PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK

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INTRODUCTION

Based on reports and questions forwarded to the Clinical Risk Managers of the Italian Network for Health Safety (INSH) from physicians working on the front line, a series of recommendations have been developed referring to documents and papers published by national institutions (ISS) and Italian and international scientific societies and journals.

We have arranged the process to describe organising the work system according to the SEIPS Human Factors approach (1).

1. Assess the work system:
   a. Team and organisation culture and communication
   b. Environment
   c. Tasks required and skills to complete tasks
   d. Equipment for patient care and to protect staff
   e. The people needed to provide care
   f. The patients who receive care
2. Develop reliable processes of care.
3. Measure the outcomes of care.

The document is work in progress and will be subject to updates by all professionals on a continuing basis. We appreciate and welcome the contribution of all those involved in COVID-19, both providers of care and patients who have received care.

(email info@insafetyhealthcare.it)

Key changes or updates between version 2.0 and 3.0 are highlighted in Red.

Changes include:

- More detailed recommendations for healthcare workers safety
- Updated recommendations about diagnosis, hospital treatment, children, pregnancy, labour and delivery, surgery, haemodialysis, oncologic patients, psychological safety of staff
- Updated criteria for de-isolation
- New cards about ophthalmology, phase 2 of emergency (characterized by reduced viral circulation), vaccinations, healthcare students’ internships
- Triage Covid-19 form
- Multimedial links: Pharmacov for drug interactions check and Virgilio, a virtual audio guide for safe doffing.
1. GENERAL RECOMMENDATIONS FOR THE WORK SYSTEM

Building the Team (including communication and team culture):

1. The emergency task force should be promptly activated with a transparent chain of command, roles and responsibilities, reliable information-sharing tools and proactive approach.
   The emergency task force should be pre-existing and meet periodically (i.e. 1-2 times/year), even in the absence of emergencies, to build the team.

2. Check frequently every day the communications sent by your institutions. Read carefully and respect them. Alternatively, print and make such communication available in the ward and share such information during handovers.

3. Clinical risk management units can support the dissemination of documents, guidelines issued by the national/regional institutions for supporting the emergency management, relatively for measures of prevention to be taken.
   Knowledge about Coronavirus transmission and spreading and clinical characteristics of the related disease (COVID-19) are continually evolving, so that indications for clinical practice change frequently, i.e. case or suspicion definition, criteria for making swabs, etc.

4. The clinical risk management units must keep in contact with front line workers and provide support. The reporting of adverse events must occur within the task-force activity and be primarily related to the core activities during the pandemic. Secondly, the reporting of Adverse Events should be encouraged to maintain the underpinning safety climate to promote, whenever possible, prompt corrective and improvement actions. Consider quick reporting tools such as confidential instant messages or audio-messages.

5. The clinical risk management units should also receive evidence of good practice, so this can be disseminated.

Tasks to be undertaken and the skills required

1. Organise brief educational training on the correct use of medical and protective devices targeted to all healthcare workers and develop video tutorials to be available on the healthcare trust website.

2. Organise refresher courses on hand-hygiene, prevention of VAP (Ventilator-Associated Pneumonia) and CLABSI (Central Line-Associated Bacterial Infection) bundles and the SEPSIS bundle for early sepsis recognition and management, lung failure and non-invasive ventilators (also by video-tutorial) to all healthcare workers (2), but in particular to the staff not in the frontline of the emergency, who could be called as replacements.

3. Organise early support of expert doctors/nurses, to educate younger doctors/nurses or colleagues from other specialities who may be called upon to replace them
4. Do not forget appropriate instructions for **environmental** disinfection (detergents, contact time, frequency) to **healthcare workers** and cleaners (3).

**Equipment needed to protect staff**

1. Contact and droplet precautions can be used in routine patient care of patients with suspected or confirmed COVID-19 (4). The infections spreads rapidly and depletion of reserves is a risk.

2. Change your PPEs to avoid cross-contamination between confirmed and suspected cases. Medical devices used for multiple patients must be disinfected between patients. In an outpatient setting, contact surfaces must also be disinfected between patients.

3. Healthcare workers must not access common areas (medical office, nurses' room, relax area, kitchen, changing rooms) or go outside the ward with PPEs worn during patient care.

4. Healthcare workers must also observe contact and airborne precautions with colleagues.

5. Avoid spraying disinfectants on coveralls, gowns or aprons to assist different categories of patients (i.e. confirmed infection and suspected infection and not infected) (81).

6. Utilise only validated disinfection systems for reusable PPEs. Decontamination with inappropriate methods reduce the protection potential of PPE and expose operators to risks for their health (generation of aerosols and respiratory side effects, falls due to slippery floors (81).

**Equipment needed to treat patients**

1. Give any patient seeking medical assistance, independently from symptoms, a surgical mask to put on, at their first contact with healthcare services (6).

2. In the dedicated care areas for patients with COVID-19, ensure that:
   a. haemo-gas analysers
   b. pulse oximeters
   c. oxygen therapy
   d. ventilator therapy equipment and suction pumps are available and well-functioning (7).

**Environment**

1. Strictly apply, without exceptions, the indications for disinfection of environments and tools (sodium hypochlorite at 0.1-0.5% or 70% ethyl alcohol solution) (8). It is not yet well known how long the virus resists in the environment, but it is inactivated by solutions based on hypochlorite and alcohol.

2. Prevent germicide deficiency by using galenic preparations.

3. Never mix detergents or disinfectants together as this could cause a toxic solution
4. To prepare diluted bleach: use a mask, rubber gloves and waterproof apron; goggles also are recommended to protect the eyes from splashes; mix and use bleach solutions in well-ventilated areas; mix bleach with cold water (hot water decomposes the sodium hypochlorite and renders it ineffective) (82).

5. Promote hospitals/buildings exclusively dedicated to Covid-19 patients care. Remember that the creation of dedicated hospitals may divert from the emergencies network. Evaluate the fallout of the timing of treatment decisions for time-dependent diseases carefully. Consider the use of underused or quiescent equipped hospitals to help meet this need.

6. Unless the activity is suspended in the outpatient (public or private) clinics:
   a. avoid gatherings in waiting rooms (recommend people to wait outside, or respect the distance of at least 1 m between seats);
   b. recommend that symptomatic subjects with fever and/or cough and/or dyspnea not to go to clinics;
   c. disseminate hygiene and health standards recommendations in the waiting room.

Patients

1. Limit patient movement within the institution and ensure that patients wear surgical masks, especially when outside their rooms

2. In the full-blown epidemic phase:
   a. reduce hospital admissions, routine outpatient clinic appointments and routine surgical procedures;
   b. regulate hospital visits
      Caregivers authorised to enter the wards should respect biosafety precautions.
   c. consider all patients with flu-like symptoms who access hospitals as potentially affected until proven otherwise;
   d. isolate, if structurally possible, patients under investigation (PUI) and probable cases (inconclusive or not available tests) in single rooms or keep 1 meter (2 meters is better) between them;
   e. isolate confirmed cases in single rooms or cohorts;
   f. create separate unclean/clean paths, with the help of external mobile structures;
   g. use a screening interview (for example see Table 5 in Appendix) to identify suspected cases among patients coming to the hospital or other medical services, authorised visitors, or caregivers
   h. per local procedures, if the criteria of case or suspicion are met, refer the subject for evaluation unless emergency treatment is required. In such case, refer subject to the unclean pathway. Do not delay emergency treatment to obtain swab.

