab | Home | 20 | 17 | 2.0 | 2.5 | 5.09 | 3.31 |
| **21** | M | 53 | Benralizumab | Home | 5 | 5 | 5.80 | 5.80 | 1.90 | 1.90 |
| **22** | F | 52 | Benralizumab | Home | 13 | 21 | 2.33 | 1.16 | 4.06 | 5.18 |
| **23** | F | 73 | Benralizumab | Home | 23 | 25 | 0.28 | 0.16 | 5.46 | 6.72 |
| **24** | M | 38 | Benralizumab | Home | 25 | 25 | 0.16 | 0.16 | 7.00 | 7.00 |
| **25** | F | 41 | Benralizumab | Home | 22 | 23 | 0.66 | 0.66 | 4.96 | 4.84 |
| **26*** | M | 56 | Benralizumab | Home | 16 | 21 | 1.8 | 0.83 | 5.18 | 5.81 |
| **27** | F | 47 | Benralizumab | Home | 20 | 18 | 1.3 | 1.3 | 6.31 | 5.53 |
| **28** | M | 64 | Benralizumab | Hospital | 21 | 21 | 0.50 | 0.50 | 4.18 | 4.18 |
| **29** | M | 53 | Benralizumab | Home | 24 | 24 | 0.00 | 0.33 | 5.18 | 4.46 |
| **30** | M | 35 | Benralizumab | Home | 25 | 25 | 0.00 | 0.00 | 4.96 | 5.09 |
| **31** | F | 54 | Omalizumab | Hospital | 17 | 15 | 1.5 | 2.00 | 4.18 | 4.06 |
| **32** | F | 22 | Omalizumab | Hospital | 20 | 20 | 1.3 | 1.3 | 5.18 | 5.81 |
| **33** | F | 16 | Omalizumab | Hospital | 21 | 21 | 0.00 | 0.00 | 4.53 | 4.53 |
| **34** | F | 52 | Omalizumab | Hospital | 20 | 18 | 1.3 | 1.3 | 6.28 | 4.53 |
| **35** | F | 38 | Omalizumab | Hospital | 18 | 19 | 0.50 | 0.66 | 5.18 | 4.43 |
| **36** | M | 61 | Omalizumab | Hospital | 13 | 15 | 2.5 | 2.0 | 2.5 | 2.5 |
| **37** | F | 64 | Omalizumab | Hospital | 22 | 22 | 1.66 | 1.66 | 3.53 | 4.53 |
| **38** | F | 59 | Mepolizumab | Home | 10 | 11 | 3.83 | 3.50 | 3.56 | 3.56 |
| **39** | M | 60 | Mepolizumab | Home | 17 | 17 | 2.0 | 2.0 | 4.6 | 4.6 |
| **40** | F | 52 | Mepolizumab | Home | 19 | 19 | 1.5 | 1.5 | 5.34 | 5.34 |
| **41** | F | 53 | Mepolizumab | Home | 11 | 10 | 0.4 | 1.2 | 3.53 | 3.53 |
| **42** | F | 55 | Mepolizumab | Home | 20 | 20 | 0.16 | 0.16 | 2.31 | 4.18 |
| **43** | F | 61 | Mepolizumab | Home | 17 | 15 | 1.5 | 2.0 | 4.53 | 4.43 |
| **44** | M | 41 | Mepolizumab | Home | 23 | 21 | 0.66 | 0.40 | 6.68 | 5.82 |
| **45** | M | 66 | Mepolizumab | Home | 23 | 22 | 0.50 | 0.40 | 6.31 | 5.81 |
| **46** | M | 45 | Mepolizumab | Home | 24 | 24 | 0.00 | 0.33 | 4.18 | 4.18 |
| **47** | M | 53 | Mepolizumab | Hospital | 23 | 21 | 0.4 | 1.2 | 6.28 | 4.43 |
| **48** | M | 38 | Mepolizumab | Hospital | 20 | 19 | 0.50 | 0.66 | 5.18 | 5.09 |
| **49** | F | 56 | Dupilumab | Home | 24 | 24 | 0.16 | 0.16 | 6.78 | 6.78 |
| **50** | F | 61 | Dupilumab | Home | 17 | 20 | 1.83 | 1.50 | 5.0 | 5.0 |

