# Risk assessment for patients with chronic respiratory and pulmonary conditions in the context of the SARS-CoV-2 pandemic

Statement of the German Respiratory Society (DGP) with the support of the German Association of Respiratory Physicians (BdP)

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## Introduction

The current SARS-CoV-2 pandemic has created uncertainty regarding the question of how to adequately protect specific groups of patients suffering from chronic respiratory and pulmonary conditions: both among physicians, who have a duty to provide patients with suitable and meaningful protection measures, and among patients, who understandably wish to optimally protect themselves from COVID-19. Assessing the risk for specific patient populations is, therefore, particularly important.

The general population is currently at high risk of contracting COVID-19 due to a lack of immunity, and only the introduction of an effective vaccine will reduce this risk. SARS-CoV-2 can also be transmitted by asymptomatic carriers, and this, in addition to its contagiousness, contributes to the rapid spread of the virus[1]. There is a possibility that SARS-CoV-2 may also be transmitted by asymptomatic animals[2]. Most COVID-19 cases are mild to moderate, and patients become symptomatic on average 11.5 days post infection (the most common symptoms are: coughing, fever, anosmia or ageusia, fatigue, muscle and limb pain; in some cases also gastrointestinal symptoms)[3]. A minority of patients develops severe COVID-19 7-10 days after symptoms start, including rapidly worsening shortness of breath, pneumonia, and respiratory distress, often requiring intensive care and mechanical ventilation[4]. In addition to pneumonia, severe COVID-19 can typically lead to thrombotic events[5], severe endothelial damage of the pulmonary vessels[6], massive release of cytokines[7], and multi-organ failure[4,8]. Approximately 20 % of patients diagnosed with COVID-19 in China experienced a severe course of the disease [9]. The Robert Koch Institute (RKI), the German government's central scientific institution in the field of biomedicine (www.rki.de), postulated (based on data reported until March 17, 2020[10]) a lower COVID-19-related hospitalization rate for Germany, which is probably due to a significantly higher testing rate of patients with mild symptoms (8–10 %). Even this number is likely to overestimate the share of severe cases since, particularly at the beginning of the pandemic, not only the severity of the illness but also the need for isolation was reason for hospitalization. This is reflected in the relatively low share of intensive care treatments (8 %) of those hospitalized (current surveys from the UK and the US show that 17–22 % of hospitalized cases require intensive care[11,12]). A model for France, which included data on the morbidity rate of people with known exposure, calculated that 3.6 % of all infected persons require hospitalization (with a strong age-dependency: 0.2 % of those under 20 years of age and > 20 % of those over 80 years of age)[13]. The currently estimated case mortality rate, which also takes into account the number of undetected SARS-CoV-2 infections, is probably less than 1 %[14,15]; an overall probability of death among those infected (Infection Fatality Ratio, IFR) of 0.7 % is assumed in France (with strong age-dependency: 0.001 % of people younger than 20 and > 10.1 % in those older than 80)[13]. Consequently,

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the mortality rate during the current SARS-CoV-2 pandemic seems to be higher than that of seasonal influenza in a severe season (0.1 %)[14,15].

The following statements refer, in particular, to the risk of progression to severe or critical COVID-19. It needs to be noted that the current data on risk factors for developing severe COVID-19 are mainly derived from China. These data can only be applied to Germany to a limited extent. Therefore, a conclusive assessment will only be possible once epidemiological data from Germany will be available[16,17]. The following sections provide answers to frequently asked questions on risk assessment based on 12 exemplary cases.

**Question 1 (General): Who is most at risk for a severe course of COVID-19?**

**Answer 1:** Current data show that older people (> 65 years of age), and people with cardiovascular diseases and/or diabetes are among those who have the greatest risk of developing severe COVID-19[12,18-30]. Obesity is a significant additional risk factor[12,16,30-33]. Men have a greater risk than women, especially in the older age group[12,13]. Chronic lung, kidney, and liver diseases[3,12,34], immunodeficiency[3], and cigarette smoking[35,36] are mentioned as further risk factors, although supporting evidence is weak in these cases. People with more than one chronic condition seem to have a significantly higher risk. In a US case series, hospitalized patients had an average of four comorbidities[33]. Nursing home residents are at a particularly high risk due to their advanced age and high incidence of multiple chronic diseases. In addition, the pathogen spreads very quickly in nursing homes because nursing staff are responsible for many residents and have close physical contact[37].