3. People who have been in contact with Covid-19 positive patients should be clinically evaluated in the locally designated sites by local Public Health Services, for epidemiological purposes and active surveillance, if symptomatic.
4. **Use broad case definitions and intensive testing strategies: it allows the epidemic outbreak to be circumscribed earlier and better.**

Aggressive contact tracing, intensive testing and home isolation have been a winning strategy in some Italian regions such as Veneto and some Asian countries (61). The value of the epidemiological link as an essential criterion for case definition is scarce in a globalised world.
2. REORGANISATION OF EMERGENCY NURSING STAFF (77, 78)

1. Define the maximum number of intensive care, sub-intensive and ordinary hospital beds that can be retrieved and activated within the organisation and an incremental activation plan (e.g. the conversion of operating rooms and sub-intensive areas into intensive care, recovery of unused hospitals) and consequently define the number of nursing staff needed at each step.

2. Make every effort to ensure numerically and professionally expert assistance concerning beds increase. The beds can be increased with less or greater economic commitment, greater or lesser time interval, the real limited resource is the human one, in terms of specialised skills that cannot be improvised.

3. Alternatively, increase the number of nurses, but provide a consistent number of nurses who are experts in intensive care in each shift. The Society of Critical Care Medicines encourages hospitals to adopt a tiered strategy of distribution of personnel in pandemic conditions (79).

4. Consider the following recovery criteria for intensive care:
   a. previous service in intensive care;
   b. current or previous service in the operating room;
   c. current or previous service in specialised intensive care (e.g. cardiology intensive care);
   d. lastly, certified training (e.g. master) even without experience, in intensive care.

5. Use similar principles for sub-intensive respiratory units, where non-invasive mechanical ventilation is practised.

6. Recall retired experienced staff.

7. Quickly activate multiple channels for nursing staff recruitment, favouring the new hiring of staff with previous experience (especially in intensive and sub-intensive care units). Consider continuing recruitment in the post-pandemic phase, if the risk of a new wave persists.

8. Caution should be used when introducing young graduates to the areas most exposed to the emergency. It is preferable to introduce them to other units and move experienced personnel to emergency sites.
3. RECOMMENDATIONS FOR DIAGNOSIS

1. The reference test for diagnosis is the search for viral RNA using Realtime-Polymerase Chain Reaction (RT-PCR). The antigen test on swabs and saliva tests are currently adopted as screening tests in selected situations.

2. The adequate specimen for Real Time-Polymerase Chain Reaction (RT-PCR) testing is a nasopharyngeal and oropharyngeal sampling. Prefer lower respiratory tract (LRT; expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage) when readily available (for example, in mechanically ventilated patients) (2). Quality of RT-PCR testing is a crucial issue. Both pre-analytical and analytical variables should be carefully taken into account, and a validation process should be performed according to ISO 15189 (3 protocols) (9).

3. The determination of anti-SARS-CoV2 IgG and IgM antibodies can be useful in the diagnostic confirmation of patients with clinical, biochemical and/or instrumental characteristics of COVID-19, but repeatedly negative RT-PCR, in addition to population epidemiological studies. Keep in mind, however, that there are different techniques with different levels of sensitivity and specificity, that the IgM are detectable 7-10 days after the onset of symptoms and the IgG not earlier than 12 days and that the viral load gradually decreases with increasing serum antibody levels. Diagnosis is confirmed if it is observed seroconversion from IgM to IgG or an increase in the IgG titer 4 or more times between the first and second determination (80).

4. Many of the most common symptoms of novel coronavirus disease (Covid-19) are similar to those of the common flu or cold. So, it is also suggested knowing which common symptoms of flu or cold are not symptoms of COVID-19. COVID-19 infection seems to rarely cause a runny nose (10).
Rhinorrhea (“runny nose”) is a not common symptom of Covid-19, and nasal congestion (“stuffy nose) is reported only by 4.8% of patients (10).

5. The most common Covid-19 symptoms are: fever (88%), dry-cough (68%), fatigue (38%), thick sputum production (34%), shortness of breath (19%), artho-myalgia (15%), sore throat (14%), headache (13.6%), chills (11%), nausea/vomiting (5%), nasal congestion (4.8%), diarrhea (3.7%).
Data from a series of 55,924 laboratory-confirmed cases of COVID-19 in China in the period up to February 2020 (11).

6. Acute alterations of taste and smell are COVID-19 symptoms.
A multi-centric European study, including over 400 subjects, reported such symptoms in over 85% of cases (12).

7. Beware of patients with gastrointestinal symptoms.
Nausea/vomiting and/or diarrhoea can be present in about 9% of cases. These symptoms have so far been one of the most frequent causes of omission or diagnostic delays (11).
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8. Atypical clinical manifestations reported in the literature are: syncope due to orthostatic hypotension, testicular pain, hemoptysis, headache, dizziness, altered mental state. In particular, cases of Guillain-Barrè Syndrome or its variant with the involvement of the cranial nerves [Miller Fisher syndrome (ataxia, areflexia, ophthalmoplegia)], meningoencephalitis, cranial polyneuritis, acute cerebrovascular events have been described (62-67).

It is important to keep these symptoms in mind so as not to incur diagnostic errors and/or dangerous exposure to healthcare professionals and other patients when presented in isolated form.

9. Cardiovascular manifestations of Covid-19 are: non-specific myocardial damage, myocarditis, myocardial infarction, arrhythmias, pulmonary embolism and heart failure, cardiogenic shock and cardiac arrest. Acute heart failure has been described as the first manifestation in 23% of cases and palpitations in 7%.

These manifestations may be due to the direct effect of the virus, the systemic inflammatory response, hypoxia, coagulopathy, but also to the effect of the drugs used. The presence of these manifestations aggravates the prognosis as well as the presence of pre-existing heart disease (68, 69).

10. Pay attention to the relationships of COVID-19 with arterial (Stroke, IMA) and venous thrombotic events (VTE), as well as the negative impact on these events in COVID-19 and non-COVID patients.

The lockdown and the fear of contagion have reduced the use of hospital for pathologies other than COVID-19, even acute. The infection is associated with a more severe prognosis in subjects with Stroke. Virus-induced coagulopathy and/or systemic inflammatory response can promote thrombotic and even bleeding events, in the case of DIC. The fear of a negative interaction between infection and the use of NSAIDs has led some patients to discontinue ASA. Antivirals, such as lopinavir/ritonavir reduce the effect of antiplatelet agents such as clopidogrel and enhance that of ticagrelor. The burden of VTE is increased by the diagnostic difficulty (hypoxia and increased d-dimer are already part of the clinical picture of COVID-19; difficulty in performing angio-CT, echocardiogram and echocolor doppler in prone patients). Diagnostic tips for VTE can be signs of deep vein thrombosis, hypoxia disproportionate to the lung picture, acute deterioration of the right ventricular function (68, 69).

11. Over time, ocular manifestations have also been described (ocular irritation, conjunctivitis, kerato-conjunctivitis, anterior uveitis, retinitis and optic neuritis 2-32% of cases) in isolated, early forms or associated with a severe course. Also, cutaneous manifestations (erythematous or herpetiform rash, especially of the trunk, diffuse urticaria, erythema pruriginous, petechial rash, livedo reticularis) can appear early or later (if later, they are probably due to immunological reactions) (83).

12. Cases of hepatitis have also been reported.

The pathophysiological mechanism of which is not yet known; possible direct infection of hepatocytes, drug toxicity, immune-mediated damage, binding to cholangiocytes through ACE2 receptors (84).