## 3. Results

Since the first day of the lockdown in Italy (March 7, 2020) until May 20, we monitored 50 consecutive severe asthmatics under biologic treatment: 7 patients under Omalizumab, 11 under Mepolizumab, 30 under Benralizumab and 2 under Dupilumab. General characteristics of the selected patients are reported in Table 1. The degree of asthma control (Asthma Control Questionnaire, ACQ-6, and Asthma Control Test, ACT) and health-related quality of life (Asthma Quality of Life Questionnaire, AQLQ Asthma) were collected before and during the global lockdown. The majority of patients treated with Benralizumab joined the PSP "*Connect 360*", which allowed the administration of the drug at home with the possibility of appointing a caregiver for the drug administration. The program also offered a nurse that answered questions on treatment and self-injection procedures, friendly reminded the injection date and also furnished a motivational coaching. Eight patients under Mepolizumab joined the PSP "*Aria di Casa*" (Home Air). A nurse, responsible for taking the drug at hospital pharmacy, administered the drug at home for those patients who could not appoint a caregiver for home administration and were not able to self-inject the medication. The self-administration was not activated for Omalizumab due to lack of local administrative approval; for these patients, as well as for those under anti-IL5 treatment who refused home administration, regular appointments at the hospital facilities were assured. We provided proper training to patients and/or caregivers on the subcutaneous injection technique of administration using the pre-filled syringe. The team of respiratory physicians and nurses guaranteed telephone support to monitor general clinical conditions. Phone contacts were scheduled the day of the home administration of biological drugs. For those patients that reported worsening of symptoms whose visit could not be postponed, we set up a specific algorithm that included, the day before the in-person visit, a phone call triage to explore the occurrence of respiratory symptoms suggestive of COVID-19 and/or the presence of a recent contact with COVID-19 positive subjects. Fig. 1 describes the algorithm used. Once guaranteed the access to the facility, the patient was instructed to follow rigid protocols (administering specific questions related to health status and measuring body temperature) to mitigate the risk of potential contagious of SARS-CoV-2 infection. The outpatient clinic was also reorganized with separated waiting areas and pathways. Fig. 2a, b and c shows changes of asthma control and health-related quality of life during the lockdown phase.

Among patients under biological therapies, two showed a rapid worsening of respiratory symptoms characterized by dyspnea, dry cough and chest pain which made it necessary to undertake the so-called "COVID-19 path" that consisted of a short hospitalization during which patients underwent a chest CT-scan, blood analysis and nasopharyngeal swab for SARS-CoV-2, which resulted negative with consequent patient discharge. Three patients had an asthma exacerbation that required OCS, following current recommendations [14]. **Among the study subjects, older individuals (i.e. those aged >65 yrs) did not show any different behavior in terms of asthma control, with respect to younger subjects.**

Due to the restrictions imposed by the pandemic, no lung function testing was performed, and any functional evaluation was postponed.

## 4. Discussion

Our experience supports the strategy that, during the COVID-19 pandemic, every effort should be made in patients affected by severe chronic respiratory diseases like severe asthma to minimize patient contact with the health-care system, planning specific pathways that allow patients to receive appropriate medical care and to continue the biological therapies administration, preventing the loss of disease control and acute severe exacerbations. We were able to achieve careful monitoring of symptoms and exacerbations by using a home-care approach, preventing as much as possible hospital admissions and accesses to emergency department. Home-monitoring medicine may be considered a useful tool even post COVID-19 pandemic. What is the lesson that we learnt from this experience? In the midst of a second wave of the SARS-CoV-2 outbreak some tips can be highlighted. Novel forms of self-monitoring and management are gaining credit especially during COVID-19 pandemic. In the last decade, new techniques have been developed to improve asthma control and to support the importance of self-management of chronic respiratory diseases; Electronic Monitoring

