its pre-pandemic stage? Or will supplementary testing need to be updated due to the delays in medical treatment? Will their tumor need to be restaged?

Given the characteristics of public health in our country, many hospitals might look to these recommendations for guidance. However, we believe that although the clinical guidelines published so far give us an idea of ẅhat to doẅith our waiting lists, the circumstances in each hospital will differ, and these guidelines merely offer theoretical recommendations on ẅhat to doör ḧow to do it in the best possible way. We call for guidelines that allow us to treat all patients in this situation - not only those with LC, but also those with other thoracic tumors that require surgical or multimodal treatment. Such guidelines would help us plan and treat patients currently on the waiting list within a reasonable time frame of less than 3 months.

Certain details need to be taken into account, such as the patient's willingness to undergo surgery at the current time, their family situation, or even the possibility that some patients have or have had COVID-19, in which case the best moment to reschedule surgery must be carefully selected. On the other hand, we may need to screen all waiting list patients for coronavirus infection. What should we do? We urgently need organization, prioritization, and treatment guidelines for the future management of these patients. We need to prioritize, not only on the basis of knowledge, but also in the knowledge that we are doing the right thing.

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Asthma and COPD in hospitalized COVID-19 patients☆

Asma y EPOC en pacientes hospitalizados por COVID-19

To the Editor,

Various studies have analyzed the presence of comorbidities and risk factors in patients with COVID-19. It is interesting to note that the frequency of chronic respiratory diseases varies widely in different countries. The number of patients with asthma and chronic obstructive pulmonary disease (COPD) in case series from hospitals in China and Italy were much lower than expected for the prevalence of these diseases.[1–4] In New York and the UK, however, the frequency is much higher.[5,6]

In a series of 140 SARS-CoV-2 patients hospitalized in Wuhan, no cases of asthma were described, and only 1.4% had COPD.[1] In another multicenter series from the same country that included 476 patients with COVID-19, 4.6% had COPD, but asthma was not mentioned among the comorbidities.[2]

In a systematic review of the prevalence of comorbidities in patients with COVID-19, also in China, Yang et al.[3] observed respiratory diseases in only 1.5% of patients. Similar results have been reported in Italy; in a series of 1,591 patients with COVID-19 seen in critical care units, 4% had COPD, but the asthma figure was so low that it is not mentioned individually.[4] This, however, contrasts starkly with data from the US and the UK.

In a series of 5,700 patients hospitalized in New York, 9% had asthma and 5.4% had COPD.[5] The figures in the UK are even higher: 19% of patients had non-asthmatic chronic pulmonary disease, and 14% had asthma[6] (which has a prevalence of 6.5% in the UK[7]), suggesting that these comorbidities are very significant risk factors.

The conflicting findings in the prevalence of chronic respiratory diseases in patients with COVID-19 in different countries, and the possibility that these diseases or their treatment may modify the risk of SARS-CoV-2 infection, have prompted us to analyze this sit-

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Table 1
Patients diagnosed with asthma and COPD.

Diagnosis	Age	Sex	Treatment
Asthma (n = 4)	66 (55–85)	3 M/1 W	LABA-CI, n = 2 IC, n = 1 SABA, n = 1
COPD (n = 12)	74 (68–88)	10 M/2 W	LABA-LAMA-IC, n = 4 LABA-LAMA, n = 6 LABA-IC, n = 2

COPD: chronic obstructive pulmonary disease; IC: inhaled corticosteroids; LABA: long-acting beta-adrenergic bronchodilator; LAMA: long-acting muscarinic antagonist; M: men: SABA: short-acting beta-adrenergic; SAMA: short-acting muscarinic antagonist; W: women.
Age expressed as median and range (minimum, maximum).

uation in our setting. We performed a retrospective observational study of cases admitted to our hospital with a diagnosis of COVID-19 to establish the frequency of asthma and COPD. The study was approved by the local ethics committee.

The electronic medical records of 168 consecutive adult patients (aged over 14 years) admitted for COVID-19 were reviewed, and a diagnosis of asthma or COPD was established when it had been recorded by an attending physician in the medical record, regardless of the diagnostic techniques used. We also recorded the number of active prescriptions for inhaled drugs. The age of the patients (median, interquartile range) was 66 years (54–77) and 66 were women (39%). Four patients (3 men) were diagnosed with asthma (2.4% of those admitted). Twelve patients (10 men) had a diagnosis of COPD (7.1% of those admitted). Table 1 shows the demographic characteristics of the sample.

The prevalence of asthma and COPD observed in our series is similar to that of the general population in Spain (around 2%–3% for asthma[8] and 10% for COPD in individuals aged over 40 years, although this disease is frequently underdiagnosed[9]). Our prevalence rates are somewhat higher than those described in China and Italy, but much lower than the US and the UK. Based on our experience with other respiratory viruses, we would expect a higher proportion of hospitalized patients with asthma and COPD, and there is evidence that patients with chronic respiratory diseases have a very high risk of requiring hospital admission for viral processes that are spread via the respiratory tract, such as seasonal influenza.[10,11] In addition, patients with COPD could be suspected of being more susceptible to SARS-CoV-2 infection because the virus uses the angiotensin-converting enzyme 2 (ACE-2) receptor as its route of entry, and expression of this enzyme is increased in patients with COPD.[12] However, in our series, only 4 patients had asthma, almost all of whom were men and none were younger than 55 years of age – figures that do not reflect the prevalence of this disease in the general population. These characteristics, together with those described in other series, could lead us to suspect that some asthma patients in Spain may be less susceptible to SARS-CoV-2 infection and COVID-19. It has been suggested that the low reported prevalence of chronic respiratory disease (especially asthma) in the series from China and Italy could be explained by 3 factors: poor recognition (which seems unlikely); a protective effect due to an immune response; and finally, a possible effect of the treatment given for these diseases.[13] We cannot rule out the possibility that patients with respiratory diseases will have taken precautionary measures (in some countries but not in others, in view of the differences described) to avoid exposure to the virus, and therefore have a lower risk of contagion.