13. Vital parameters measurement (respiratory rate and peripheral saturation O2 in ambient air, SpO2 are recommended) and walking test are fundamental to monitor patients managed at home. In addition, it is recommended to perform a blood gas analysis in ambient air if SpO2 <94%, at triage or as soon as possible, for those who come to the hospital (13, 14).
14. Do not rely only on PO2 <60 for the diagnosis of respiratory failure, always calculate the P/F, especially in young subjects.

15. Define a "COVID-19 profile" for the rapid order entry of blood tests, including the following tests: blood count, C-RP, creatinine, blood glucose, albumin, AST ALT, bilirubin, pneumococcal and urinary legionella agents, mycoplasma and chlamydia test, PT-INR, troponin and procalcitonin.

16. Chest X-rays have limited sensitivity in the early stages of Covid-19 pneumonia. A CT scan is more sensitive but raises logistical problems. If ultrasounds competencies are available, use chest US, but disinfect US probes after contact with every Covid-19 suspected or confirmed patient (15).

17. Monolateral lung infiltrates do not exclude COVID-19. They have been described in 25% of cases (15).

18. The most common reported laboratory abnormalities in Covid-19 patients are: Lymphopenia (35-75%), increased C-RP (75-93%), LDH (27-92%), ESR (up to 85% of cases), hypoalbuminemia (50-98%) and anemia (41-50%). Data from a systematic revision of literature (16).

19. The following negative prognostic factors have been reported: leukocytosis, neutrophilia, increased procalcitonin, LDH, AST, ALT, total bilirubin, creatinine, troponin, d-dimer, PT and hypoalbuminemia, lymphopenia. Even thrombocytopenia is associated with severe disease (16, 17). Severe lymphopenia and lymphocytes count fall during the first 4 days since hospital admissions have been associated with higher mortality. Increased white blood cell count, neutrophil count and procalcitonin could reflect bacterial superinfection, while increased d-dimer and PT diffuse intravascular coagulation (DIC), reported in up to 75% of patients who died (16).

20. History of smoking, older age, co-morbidities, respiratory failure, maximum body temperature on admission ≥37.3°C, albuminemia<4 mg/dl, higher SOFA score, d-dimer >1000ng/ml would be risk factors for disease progression (severe or critical disease/death) (18, 70).

21. Do not forget other respiratory infections (legionella, pneumococcus, mycoplasma, chlamydia, other respiratory viruses) and non-infectious disorders, even during epidemics. Always take an accurate clinical history and physical examination, look for other pathogens and aetiologies, consider blood cultures and antibiotics if appropriate. During epidemics, it is crucial to avoid availability bias that means diagnose all infections due to epidemic agents. Further, WHO recommends investigating other pathogens, as co-infections have been reported.

22. Avoid restrictions on caregivers’ access. This can negatively affect the diagnostic and therapeutic process, through the loss of useful information (clinical history, symptoms evolution, allergies, etc.), especially in elderly and/or uncooperative patients. In this
Use disease severity stratification for the choice of the treatment setting (home, ordinary, sub-intensive or intensive care unit).

WHO distinguishes 6 clinical syndromes associated with COVID-19: mild disease, moderate disease (pneumonia), severe disease (severe pneumonia), ARDS, sepsis and septic shock. Patients with the mild or moderate disease do not have any signs of dehydration, sepsis or shortness of breath and can be treated at home. Such decisions will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and conditions at home, including the presence of vulnerable persons in the household (2).

Pay attention to older people and immunocompromised subjects as they can present vague and/or atypical symptoms (fatigue, reduced alertness, reduced mobility, diarrhoea, loss of appetite, delirium and absence of fever) (2).

Immediately notify the Public Health Officials of Covid-19 positive patients (use infectious disease notification forms) (19).
4. RECOMMENDATIONS FOR HOSPITAL TREATMENT

1. Since there are no proven treatments, anti-rheumatic, antiviral, immunomodulatory and immune plasma treatments used so far should not be administered outside of clinical trials (2).

2. Before prescribing antiviral drugs, verify drug-drug and drug-disease interactions, pay particular attention to oral anticoagulants that could be substituted by low molecular weight heparin. Current antiviral therapy schemes include drugs such as lopinavir/ritonavir, chloroquine or hydroxychloroquine, darunavir, cobicistat, tocilizumab, remdesivir (14, 20) which present interactions with antibiotics, antiarrhythmics, statins, anti-angina, etc. (table 1, 2, 3, 4).

3. Be aware of the risk associated to the combination of chloroquine/ hydroxychloroquine and macrolides (QT elongation and fatal arrhythmia); so look for other concomitant therapies able to prolong QT interval, check QT interval at baseline and during the therapy.

4. Beware of the concomitant presence of antiphospholipid antibody syndrome, porphyria, myasthenia gravis and favism (possibly G6PDH dosage), before prescribing chloroquine or hydroxychloroquine. The last meta-analysis showed that hydroxychloroquine does not reduce mortality or mechanical ventilation (85).

5. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are safe and should not be discontinued during Coronavirus epidemics (21).

6. To date, there is no strong evidence for or against the use of NSAIDs in a person diagnosed with COVID-19. Clinicians must weigh the risk and benefits on an individual basis (22).

7. Administer oxygen therapy up to 5 L/min by nasal cannula or up to 6-10L/min by Ventimask or 10-15L/min with face mask with reservoir and titrate flow rates to reach SpO2 ≥90% in non-pregnant adults and SpO2 ≥92-95% in pregnant adults (2).

8. High-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) should only be used in selected patients with hypoxemic respiratory failure (P/F next to 300 for HFNO and 250-300 for NIV), but with alerts and with preserved ventilator dynamics. Monitor closely for clinical deterioration (7, 23).

9. Avoid HFNO or NIV in patients with hypoxemia and hemodynamic instability, hypercapnia, multi-organ failure and sensory impairment.

10. Do not prolong HFNO or NIV for over 2 hours in the case of failure to improve (HFNO:
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respiratory rate ≥24/min, NIV: respiratory rate ≥28/min and/or worsening P/F for both) (7, 23).
High flow nasal cannulas and non-invasive ventilation are not recommended in viral pandemics, based on
studies conducted in influenza and MERS (7).

11. Avoid nebulisation therapies for the potential spread of pathogens.
Nebulisers generate aerosol particles that can carry bacteria and viruses deep into the lung. The risk of
infection transmission may increase with nebulisers as they can generate a high volume of respiratory
aerosols that may be propelled over a longer distance than in natural dispersion patterns. Nevertheless, the
larger particles may cause cough in both patients’ and bystanders’ and increase the risk of spreading the
disease. So, nebulisers in patients with pandemic COVID-19 infection have the potential to transmit
temporally viable COVID-19 to susceptible bystander hosts (24).

12. Administer intravenous fluids only if needed.
Excessive fluid administration could aggravate oxygenation and be dangerous, especially in settings where
mechanical ventilation is not readily available.

13. Use steroids only in patients with the severe or critical disease and/or for other
indications (i.e. exacerbation of COPD or asthma, septic shock/ARDS) (84).
Steroids were not associated with benefits, but rather with damage in the 2003 SARS epidemic and a delay
in virus clearance in Middle Eastern Respiratory Syndrome (MERS) of 2012 (2). Two recent systematic reviews
showed that steroids probably reduce mortality and mechanical ventilation need (84,85)

14. Assess thromboembolism and bleeding risk of every patient and provide appropriate
thromboprophylaxis.
Consider that recovery times, and therefore hypomobility of a subject with COVID-19 are long (at least 15
days in mild forms and up to 6 weeks in severe/critical ones). Diffuse intravascular coagulation (DIC) can
complicate the course (2,14).