**Question 2 (Mild to moderate asthma): I am a 58-year-old teacher. I have moderate, well-controlled asthma, and regularly use inhaled medications. Does this make me a risk patient? Can I go back to work without being at risk when schools reopen?**

**Answer 2:** There is no evidence to date that people with asthma have a higher risk of severe COVID-19[12,18-28]. It is even hypothesized that patients with asthma may have a lower risk due to a decreased expression of the ACE-2 receptor responsible for the uptake of SARS-CoV-2 in the airways, especially in patients with allergies[38] and/or type 2 inflammation[39]. There is currently also no evidence that inhaled corticosteroid therapy (ICS) for the treatment of asthma might increase the risk of developing severe COVID-19. Since ICS therapy generally reduces the risk of asthma exacerbations and may additionally decrease the expression of the ACE-2 receptor in the airways[40], a protective effect is suspected instead[41]. Interruption of ICS therapy may contribute to a severe worsening of a patient's asthma and, hence, will likely contribute to a severe disease progression in the event of a COVID-19 infection. During the SARS-CoV-2 pandemic, inhalation therapy, and in particular ICS therapy, should therefore be maintained unchanged for patients with well-controlled asthma. Separate and detailed statements by DGP (DGP statement on asthma therapy with inhaled corticosteroids, www.pneumologie.de) and GINA (https://gi-nasthma.org/recommendations-for-inhaled-asthma-controller-medications) are available.

Allergen immunotherapy should also be continued. A separate EAACI statement is available in this regard[42]. We therefore suggest that properly medicated asthma patients with no signs of acute symptoms can work in schools as long as the recommended hygiene measures are consistently followed.

**Question 3 (Severe asthma): I am a 48-year-old executive. I have severe asthma. I am taking high doses of inhaled or corticosteroids every day plus a biologic. Until now, the biologic was administered by my respiratory physician at regular intervals. Can I continue to work at my job? Should I self-isolate at home? Should I rather inject the biologic myself at home?**

**Answer 3:** So far, there is no evidence that patients taking biologics for chronic inflammatory conditions would generally be at a higher risk of developing severe COVID-19[43,44]. Although specific epidemiological data regarding the role of biologics for asthma treatment in the COVID-19 situation are not yet available, it is recommended to continue the biologics in patients with severe asthma, especially to avoid the necessity of a systemic corticosteroid therapy and exacerbation-related hospitalization: A separate statement of the German Society for Allergology and Clinical Immunology (DGAKI) on this topic is available (https://dgaki.de/biologika-therapie-u-covid-19). Patients with well-controlled severe asthma, who do not show acute symptoms, can continue to work outside their homes as long as the RKI recommendations are strictly followed. Self-administration of a biologic at home (which has been approved for omalizumab, mepolizumab, benralizumab, and dupilumab in Germany) should be preferred in order to reduce contact with medical facilities and thus minimize the risk of contact with patients infected with SARS-CoV-2.

**Question 4 (COPD): I am a 68-year-old man with COPD. I had a heart attack three years ago, and I suffer from high blood pressure. I currently still smoke 3–4 cigarettes per day. Can I continue to take my high blood pressure medication (e.g., ramipril) and continue with inhalations? Should I be vaccinated against pneumococcal infections? Should I shelter at home for the duration of the coronavirus crisis? Can I see my children and grandchildren?**

**Answer 4:** COPD patients are at a higher risk of a more severe course of a COVID-19 infection[11,12,29,45-47]. COPD patients with cardiovascular comorbidities have a significantly increased risk[18-26]. Guideline-directed therapy should generally be continued in COPD patients. So far, there is also no evidence that inhaled corticosteroids would have an unfavorable effect on the prognosis of patients with COPD. Likewise, high blood pressure medication, including ACE inhibitors (such as ramipril) or sartans, should be continued. There is no evidence that these drugs would increase the risk of severe courses[48,49] (there is even evidence that ACE-inhibitor therapy may reduce the risk of a severe progression of the disease[29]). It is strongly recommended to stop smoking cigarettes. Equally, vaccination against pneumococcal infections is also strongly recommended if not already done. In the absence of signs of COVID-19, sheltering at home is not necessary. However, all RKI recommendations, including distancing rules and hygiene measures, should be rigorously followed.