The possibility that inhaled treatment influences the risk of SARS-CoV-2 infection is not based solely on prevalence data among those admitted with COVID-19. In *in vitro* models, inhaled corticosteroids (alone or in combination with bronchodilators) have been shown to suppress coronavirus replication and cytokine production.[14] Therefore, it could be interesting to evaluate whether the use of these drugs could have a protective effect against SARS-CoV-2.

In conclusion, patients with asthma or COPD in our setting do not seem to be at higher risk of admission for COVID-19. Our data show that the prevalence of asthma or COPD among patients admitted for COVID-19 is similar to that estimated in the general population, and significantly lower than our experience with other respiratory viral diseases would lead us to expect.

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Hydroxychloroquine as Prophylaxis for Coronavirus SARS-CoV-2 Infection: Review of the Ongoing Clinical Trials

Hidroxicloroquina como profilaxis para la infección por coronavirus SARS-CoV-2: revisión de los ensayos clínicos en curso

Dear Editor:

At the time of writing this document the entire planet is facing the pandemic caused by the SARS-CoV-2 virus. Contrary to the initial thoughts that most infected patients had symptoms, according to data from China collected in April 2020, at the time of the diagnosis, up to 80% of those confirmed to have the disease are asymptomatic, becoming an important source of contagion.[1–3] Pan et al. reported that health workers in Wuhan (China) had a significantly higher risk of becoming infected (daily confirmed case rate in local health care workers was 130.5 per million while in the general population it was 41.5 per million).[4]

In this light, the scientific community is discussing the use of chemoprophylaxis in people at higher risk of infection using several alternatives including antimalarials (chloroquine or hydroxychloroquine) and antiretrovirals (lopinavir-ritonavir).[5–10] There is an increased interest in use of chloroquine and hydroxychloroquine, two medications that have experimentally shown to have antiviral capabilities and prophylactic potential.[11,12] Lee et al. recently reported good results in an observational study in South Korea after a large COVID-19 exposure event in a hospital. At the end of quarantine, after receiving post-exposure prophylaxis with hydroxychloroquine (400 mg daily for 14 days) all follow-up PCR tests were negative in 211 individuals exposed to the index case.[13] Certain countries have already adopted chemoprophylaxis schemes; on March 22nd, 2020, the Indian Council of Medical Research's National Task Force for COVID-19 issued a national recommendation to use hydroxychloroquine for prophylaxis against SARS-CoV-2 infection (400 mg twice a day on day 1, followed by 400 mg once weekly for 7 weeks).[14]

We conducted a search (updated to April 15th, 2020) on the website https://clinicaltrials.gov/. Using the keywords COVID-19 and hydroxychloroquine we found a total of 90 projects registered. Twenty-five of those projects included the use of prophylaxis in non-infected population (Table 1)

Institutions from 13 countries are leading those projects, 13 of them from the United States, 2 from Mexico, 2 from Spain and 2 from France. Turkey, Colombia, Austria, South Korea, Singapore, United Kingdom, Thailand, Australia and Canada, have institutions leading one project (there are more institutions than projects, because some have shared leadership).

There is a significant variability in the number of participants among the studies. The estimated number of participants to be enrolled ranges between 45 and 55,000 with an average of $5588 \pm 13{,}139.2$, and a median of 1212 participants. Only 3 (12%) studies plan to enroll more than 4000 participants; those 3 studies will include 70,000 participants which corresponds to 50.1% of the total potential recruitment of the 25 protocols (NCT04334148, NCT04303507 and NCT04333732).

There is a significant variability among protocols regarding hydroxychloroquine maintenance dose, which will be between 200 and 600 mg. The frequency is also highly variable: seventeen protocols will use daily prophylaxis for a period from 4 days to 12 weeks and 9 protocols plan to evaluate weekly use for a period of 3 to 24 weeks. Thirteen (52% of 25) protocols will use an initial loading dose ranging between 400–1400 mg taken on the first day. In three other protocols, 2–4 days of loading doses of 400 mg/day will be indicated.

19 clinical trials will evaluate pre-exposure prophylaxis and 6 post-exposure prophylaxis. In 9 of the pre-exposure prophylaxis studies and 4 of the post-exposure prophylaxis studies, a loading dose of 800 mg of hydroxychloroquine will be started on the first day. In an additional multicenter pre-exposure prophylaxis study, which plans to recruit 15,000 participants (NCT04334148), they will use a higher loading dose on the first day: 1200 mg of hydroxychloroquine.

We evaluated the exclusion criteria among protocols by grouping into several possible categories. Most common criteria used by protocols to exclude patients comprised allergies to 4-aminoquinolines (hydroxychloroquine, chloroquine) in 20 studies (80%); retinopathy in 19 (76%); history of a prolonged QT syndrome, use of medications that prolong the QT/QTc interval or risk factors for torsades de pointe in 17 (68%); nephropathy in 16 (64%); pregnancy or breastfeeding in 14 (56%); concomitant use of other medications with potential pharmacological interaction with 4-aminoquinolines in 13 (52%); liver disease in 13 (52%); psoriasis