15. Consider pharmacological and non-pharmacological prophylaxis (mobilisation and
hydration) of venous thromboembolism, depending on the bleeding risk, also in
patients managed at home or discharged from the hospital, if they have additional risk
factors (e.g. cancer, bedding, previous VTE...) (68).

16. Low molecular weight heparins represent the anticoagulants of choice in COVID-19. For
reasons of manageability, compatibility and risk of exposure of healthcare
professionals, unfractionated heparin should be reserved for patients with severe renal
failure or candidates to invasive procedures (68).

17. Assess the risk of pressure ulcers and implement preventive interventions (Anti-
decubitus mattress, frequent change of position, skincare, attention to hydration, etc.).

18. Vital parameters, including respiratory rate, peripheral oxygen saturation (SpO2) and
arterial blood gas analysis results must be monitored closely during a hospital stay due
to insidious presentation of severe hypoxemia in this disease. Intra-arterial radial
catheters insertion is to be considered to reduce arterial punctures, even outside ICU.

19. Consider medical early warning scores (e.g. NEWS2) that facilitate early recognition
and escalation of treatment of the deteriorating patients (2).
20. Also monitor white blood cells, lymphocytes and platelets count, LDH, procalcitonin, hemocoagulation parameters, liver and kidney function: they are considered alarm flags (13, 16, 17).

21. Be aware of the possible development of severe form around 7 days after symptom onset (13).

22. If a patient reports a SpO2 ≤90% in free air or ≤92% in COT and /or presents FOR ≥30 acts/min and/or severe respiratory distress, intensive care therapist consultation must be required (25).

23. Use biosafety precautions when handling oxygen therapy devices (23); cover the patient's face with a surgical mask during HFNO or C-PAP (23); to reduce the risk of aerosolisation, possibly use a dual or single circuit non-invasive ventilator with an integrated expiratory valve and the helmet as an interface (7).

24. Because of the risk of Strongyloides stercoralis hyperinfection with steroid therapy, diagnosis, or empiric treatment should be considered in endemic areas if steroids are used (86).

25. People with Covid-19 are at high risk for delirium, so assess them by validated tools, implement prevention strategies and treat promptly in case of detection (2). Accurately check drug-disease and drug-drug interactions in cases of pharmacological treatment of delirium.

26. Covid-19 infection is characterised by a long duration of symptoms, so evaluate nutritional status on admission to hospital to prevent malnutrition.

27. Consider communication impairments of patients, especially if they are older or have a cognitive or auditory impairment and adjust your communication modality (2). Facemasks can enhance such problems.
5. ETHICS OF TREATMENT DECISIONS

This is a complex issue which needs to be decided in the local setting as per previous ethical frameworks.

We recommend that the ethical decision-making process is developed in anticipation of making complex decisions, rather than in reaction to the need to make a decision.

With regard to the management of patients affected by COVID-19 in intensive care, we offer some references which may assist in developing the local ethical guidelines (25, 26, 27, 28).

Other important publications (not included among references):

- Giacomo Grasselli, Antonio Pesenti, Maurizio Cecconi. Critical Care Utilisation for the COVID-19 Outbreak in Lombardy, Italy Early Experience and Forecast During an Emergency Response. JAMA published online March 2020 https://jamanetwork.com/journals/jama/fullarticle/2763188


6. RECOMMENDATIONS FOR SURGERY

These recommendations apply to the medical staff of the operating departments concerning cases of COVID-19.

1. An operating room maintained at a negative pressure with a high-frequency air exchange (at least 25 cycles/h) or designated 'contaminated' surgery-only is sensible (71).

2. Surgical patients suspected or positive for SARS-CoV-2 infections should follow the local management protocol, which may include:
   a. wearing specified bracelets and surgical masks,
   b. having their medical records marked with warning labels
   c. being brought through defined routes and lifts to the special isolation area for recovery (72).

3. A dedicated portable ventilator should be used when managing infected ICU patients, switching off the gas flow and closing the endotracheal tube to reduce aerosol production when connecting to the operating room ventilator. The gas sampling tube should be protected by a high-efficiency particulate air (HEPA) filter, and the soda lime should be changed regularly (73). Anaesthetists should use three-level protective measures with HEPA filters on both of the circuit's limbs and consider disposable components (73).

4. Surgeons and personnel not needed for intubation should remain outside the operating room until anaesthesia induction/recovery, and intubation/extubation, are completed by the anaesthetist. (Minimum time before the entrance of the surgical team depends on the type of PPE and the characteristics of the room - refer to the local indications).

5. Patients with COVID-19 may need to undergo emergency and/or emergency surgery. The following recommendations should be observed:
   a. the patient wears the surgical mask until the IOT.
   b. the surgical team wears masks with FFP2/FFP3 filters, especially if the patient is symptomatic
   c. the anaesthetist and/or nurse assigned to anaesthetic assistance wears an FFP2/FFP3 filter
   d. after intubation, the patient's airways are protected with TNT light drapes compatible with anaesthetic assistance
Protection level of the surgical gowns depends on the type of procedure. Level 4 is the highest fluid and microbial barrier, and is needed for lengthy, fluid-intensive procedures; level 3 is indicated as moderate fluid barrier protection (74).

6. The number of healthcare professionals present during the procedure should be limited to only those essential for patient care and procedure support (no visitors or observers allowed, no teaching/academic activities).

7. Consider a laparoscopic approach only after strictly evaluating the risk/benefit to both patient and staff. Precautions during laparoscopic surgery may include:
   
   a. lower intra-abdominal CO₂ pressure  
   b. closed smoke suction system with ultra-low particulate arrestance filter (ULPA)  
   c. minimal incisions for trocars placement (using balloon trocar, if available)  
   d. evacuation of all smoke before the specimen extraction

8. Identify explicit priority criteria for elective surgical interventions to be performed even during an emergency (e.g. oncological interventions at high risk of progression or complication) (75).

9. It is recommended to perform a sanitisation and disinfection of the operating room for at least 1 hour, at the end of the intervention.

10. Team working organisation:

    To stay healthy and maintain the continuity of care, surgical teams should be divided into senior and junior doctors and work for 2 weeks. After the 2 weeks, a new team will release the other. This will allow for easier replacement of team members should they fall ill, restrict potential containment of the virus to smaller staff numbers, and provide the ability to maintain some service provision and clinical care.

11. It is recommended that all the operating material be disposed of through special waste routes and use disposable material/TNT.
7. RECOMMENDATIONS FOR PREGNANT WOMEN

1. It is recommended that pregnant women observe general prevention measures, including using masks.
   There is no evidence that the mask is hazardous to the mother and/or the foetus (87).

2. Reduce pregnant women’s access to prenatal care, limiting it to essential visits and high-risk cases only (29).
   There is no evidence of an increased risk of unfavourable maternal or foetal outcomes in the case of Covid-19. However, evidence relating to influenza and SARS-COV1 can infer that the pregnant woman is at high-risk.

3. Infants born to mothers with confirmed COVID-19 should be presumed to be infected. As such, these infants should be isolated from others (30) and tested at 0, 2, 7 and 14 days.
   Mother-to-foetus (vertical) transmission is possible and accounts for about 30% of cases (88). A meta-analysis of 176 cases showed that about 50% of infected infants were asymptomatic, while the other 50% had similar characteristics to those described for the adults (89).