Getting together with children or grandchildren should be avoided in the current situation, and patients should preferably keep in touch over the phone or by video conference.

**Question 5 (Cystic fibrosis): I am a 22-year-old student with cystic fibrosis. I take my medication regularly and have been receiving treatment at a cystic fibrosis outpatient unit since I was a child. Should I keep my current appointments with my physiotherapist? Should I stay at home for the duration of the**

**coronavirus crisis? Should I continue to take my medication as before and also continue the inhalation therapy?**

**Answer 5:** So far, only very few case reports are available on the course of COVID-19 in patients with cystic fibrosis (CF) or conditions related to bronchiectasis of other causes[50,51]. Generally, it can be assumed that patients suffering from these conditions are at a higher risk of having a more severe course of COVID-19 due to the impaired compensation mechanisms of their structurally damaged lungs. There is data from individuals with CF from a survey of 56 patients conducted by the European Cystic Fibrosis Society Clinical Trials Network (ECFS-CTN) (version: May 20, 2020), which shows predominantly mild clinical manifestations of the SARS-CoV-2 infection (however, 3 out of 56 patients died, corresponding to 5.4 %; the data is updated weekly and available at: https://www.ecfs.eu/covid-cf-project-europe). It should be noted in this context that CF patients often already observe excellent basic hygiene and are younger than other patient groups. An additional risk could be posed by concomitant diabetes. It is generally recommended that patients with CF or bronchiectasis of other causes should continue with their basic therapy consisting of medication and non-medicinal therapies. This also generally applies to a potentially necessary breathing therapy, which should, however, be performed independently by the patient. Individual arrangements should be made for therapy sessions in the offices of a respiratory physiotherapist. Many therapists are already offering video sessions and are (temporarily) also permitted to bill for them. Likewise, clinically indicated outpatient and inpatient antibiotic therapies should be continued as before. It is not necessary for patients who show no signs of COVID-19 to stay at home permanently (and this is also not reasonable in light of the numerous positive aspects of physical exercise). The RKI's behavioral recommendations should, however, be strictly followed.

**Question 6 (Interstitial lung disease): I am a 72-year-old man, and I have rheumatoid lung disease. I am regularly taking methotrexate (15 mg/week) and prednisolone (5 mg/day). I am on long-term oxygen therapy (2 liters of O2/min via nasal cannula). Can I even dare to leave the house during the coronavirus crisis? Should I keep taking my meds? Should I continue with oxygen therapy?**

**Answer 6:** It is suspected that interstitial lung diseases (ILD), including pulmonary fibrosis, are associated with a higher risk of severe illness from COVID-19. However, no data is currently available in this regard. Similar considerations apply to the treatment of ILD with immunosuppressant drugs. However, there is very little data available on this, and the temporary discontinuation of an indicated immunosuppressant therapy is associated with a potential worsening of the underlying disease (making an even higher dose of immunosuppressants necessary). The indication for immunosuppression should, however, be reviewed. If a continuation of the therapy is indicated, it should be continued without modification and at the lowest possible dose. Only if the patient or a household member tests positive for SARS-CoV-2 should immunomodulators such as azathioprine or methotrexate be discontinued (in accordance with the recommendations of German rheumatologists, www.dgrh.de) until clinical improvement is achieved. The prednisolone therapy should be continued at the lowest possible dose. Since antifibrotic agents in idiopathic pulmonary fibrosis (IPF) protect against acute exacerbations that may develop in ILD in the context of a viral infection, this therapy should be continued until reliable data will be available[52,53]. It is not necessary for patients who show no signs of COVID-19 to stay at home permanently (and this is also not reasonable in light of the numerous

positive aspects of physical exercise). The RKI's behavioral recommendations should, however, be strictly followed. Oxygen therapy should be continued.