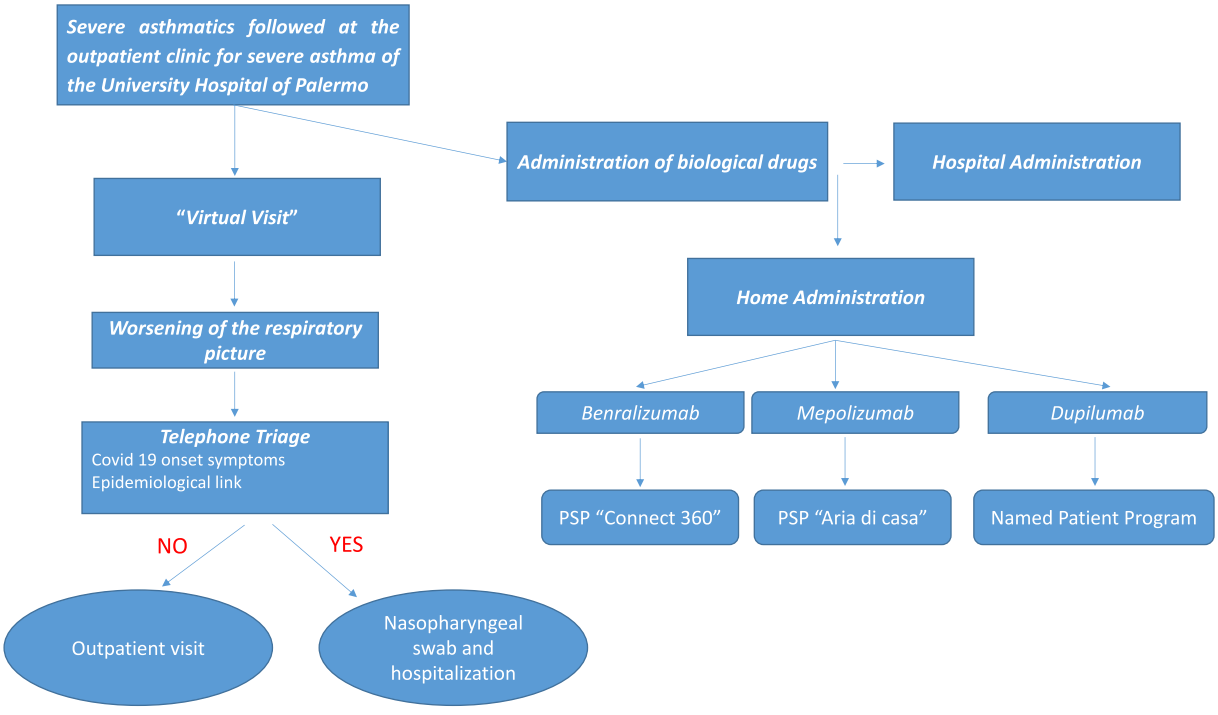


**Fig. 1.** Algorithm used to treat and monitor severe asthmatic patients.

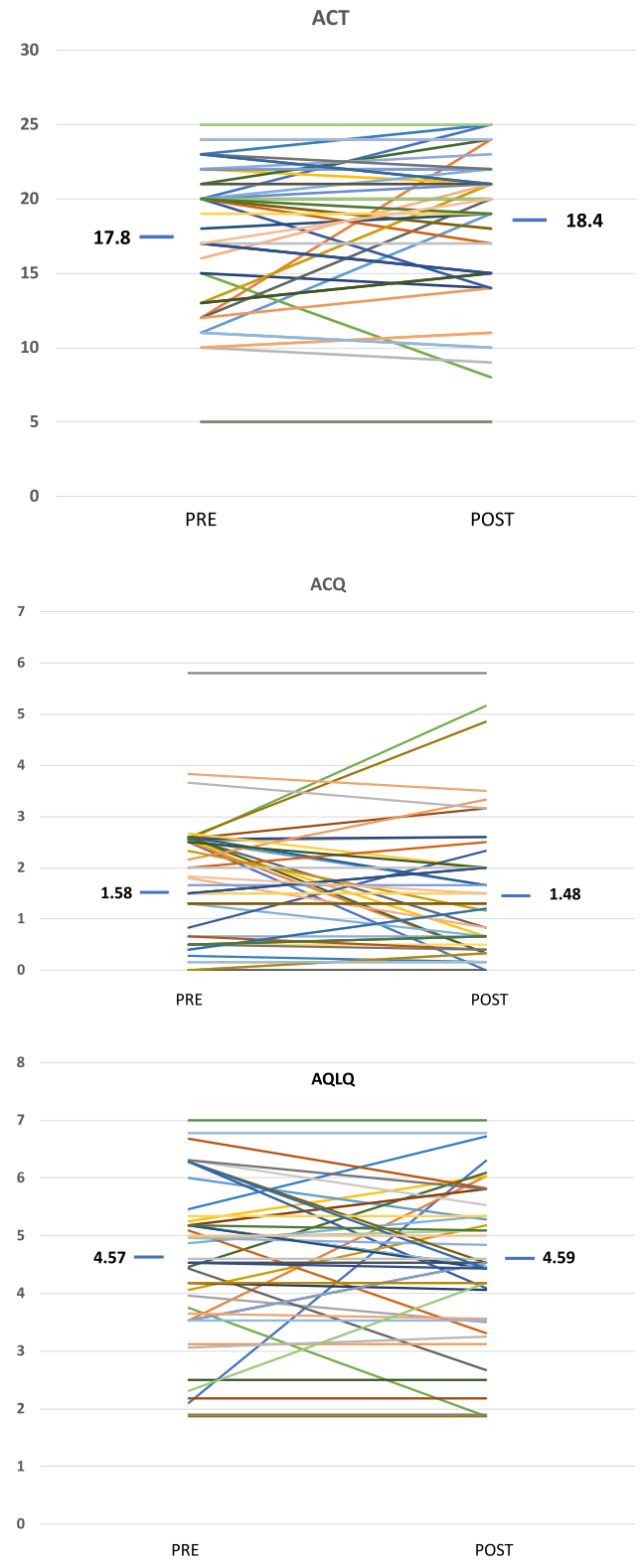


**Fig. 2.** Individual data of ACT (a), ACQ (b) and AQLQ (c) registered when patients started a new biological treatment before (PRE) and during (POST) the lockdown phases.

Devices (EMDs) are now considered the gold standard to monitor adherence to treatment for asthma considering that they provide objective data, not biased by patient self-report, which increase its feasibility in children [15,16]. Mobile phone applications have had a rapid development and are used in many fields including healthcare and medicine, helping physicians in monitoring symptoms and adherence and giving patients a rapid feedback and a better consciousness of their asthma and medication tracking. These strategies are commonly available although many of these are not evidence-based, and further studies are needed to evaluate their efficacy in specific asthma-control endpoints [17]. In addition, there is no doubt that telemedicine has become crucial in order to maintain the control of asthma symptoms in the most severe forms of asthma; the World Health Organization (WHO) defines telemedicine "The delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities" [18]. Evidence from studies so far has not clearly proved whether the introduction of telemedicine in asthma is effective in decreasing exacerbations, even the most severe that led to emergency department or hospitalization [19], even though it has been shown its potential effectiveness in improving asthma control and quality of life in adults, a cardinal pillar in asthma management and prevention of flares related to asthma [20]. Therefore, we support the introduction of telemedicine as a new and valuable additional approach to the asthma standard of care, although further studies are needed to explore its feasibility and efficacy in clinical practice, with a particular focus on severe and uncontrolled asthma. When telemedicine is not applicable, a re-organization of healthcare services, aiming at stratifying patients and dedicating specific areas where patients with suspected COVID-related respiratory disease could receive the necessary health care assistance has demonstrated to be effective in reducing the risk of infection [21].