4. Infants should be separated (i.e. in an individual room) from the mother with confirmed or suspected Covid-19 until the precautions based on the transmission risk of the mother are suspended. This precaution should be thoroughly discussed between the care team and the mother, considering the clinical condition of the mother, her desire, the risk of disease transmission with the appropriate precautions (low) and the benefits of non-separation, including the protective potential of colostrum, breastfeeding and feeding time (29, 30).
   Recent indications from the CDC do not consider confirmed disease a reason to separate mother and child, even in preterm or low weight or to avoid skin-to-skin or rooming-in practice (90). However, a meta-analysis of 176 cases revealed the lack of separation of mother and newborn - if the mother is symptomatic, and therefore, particularly infectious, it significantly increases the risk of neonatal infection (89).

5. The discharge of mothers after childbirth must follow the recommendations for Covid-19 or suspected patients (29).

6. In the case of a woman with suspected SARS-CoV-2 infection or with COVID-19, according to her clinical conditions and desire, breastfeeding should be started and/or maintained directly on the breast or with squeezed breast milk. If mother and child must be temporarily separated because of mother clinical conditions, one should help the mother maintain milk production through manual or mechanical/electric squeezing (30).
   In a limited series reported to date, the virus’s presence in the breast milk of infected women has not been reported, but anti-SARS-cov2 antibodies have been found (29). So breast milk would be protective.
7. In the hospital or at home, a mother with confirmed COVID-19 or symptomatic should take all possible precautions to avoid spreading the virus to the baby, including washing hands before touching the baby and wearing a face mask when she is within 2 meters, like during breastfeeding. If using a manual or electric breast pump, the mother must wash her hands before touching the breast pump or parts of the bottle and wearing a mask during feeding. If possible, ask another healthy person, not at risk of the severe forms of COVID-19, preferably cohabiting, to give milk to the baby, always taking care to wash your hands first and wear a mask (30).

It is not yet known whether COVID-19 can be transmitted through breast milk. At present, the main concern is not whether the virus can be transmitted through breast milk, but rather whether an infected mother can transmit the virus through respiratory droplets during breastfeeding (29).

8. When assisting the delivery of women with confirmed or suspected Covid-19, staff must use the safety precautions provided for non-pregnant patients (30).

9. Serological screening, followed by swab monitoring every 5-7 days from the 37th week of gestation, may help avoid urgent swabs during active labour or delivery in an unclean pathway.

10. Centralising all non-imminent deliveries of women with confirmed infection at a referral centre can reduce nosocomial contamination. Some centres also adopt the practice of induction at 40 + 1 weeks for this purpose.

11. Partner's or other beloved person's access to the delivery room must be filtered by a screening interview (see Table 5 in Appendix 29) and/or by an oral-nasopharyngeal swab, depending on the local epidemiology.

12. Pregnant women with suspected or confirmed SARS-COV2 infection should be treated with supportive therapies while considering pregnancy's physiological characteristics (2).

13. The use of experimental therapeutic agents outside of a research study should be guided by an individual risk-benefit analysis based on the potential benefit to the mother and the foetus's safety, with the consultation of an obstetrician specialist and an ethics committee (2).

14. The decision to proceed with a preterm birth is based on many factors: gestational age, maternal conditions and foetal stability, and requires a collegial evaluation by obstetric, neonatal and intensive care specialists (depending on the mother's condition) (2).

15. Positivity in itself to Coronavirus is not an indication for a caesarean section which in these patients should only be performed based on other obstetric or medical indications (30).
16. In COVID-19 pregnant women, be very cautious in inducing lung maturity with corticosteroids, since these drugs seem to worsen the course of the infection. If possible, evaluate each case with a neonatologist.
8. RECOMMENDATIONS FOR PEDIATRIC PATIENTS

Keep in mind that:

1. Children and infants may be affected, but more often with asymptomatic or mild symptoms, without fever or pneumonia, more often with malaise, rhinitis and gastrointestinal symptoms (31, 32)
   It is hypothesised that this may be due to various reasons including more effective immune responses, a different expression of ACE2 receptors and the presence of other viruses that limit the spread of SARS-CoV2 in the respiratory tract of children (84)

2. Leukocytes are often normal, even if some have leukopenia; lymphopenia is much less frequent in children (32) (76)

3. Among the instrumental investigations, chest X-ray is often silent, while the CT scan is more sensitive (31, 32). Pulmonary consolidations with a halo sign on CT are typical in children (32).

4. Covid-19 severe/critical forms are less represented in children. However, in such cases, the symptoms are respiratory and sometimes neurological and/or cardiovascular. About 2 weeks after infection onset, some children can present a multisystemic inflammatory syndrome that can manifest with various clinical pictures: a Kawasaki-like vasculitis, acute myocarditis or macrophage activation syndrome.

5. In autumn and winter, many other viral diseases with similar symptoms can affect children, particularly influenza-like infections. It is therefore recommended that both parents and caregivers are vaccinated against influenza.

6. For the same reason, rapid virological diagnostic tests should include, in addition to Covid-19, other Coronaviruses, influenza, RSV, rhinovirus, and human metapneumovirus.

7. The criteria for the definition of Acute Respiratory Distress Syndrome (ARDS) and septic shock, the guidelines for the management of sepsis and septic shock, and non-invasive ventilation in children are different from those of adults (2).

8. Children desaturate more easily during intubation; therefore, it is vital to pre-oxygenate with 100% O2 with a mask with a reservoir before intubating (2).

9. Most of the drugs used for Covid-19 are not authorised for paediatric patients due to the difficulty of conducting randomised studies in this period of life.

10. A rectal swab may be useful in children to determine the timing of the termination of quarantine.
Some authors have used the cycle threshold values of the serial rectal and nasopharyngeal swab tests to indicate viral load. Interestingly, the measurements have indicated that viral shedding from the gastrointestinal system could be greater and last longer than the respiratory tract (33, 34).
9. RECOMMENDATIONS FOR HOSPITAL DISCHARGE

1. A patient with fever but without respiratory failure (normal EGA and walking test) and a normal chest x-ray, <70 years and without risk factors (lung disease, diabetes mellitus and/or heart disease) can be discharged from the emergency room (14, 20) with a request to isolate at home while waiting to run the swab sampling or its result.

The discharging physician:

a. Must obtain a telephone number to contact the patient for swab sampling and/or to communicate the result;

b. Provides information on how to access the swab (where and when).

Suppose the swab test does not occur in the emergency department but is performed elsewhere to another area or hospital. In that case, it is strictly suggested to use systems to avoid the loss of information.

The facility/service running the buffer must report the result as soon as it is available to the patient and, if positive, to the Public Health Department for establishing active monitoring.

2. At the end of the hospitalisation, write clearly on the discharge letter:

   a. CLINICALLY CURED patient (patient with clinical symptoms resolution for at least 3 days, but swab still positive) (35) or
   b. CURED patient (patient who, in addition to symptoms resolutions, has negative swab (35).

CLINICALLY CURED PATIENT: write clearly on the discharge letter the requirements to be observed in the home quarantine until the swab is negative, and how to swab. Although there is no clear supporting evidence, it is considered appropriate to suggest patient retesting no earlier than 7 days, if positive.

If long-term swab positivity persists, the subject, asymptomatic for at least 7 days, is considered cured 21 days after the onset of symptoms (excluding anosmia and dysgeusia) (35).

3. DISABLED PATIENT, a person with a positive swab or whose result is not yet known:

   a. Write the requirements of home isolation on the discharge letter (up to 14 days from contact with the infected person)
   b. Provide a telephone number to communicate buffer result;
   c. Communicate swab results as soon as available to the patient and carer and, if positive, to public health trusts, to establish active monitoring (19).