**Question 7 (Patients with lung transplants): I am 53 years old. I had a double lung transplant 3 years ago. I am regularly taking a large number of medications, and I pay close attention to all recommendations regarding my diet and lifestyle. Can I leave the house during the coronavirus crisis? Should I continue taking all these medications as before?**

**Answer 7:** In theory, the risk of severe progressions of COVID-19 in patients with lung transplants could be increased due to the required immunosuppression. On the other hand, *in vitro* data for both ciclosporin and tacrolimus indicate that both drugs have an inhibitory effect on virus replication. No substantial case series on lung transplant patients with COVID-19 have been published so far. The course of the illness in the first published lung transplant recipient with COVID-19 was moderate[54]. In a case series of 90 organ transplant patients with COVID-19 from New York (including 17 patients with lung transplants), 76 % of patients were hospitalized, 24 % were intubated, and 18 % died[55]. In other case series of transplant patients with COVID-19, which did, however, not include patients with lung transplants, 25–28 % of those infected died[56-58], including 2 patients who were initially not thought to require hospitalization[57]. Therefore, increased attention is to be paid to transplant patients who have only mild clinical symptoms. Routine adjustment of immunosuppression is currently not recommended for lung transplant patients infected with SARS-CoV-2. It is also not recommended to prophylactically adjust an immunosuppressive therapy in the context of the coronavirus crisis. Only in cases with severe COVID-19, a temporary discontinuation of mycophenolate mofetil and azathioprine under close monitoring is recommended. Interactions of immunosuppressants, antivirals, and additional medications administered to treat COVID-19 need to be taken into consideration when treating lung transplant patients. It is not necessary to stay at home permanently (and this is also not reasonable in light of the numerous positive aspects of physical exercise). The RKI's behavioral recommendations should, however, be strictly followed.

**Question 8 (Lung cancer): I am 71 years old and have lung cancer. I am currently treated with chemotherapy. One bone metastasis was treated with radiation therapy 3 months ago, the treatment of another one is pending. Should the chemotherapy be continued during the current coronavirus crisis? Should the radiation therapy take place? May my children visit me?**

**Answer 8:** There are only very few case reports of lung cancer patients who contracted COVID-19[59]. A case series from New York includes 11 lung cancer patients with COVID-19; 55 % of them died[60]. Based on current knowledge, cancer patients, in general, have a higher risk of developing severe COVID-19[60,61]. On the other hand, it has been hypothesized that, in some patients, immunosuppression as part of cancer therapy may prevent the massive release of cytokines that is typical of severe COVID-19 and thus counteract progression to a severe disease state[62].

However, due to the many different subtypes, disease stages, cancer therapies and prognoses, the range of lung cancer types is so broad that risk assessments and recommendations can only be made on a case-by-case basis. In general, surgeries, systemic therapies, or radiotherapy are of vital importance for patients and should, therefore, whenever possible, neither be postponed nor canceled[59]. The German

(www.dgho.de) and the European (www.esmo.org) cancer societies have issued separate recommendations for the treatment of cancer in the context of the SARS-CoV-2 pandemic, with the latter providing highly specific, hierarchically structured recommendations (three different levels) for diagnostics and all types of local/systemic tumor therapies in lung cancer. The RKI's behavioral recommendations also apply to lung cancer patients, and all visitors should strictly follow the RKI's hygiene rules. However, regarding contact restrictions, the decision whether or not visits by relatives or friends should be allowed must be made on a case-by-case basis depending on the patient's prognosis; a general ban on visits is not appropriate.

**Question 9 (Sleep apnea syndrome): I am 74 years old and weigh 120 kg. I've never smoked, and, apart from my high blood pressure, I have no other chronic diseases. In the past, I used to feel extremely exhausted when I woke up in the morning and remained very tired during the day. Since using CPAP therapy regularly, I feel fresh when I wake up in the morning and can work in my garden all day long. Do I belong to a group with a risk of severe disease progression? Will I soon be able to have a big barbecue party in my garden again?**

**Answer 9:** For patients with obstructive sleep apnea syndrome who need to use CPAP (continuous positive airway pressure) therapy every night, an increased risk can neither be excluded nor confirmed based on currently available data. A separate statement of the German Sleep Society (DGSM) is available on this subject (www.dgsm.de/downloads/aktuelles/Stellungnahme der DGSM_22April2020.pdf). However, the combination of obesity[16,31-33] and arterial hypertension[18-28] is generally associated with an increased risk of severe COVID-19. The RKI behavioral recommendations should, therefore, be strictly followed, and parties or social gatherings with friends should be avoided for the time being. The coronavirus crisis should also be seen as an opportunity to tackle weight reduction, which offers many benefits.