Most importantly, the advantage of self-administered medications has been highlighted in terms of reducing healthcare costs caused by the reduced need for clinic visits and improving convenience for both patients and health care providers [22–24]. The possibility of self-injections for patients with severe asthma under treatment with monoclonal antibodies may be considered as a viable alternative to the periodic administration of the medication in hospital settings, and offers patients the opportunity of being able to self-inject at home. Bernstein et al. [25] showed that the self-administration of mepolizumab has the same success both in-clinic and at home without the report of new safety concerns and of device failures that affected injection success. Therefore, for those patients who are open to the idea of self-administration of their medication, this option may be included as a valuable alternative, especially during COVID-19 pandemic.

We were able to show that the outcomes were not affected by age. Although the proportion of older subjects did not allow to perform a comprehensive analysis, our findings indicate that the same home strategies can be safely applied to elderly asthmatics. This is not a trivial issue, given that older subjects may experience difficulties in accessing hospital facilities and are affected by high rates of mortality. Indeed, asthma affects older adults to the same extent as younger subjects; however, the management of asthma in the elderly population is complicated by specific features such as the occurrence of comorbidities or low adherence to treatment [26]. Therefore, the potential to safely use biological drugs in this population could strongly improve the outcomes of asthma treatment.

Taken together, our observations reassure on the extended use of home monitoring of severe asthma and self-administration of monoclonal antibodies in the post-COVID era. We envision the application of novel strategies to manage the most severe forms of asthma that implement the use of telemedicine, thus allowing to safely and efficaciously follow the patients remotely.

## 5. Conclusions

Although further studies are needed to support our conclusions, we

confirmed that self-management and home-monitoring systems with a remote coach and assistance does not change patient's outcome and helps clinicians to better follow-ups of severe asthmatics even during COVID-19 pandemic. Home monitoring of asthma patients and objective assessment of symptom levels might also allow early intervention and prevention of exacerbations reducing healthcare costs.

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