4. Any patient destined for a nursing home, rehabilitative, hospice, long-term or similar health facility or referred to integrated home care, should have a negative test before discharge. For further details, see section 16.
10. RECOMMENDATIONS FOR HOME ISOLATION AND DE-ISOLATION (35, 36, 37)

1. Provide prevention measures and explain them to patients in home isolation, using designs, charts or pictures.

2. Give clear information on symptoms that should cause concern: promote information diffusion of telephone numbers to call in case of their occurrence.

3. Provide call centres, online chats, FAQs and video tutorials to consult in case of concerns or questions.

4. De-isolation:
   a. for persons who never developed symptoms - the date of the first positive viral diagnostic test (PCR or antigen) for SARS-CoV-2 RNA should be used in place of the date of symptom onset and isolation. Other precautions can be discontinued 10 days after.
   
   b. for symptomatic persons - isolation and precautions can generally be discontinued 10 days after symptom onset and resolution of symptoms for at least 3 days

   c. a limited number of persons with severe illness may produce replication-competent virus beyond 10 days that may warrant extending the duration of isolation and precautions for up to 20 days after symptom onset; consider a consultation with infection control experts.

   d. two consecutive negative SARS-CoV-2 RT-PCR test results, ideally in 24 hours, are recommended to discontinue isolation for immunocompromised and severely ill patients, especially if they are to be transferred to other units within the hospital or discharged to an LTCF.

5. For persons previously diagnosed with symptomatic COVID-19 who remain asymptomatic after recovery, retesting is not compulsory within 3 months after the date of symptom onset for the initial COVID-19 infection, unless they develop new symptoms consistent with COVID-19 and an alternative aetiology cannot be identified by a provider, especially in the event of symptoms develop within 14 days after close contact with an infected person. Persons being evaluated for reinfection with SARS-CoV-2 should be isolated under recommended precautions while undergoing evaluation. If reinfection is confirmed or remains suspected they should remain under the recommended SARS-CoV-2 isolation until they meet the criteria for discontinuation of precautions.
11. RECOMMENDATIONS FOR PERSONS IN QUARANTINE (38)

1. Information sharing is a critical factor for a successful quarantine; quarantined persons must be continuously informed and updated on the epidemic progress.

2. Provide food, any necessary drugs, and other materials without making people feel abandoned or alone.

3. The quarantine period should be in keeping with the health authority requirements, and the duration should not be modified except in extreme circumstances.

4. Voluntary quarantine is associated with less stress and fewer long-term complications; therefore, it is crucial to explain clearly the reasons for such suggested behaviours.

5. Public health officials should stress the selfless choice of self-isolation.

Quarantined healthcare workers can work on office-based work while at home. They could contribute by making suggestions and staying in touch via social media.
12. RECOMMENDATIONS FOR ONCOLOGIC AND IMMUNOSUPPRESSED PATIENTS

1. Do not indiscriminately discontinue antineoplastic or immunosuppressive therapies. (39-41).

2. In cancer patients, consider the possibility of postponing the treatment cycle on a case-by-case basis (39).

3. Immunosuppressant withdrawal is indicated if symptoms suggestive of infection appear (41); in this case, it is good practice to inform the physician responsible for the treatment promptly.

4. Steroids can be continued, but with caution (41).

5. New immunosuppressant prescriptions or dose increases are not recommended during an epidemic (42).

6. Consider the switch from parenteral drugs to others that can be administered at home (e.g. subcutaneously) to reduce outpatient clinics visits (39).

7. Ensure non-deferred outpatient visits and postpone visits for long-term follow-up, after remote evaluation (telephone, email, etc.) (39, 41).

8. Do not allow visitors in the therapy rooms and allow a maximum of one visitor per patient in hospital stays (39).

9. Use a screening interview (see Table 5 in Appendix), preferably the day before, to filter day hospital visits, elective hospitalisations or home visiting; interview the patient and any accompanying person (in the case of a disabled patient) (40).

10. Perform oro-nasopharyngeal swab at least 48h before starting antineoplastic treatment in naïve patients (40).

11. According to local resources and epidemiology, consider periodic monitoring by oro-nasopharyngeal swabs for patients on oncologic treatments and healthcare operators who assist them (40).

12. In Covid-19 positive oncologic patients, stop antineoplastic treatment. There are no studies about starting or continuing treatment in asymptomatic patients, and a 2-week
stop does not aggravate the prognosis. In the case of persisting Covid-19 positive tests, clinicians should decide on an individual basis (40).

Please also refer to the General Recommendations (section 1) for other indications relating to outpatients’ clinics.
13. MORTUARY/MORGUE OPERATING PROCEDURES

Management of the deceased body with suspect, probable or confirmed COVID-19 respiratory infection

1. The proposed procedure is aimed at the safe management of the phases of acceptance, handling, custody, and discharge of the body with suspected, probable or confirmed diagnosis of COVID-19 (43). It is recommended that:

   a. The acceptance and handling of the body must be done by personnel equipped wearing the recommended PPE;

   b. The body must be positioned on a sanitised metal stretcher for custody and subsequent investigations;

   c. At the end of the investigations, the body must be placed clothed in the coffin and wrapped in a sheet soaked in disinfectant solution;

   d. If the corpse must remain in the mortuary, pending or after the investigations, the corpse must be placed in a specific closed body bag and stored in a dedicated refrigerated room;

   e. All the equipment used must be subjected to sanitisation at the end of the handling and transport operations.

2. Recommendations for autopsy investigation in cases of suspect, probable or confirmed COVID-19. For the safe and effective performance of HG3 (Hazard Group 3) autopsy investigations, it is recommended that:

   a. A generic risk assessment and universal standard precautions are adopted;

   b. Knowledge of possible pathological findings are highlighted;

   c. Standard Operating Procedures (SOP) for the management of autopsies with high biological risk are implemented.

3. The use of universal precautions effectively protects against most risks related to SARS-CoV-2 infection. Professionals have a duty to carry out a risk assessment for each case to prevent actions that could put operators at risk (44).
4. At the end of the autopsy investigations, the body must be positioned in a body bag and transported in a refrigerated room.

5. Disinfect the outside of the body bag with a hospital disinfectant applied according to the manufacturer’s recommendations. In this phase, it is also recommended that each operator involved in the movement and exit phases of the body wear suitable PPE.

6. Following an autopsy on a subject with suspect or confirmed COVID-19, the following recommendations for the disinfection of the autopsy room should be applied:
   
   a. keep ventilation systems active during cleaning;
   
   b. wear disposable gloves when cleaning and handling cleaning or disinfectant solutions;
   
   c. dispose of gloves after cleaning; do not wash or re-use the gloves in any case;
   
   d. use eye protection, such as a visor or goggles, if splashing is expected;
   
   e. if necessary, use respiratory protection based on the type of detergent or disinfectant;
   
   f. wear a long-sleeved waterproof device to protect skin and clothing;
   
   g. use disinfectants effective against human coronaviruses;
   
   h. clean the surfaces and apply the disinfectant, ensuring an adequate contact time for effective disinfection;
   
   i. comply with the safety precautions and warnings indicated on the product label (for example, allow adequate ventilation in restricted areas and ensure correct disposal of the unused product or used containers);
   
   j. avoid application methods that cause the production of splashes or aerosols.