**Question 10 (Neuromuscular disease): I am 62 years old and suffer from a rare neuromuscular disease. I need non-invasive ventilation every night because my lungs cannot get enough oxygen otherwise. Would I even stand a chance of recovering and getting my previous life back if I had the coronavirus? Maybe I should refuse to even be placed in an intensive care unit?**

**Answer 10:** Patients with neuromuscular diseases who require non-invasive ventilation (NIV) suffer from a severe ventilatory insufficiency. Although epidemiological data in the context of the SARS-CoV-2 pandemic are not yet available for this group of patients, a significantly increased risk of severe COVID-19 disease progression must be assumed, as these patients lack ventilatory compensation capacity in the context of COVID-19 pneumonia. Therefore, these patients may need to be intubated earlier as long as no therapy goal-related restrictions apply. In addition, these patients are expected to experience a difficult weaning from invasive mechanical ventilation. This further limits the prognosis, even if ventilation in intensive care is primarily successful[63]. The underlying condition may even further reduce the quality of life after an extended period of COVID-19 pneumonia. This should be discussed in detail with the respective patient[64]. The patient should draw up a detailed and specific advance directive after personal consultation with his/her treating physician, following careful consideration. Irrespective of this, however, the options of NIV in the acute setting should be used if the patient contracts COVID-19, as this may avoid the need for intubation/invasive ventilation[65].

**Question 11 (Tuberculosis): I am 43 years old and had pulmonary tuberculosis 20 years ago. The illness was treated over 6 months using a combination of different pills. Several X-ray images of my lungs were taken afterward, and my doctors confirmed that my tuberculosis had healed without lasting sequelae. I have not had any symptoms since then. Does this history make me a risk patient for severe COVID-19? Would I be a risk patient if I was currently under tuberculosis medication?**

**Answer 11:** There is little data on SARS-CoV-2 infections in patients who have recovered from tuberculosis. Presumably, the likelihood of developing severe COVID-19 after a successfully treated tuberculosis without lasting damage is not increased. It has been hypothesized that the immune system's exposure to mycobacteria (e.g., through BCG vaccination[66,67]) might even strengthen the body's defense against the virus: this has, however, not yet been proven. Tuberculosis may lead to subsequent lung damage such as bronchiectasis, fibrosis, or COPD[68,69], and this would, in all likelihood, increase the risk of severe COVID-19 progression (see cases 4, 5, and 6 presented in this statement). Two small Chinese studies suggested a more severe course of COVID-19 in patients with tuberculosis[70,71], but this was not confirmed in another study[72]. Due to the very small number of published cases, a final assessment is not yet possible, and patient's comorbidities must also be taken into consideration. Even under the current difficult conditions, it is of decisive importance for the success of tuberculosis therapy that patients go to all necessary doctor's appointments and avoid therapy interruptions: The WHO consequently recommends the systematic continuation of tuberculosis therapy in the context of the SARS-CoV-2 pandemic (www.who.int).

**Question 12 (Pulmonary embolism): I am 61 years old, never-smoker and not overweight. Three years ago, I was diagnosed with pulmonary embolism. However, no trigger or genetic cause was identified. I used to take an anticoagulant medication until two years ago; since then I have not had another pulmonary embolism. I read that coronavirus infection can cause pulmonary embolisms. Am I at higher risk for severe illness from COVID-19? Should I take the anticoagulant again, to prevent COVID-19-related embolism?**

**Answer 12:** Cases of thrombosis and pulmonary embolisms associated with SARS-CoV-2 infection have been reported repeatedly[5,6,73,74]. Laboratory parameters indicating a tendency to develop blood clots as a result of the strong inflammatory response to the viral infection (including elevated d-dimers) were frequently observed, in more than 50 % of cases[18]. The percentage of patients with confirmed pulmonary embolism and/or deep vein thrombosis is also high, on average 25 %[75-78] (and possibly even higher[5]), even though the findings collected until now were obtained without a control group. They are, therefore, not very robust. These observations mean that thrombosis prophylaxis (with heparin injections) is always required if a patient with *confirmed* COVID-19 needs to be *hospitalized*[79,80]. This applies in all cases, and especially for patients with a history of thrombosis or pulmonary embolism who consequently carry a higher risk of thrombosis. On the other hand, it should be underlined that, based on current knowledge, these patients are not at increased risk in the context of COVID-19 (compared to the general population), and, above all, there is no indication for comprehensive prophylactic anticoagulation at home. Patients with a history of pulmonary embolism who are no longer taking anticoagulants should generally, and especially during the COVID-19 epidemic, observe the general precautions (such as avoiding extended immobilization and ensuring adequate fluid intake). However, if they present with suspected COVID-19 symptoms to their primary care physician or the emergency department of a hospital, their history of pulmonary embolism or