7. Regarding environmental disinfection, the available evidence has shown that coronaviruses are effectively inactivated by adequate sanitisation procedures that include the use of common hospital disinfectants, such as sodium hypochlorite (0.1% - 0.5%), ethanol (62 - 71%) or hydrogen peroxide (0.5%). There is currently no evidence to support a greater environmental survival or a lower sensitivity of SARS-CoV-2 to the aforementioned disinfectants (45).
a. Hard and non-porous surfaces can be cleaned and disinfected as previously described.

b. Equipment such as cameras, telephones and keyboards, and all objects that remain in the autopsy room should be handled with gloves and appropriately disinfected after use.

c. Cleaning activities must be supervised and periodically checked to ensure that the correct procedures are followed. Sanitation personnel must be properly trained and equipped with suitable PPE.

d. After cleaning and removing the PPE, wash hands immediately. Avoid touching the face with gloved or unwashed hands.

e. Environmental disinfection must include cleaning with water and detergent soap on all vertical and horizontal surfaces, followed by disinfection with hospital disinfectants effective against SARS-CoV-2.

f. For environmental decontamination, it is necessary to use dedicated or disposable equipment. Reusable equipment must be decontaminated after use with a chlorine-based disinfectant. The use of special trolleys is strongly recommended, different from those used for cleaning common areas.

g. The instruments used for autopsies should be autoclaved or treated through chemical sterilisers.
1. Create a healthy work, ethos and environment during crises and have systems to deal with any subsequent distress and disorder.

2. Organisations which have the foresight to prepare their staff to deal with trauma might consider using interventions such as PFA. Psychological First Aid is a humane, supportive response to a fellow human being who is suffering and who may need support.

3. Consider the factors that negatively affect the psychological wellbeing of staff:
   a. concerns over contracting the illness
   b. concerns for the safety of their family
   c. witnessing the death of colleagues
   d. isolation from family and colleagues
   e. a sense of being underappreciated
   f. the extended length of the epidemic

4. Reduce mental health stigma. The best way to reduce stigma is to raise awareness of mental health issues and tell people that it’s quite normal to feel that way and have those feelings.

5. Educate healthcare workers who are exposed to trauma about the effects of cumulative stress. The training should be delivered online because they can do it at their convenience, or via educational leaflets, rather than finding the time to spend on a day course.
   The education about psychological trauma may lead to better understanding, better recognition of symptoms in oneself and others, less judgment, reduced stigma, and positive relationships with others in the workplace can positively impact psychology.

6. Maintain teamwork and effective leadership while at the same time providing individuals with the opportunity to provide input into the decisions that affect their lives.
   Staff often experience severe emotional stress during viral outbreaks. The nursing staff often feels the greatest level of stress due to their constant contact with sick patients, who may not be improving despite the nursing staff’s best efforts. Physicians usually cope somewhat better with this situation because they can make treatment decisions and are less directly involved in implementing patient care.

7. Be receptive to suggestions from nursing staff and support personnel.
   Input is empowerment and provides a sense that critical staff retain some control over their situation. If suggestions are not acted on, clear explanations of why they were not should be provided, and alternatives should be explored.

8. The administration needs to be supportive of staff and not be seen as pedantic or overly controlling.
   In cases where staff and support personnel did not feel appreciated or listened to, there was a high degree
of dissatisfaction and an increased occurrence of absenteeism and staff strikes, which further reduced personnel in an already-strained system.

9. Keep in mind that lack of clarity around tasks is associated with significant stress, and poor leadership is linked to staff stress (includes ad hoc planning) (96).

10. Make an effort to ensure that your office and/or organisation has a viable plan to monitor the course of the outbreak and take rapid and appropriate action if needed.

As a healthcare worker,

11. Take care of yourself and your loved ones. Healthcare providers are not invulnerable to experiencing their own emotional distress during outbreaks, and this distress can be compounded by caring for sick and distressed patients.

12. Make sure your basic needs are met, including eating, drinking, and sleeping. Take a break when you need one; check in with loved ones; practice strategies to reduce distress (listed above) and monitor yourself for stress reactions too.

13. reframe negative experiences in a positive way (97)

14. look for opportunities to express gratitude (97)

15. separate work from private life; avoid media exposure about Covid-19 (97)

16. Adopt the "Three Good Things" as a stress management technique. At the end of the shift, operators are invited to think: "What are three things that went well today and what was my role in making them happen?" (98)

Such strategies are useful to increase happiness and decrease burnout as a result.
15. RECOMMENDATIONS FOR MENTAL WELLBEING OF PATIENTS (48, 49)

1. Medical and mental health clinicians are likely to encounter patients experiencing various levels of emotional distress about the outbreak and its impact on them, their families, and their communities.

We must consider that COVID-19 patients have prolonged hospital stays. In the early stages, they will experience the concern of having a severe manifestation of the disease with the possibility of being intubated. Staff shortages may impact on their treatment.

2. Providers should acknowledge uncertainty about emerging diseases and help patients understand that there is often an emotional component to potential health concerns.

3. Providers should be aware that the symptoms might extend beyond classic mental health symptoms, including relational struggles, somatic, academic, or vocational issues.

4. Every person, including mental health providers, can either react in fear, anger, or despair and regress or choose resilience and play an active part in the solution.

5. Providers should also consider the following recommendations for promoting patients’ mental wellbeing during emerging infectious disease outbreaks:

   a. Be informed: Obtain the latest information about the outbreak from credible public health resources to provide accurate information to your patients.

   b. Educate: Healthcare providers are on the front lines of medical intervention and in a position to influence patient behaviours for protecting individual, family, and public health.

      Psycho-education is of utmost importance in the aftermath of disasters. Patient education plays a critical role in containing the disease and mitigating emotional distress during outbreaks. Depending on the nature of the outbreak, this can range from education about basic hygiene such as hand-washing and cough etiquette, to more complex medical recommendations for prevention, diagnosis, and treatment.

6. Let patients know what you, your office, or your organisation are doing to reduce exposure risk.

7. Correct misinformation

   In this age of social media, misinformation can spread quickly and easily, causing unnecessary alarm. If patients present you with inaccurate information about the outbreak, correct their misconceptions and direct them to vetted public health resources.

8. Limit media exposure.
The excess media exposure to coverage of stressful events can result in negative mental health outcomes. Use trusted media outlets to gather the information you need, then turn them off—and advise your patients to do the same.

9. **Anticipate and counsel potential emotional stress**

Emotional distress is a common mental reaction in uncertain and potentially life-threatening situations, such as the COVID-19 epidemic. An excellent first step for mitigating your patients' stress is to acknowledge that it exists and help normalise it ("I see that you’re stressed, and that’s understandable. Many people are feeling this way right now.").

10. **Teach people to recognise the early signs of emotional stress, including anxiety, fear, insomnia, difficulty in concentration, deteriorating interpersonal relationship, situation avoidance at work or daily living, unexplained physical symptoms, and increased use of alcohol or tobacco.**

This will help them become more aware of the state of their mental health and stress address emotional stress before it becomes difficult to manage.