venous thrombosis must absolutely be mentioned, so that, if the COVID-19 suspicion is confirmed and the patient is hospitalized, thrombosis prophylaxis can be started without delay[81,82]. If these patients exhibit parameters indicating a tendency to form blood clots, intensified anticoagulation may be advisable in individual cases[79,83].

**Conclusion**

We want to stress, once again, that patients with chronic respiratory diseases should, in general, strictly follow the RKI recommendations, in particular concerning the distancing and hygiene rules, and have the recommended vaccinations (www.rki.de). As long as distancing rules, hygiene rules, and a patients' current symptoms are strictly observed (no participation of patients who have acute symptoms of any degree of severity), small-group exercises for people with pulmonary conditions may be continued. If this is not possible, patients should continue to exercise at home. Group training sessions in the context of structured training programs conducted in medical offices should not take place at the moment. However, the owners of such practices can offer customized instruction (at least in inhalation techniques) and refer to training dates in the future. The German Airway League is currently developing internet-based training programs and offers comprehensive information and additional inhalation training videos (www.atemwegsliga.de) for patients. There is a detailed separate DGP statement on the clinical management of COVID-19 (Position Paper for the State-of-the-Art Application of Respiratory Support in Patients with COVID-19)[65].

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**Abbreviations used in this paper**

| | |
|---|---|
| ACE inhibitor | **A**ngiotensin-**C**onverting-**E**nzyme inhibitor (a blood pressure lowering agent) |
| CF | **C**ystic **F**ibrosis (also known as mucoviscidosis) |
| COBRA | **C**hronic **O**bstructive **Br**onchitis with and without emphysema<br>**O**utpatient training program for patients living with COPD |
| COVID-19 | **Co**rona **Vi**rus **D**isease 2019 (a disease caused by SARS-CoV-2) |
| CPAP | **C**ontinuous **P**ositive **A**irway **P**ressure (treatment of the sleep apnea syndrome) |
| DGAKI | German Society for Allergology and Clinical Immunology<br>(**D**eutsche **G**esellschaft für **A**llergologie und **K**linische **I**mmunologie) |
| DGHO | German Society for Haematology and Medical Oncology<br>(**D**eutsche **G**esellschaft für **H**ämatologie und Medizinische **O**nkologie) |
| DGP | German Respiratory Society<br>(**D**eutsche **G**esellschaft für **P**neumologie und Beatmungsmedizin) |
| DGRh | German Rheumatology Society<br>(**D**eutsche **G**esellschaft für **Rh**eumatologie). |
| DGSM | German Sleep Society<br>(**D**eutsche **G**esellschaft für **S**chlafforschung und Schlaf**me**dizin) |
| DZK | German Central Committee against Tuberculosis<br>(**D**eutsches **Z**entral**k**omitee zur Bekämpfung der Tuberkulose) |
| ESMO | **E**uropean **S**ociety for **M**edical **O**ncology |
| GINA | **G**lobal **In**itiative for **A**sthma |
| ICS | **I**nhalative **C**ortico-**S**teroide (basic asthma therapy) |
| ILD | **I**nterstitial **L**ung **D**isease |
| IPF | **I**diopathic **P**ulmonary **F**ibrosis |
| NASA | National outpatient training program for adults living with asthma<br>(**N**ationales **A**mbulantes **S**chulungsprogramm für erwachsene **A**sthmatiker) |
| NIV | **N**on-**I**nvasive **V**entilation (through a mask) |
| RKI | **R**obert **K**och **I**nstitute |
| SARS-CoV-2 | **S**evere **A**cute **R**espiratory **S**yndrome **Co**rona-**V**irus **2** |
| WHO | **W**orld **H**ealth **O**rganisation |