11. **Discuss strategies to reduce distress, which can include:**

   a. Being prepared (e.g., developing a personal/family preparedness plan for the outbreak).
   b. Taking simple preventive measures (e.g., frequent handwashing).
   c. Maintaining a healthy diet and exercise regimen.
   d. Talking to loved ones about worries and concerns.
   e. Engaging in hobbies and activities you enjoy, to improve your mood.
   f. If a patient is experiencing severe emotional distress or has a diagnosable mental illness, refer them for specialised mental health care.
16. RECOMMENDATIONS FOR HOSPITAL AND RESIDENTIAL PSYCHIATRIC FACILITIES (50, 51)

1. Team organisation and immediate isolation of the structure
   a. Assign specific responsibilities to clinical and management figures and designate a contact person for COVID-19, who is in constant contact with the local emergency team
   b. Close Outpatient Clinics and Day or Semi-residential Centers
   c. Cancel visits of relatives, friends and consultants
   d. Consider the possible return of less severe patients to the families until the end of the emergency, illustrating the infection prevention measures

2. Infectious risk containment actions
   a. Provide surgical masks, measure body temperature, assess Covid-19 related symptoms and contacts and require hand-wash for any healthcare worker (HCW) entering the facility. If there is a history of close contact with positive COVID-19 and/or even mild symptoms, they should not be accepted within the facility
   b. HCWs should always be assigned to the same department and the same section during the emergency
   c. Monitoring of the patient's clinical condition should be carried out at least twice a day
   d. Rehabilitation activities must be reformulated on a "visible" social distancing since the use of masks is not conceivable, nor hands washing is practicable
   e. In residential facilities rehabilitation activities should be carried out mainly outside
   f. Identify an isolation zone to be reserved for suspicious cases, pending diagnostic confirmation (COVID-19 area). The COVID-19 area should be set up in an area wholly detached from the rest of the department, possibly with an independent entrance. It must be sanitised at least 2 times a day, keeping it always ready, even in the absence of cases to be isolated
   g. Swabs should be performed immediately on any suspicious case and his/her contacts
   h. Immediate isolation of the positive patient and close contacts
   i. The clinical management of COVID-19 requires a multidisciplinary medical team including infectious disease specialist, anaesthetist, internist and psychiatrist
   j. Beware of the numerous therapeutic interactions of psychotropic drugs
3. **Actions aimed at protecting HCWs**

   a. Arrange beds and bathrooms with shower, available exclusively to operators
   b. Identify the Operators who may be available to remain in the isolation area for at least 15 days, in case of a positive COVID-19 patient case
   c. Provide HCWs with the necessary PPE in case of a suspected or confirmed COVID-19 patient
   d. Teach them about PPE donning/doffing
   e. Set up a decontamination space outside the COVID-19 area to be used by personnel who should go into the COVID-19 area for an emergency

4. **Communication**

   a. Organise video calls between patients and family members or send them short videos
   b. Organise video conferences to replace team meetings
17. RECOMMENDATIONS FOR LONG-TERM FACILITIES AND NURSING HOMES

(52, 53)

GENERAL ACTIONS

1. External access only allowed to facility operators; social and health services, general practitioners and support administrators, if necessary

2. Unloading of goods in the external area and collection by personnel equipped with PPE

3. Limit, as far as possible, hospitalisation for specialist visits and instrumental examinations

For other indications, see also Recommendations for hospital and residential psychiatric facilities (points 1-2).

SPECIFIC ACTIONS

1. Organise two functional areas, possibly with single rooms and dedicated staff:
   a. a "filter" area for the reception of new guests, equipped with a doctor's certificate of absence of symptoms/suspect contacts and/or negative swab; or guests returned from the hospital with a diagnosis other than COVID-19 and negative swab before discharge
   b. "isolation" area inside the residence for suspect cases awaiting diagnostic confirmation; guests who have returned from the hospital who have only been cured clinically (swab still positive); or to treat confirmed cases, if highly specialised care is not necessary (hospital).

2. In case of a network of residences, identify an entire facility dedicated to COVID-19 with a "filter" and "isolation" area

3. Limit visits by GPs or specialists, and individual physiotherapy activities, to those considered absolutely necessary and non-deferrable

4. Suspend group activities and the sharing of common spaces within the structure

For other indications, see Recommendations for hospital and residential psychiatric facilities (points 3-4).
18. RECOMMENDATIONS FOR GENERAL PRACTITIONERS

INFECTION PREVENTION AND CONTROL AND OFFICE ORGANISATION

1. Prepare organisational procedures to limit attendance (e.g. visits by appointment) and regulate access through standardised telephone triage (54), aimed at stratifying the risk of COVID-19 and the urgency of other problems.

2. Prevent people with fever and/or respiratory syndromes to attend the office.

3. Allow a maximum number of people per area (m2) and per hour, so that no more than 2-3 people are simultaneously in the waiting room at a minimum distance of 2 meters and for more than 15 minutes (8).

4. Promote and implement the electronic transmission of prescriptions.

5. Make available and mandatory the use of personal protective equipment (PPE), the disinfection of hands and shoes, and body temperature measurement at the entrance (thermo-scanner) for patients (55).

6. Arrange for proper disposal, at the end of each visit, of the disposable material of patients and staff, according to the procedures for special biohazardous waste, in closed disposable bags sprinkled with disinfectant and stored in specific rooms.

7. Prepare sanitisation and ventilation procedures: sanitise the medical room (surfaces, used equipment, examination table) after each visit and at the end of each day with solutions based on 0.5% sodium hypochlorite or ethyl alcohol solution at 70% (8).

8. Provide administration staff with PPE and proper training (FAD, video tutorial, poster, etc.).

9. Upon arrival in the office, the physician must wear a washable uniform (at least 2 should be available), working closed shoes and wear PPE (FFP2, disposable goggles and gloves for non-suspicious cases; FFP3, disposable gown, disposable waterproof full suit, headset, glasses, visor, cover shoes and 2 pairs of gloves for visits of suspicious cases). Disposable devices must be changed on each visit.
AT THE DISTRICT LEVEL

1. Establish special continuity of care units that support general practitioners in home management (swabs, laboratory tests, home surveillance).
   Early identification and treatment at home are useful to reduce the congestion of hospitals and intensive care in particular, as they would be associated with a lesser evolution of the disease.

IDENTIFICATION and MANAGEMENT OF SUSPECTED or CONFIRMED CASES (63)

1. Have triage cards based on checklists - better if computerised - that include items for the identification of suspected cases, for the stratification of severity (56), the choice of the appropriate setting and appropriate treatment, and the mandatory reports according to national and local provisions (to the Public Health units and special continuity units, in case of home management)

2. Keep active contact with COVID-19 patients by telephone or through other communication tools (email, WhatsApp, telemedicine) for clinical-prognostic reassessment, at different intervals depending on the clinical severity. Ensure 12-hour availability when needed (in case of onset or worsening of symptoms), including holidays and pre-holidays.

3. Inform - by written instructions, or video tutorials sent by email - all patients on how to prevent contagion, disinfection measures (places and hands), respiratory etiquette, social distancing and the behavioural rules for home isolation

4. Off-label therapies must be prescribed after checking contraindications and/or interactions with other drugs taken by the patient and after the patient’s informed consent.

COMMUNICATION

1. The information flow must be constant, computerised and traceable, possibly using electronic media and telemedicine and teleconsultation systems (57)

2. Reporting suspicious and/or symptomatic cases to special units of care continuity for diagnostic confirmation and home care must be carried out in a traceable and timely way through any available communication channel (i.e. WhatsApp, email, portal, app, etc.)
3. The swabs and/or serological tests results must be returned to the GP in a traceable way to be recorded in the electronic medical record.

4. Teams of care continuity, GPs and the hospital must work together as an integrated team using available tool to efficiently communicate each other (e.g. Messenger Apps, WUP, mobile phones, emails, shared software, teleconsultation) regularly and continuously, to share information about the patient's journey including tests results, clinical condition and monitoring any ongoing therapy, hospital admissions and discharge. The team must keep in contact with all of the people who need support through regional and national information campaigns regarding public health interventions to decrease infections.

5. Carry out regular pro-active phone calls aimed at the assessment of the most fragile people (the elderly, disabled, or with chronic conditions)

OUTCOME MEASURES FOR GENERAL PRACTITIONERS

1. The hospitalisation rate for COVID-19

2. The mortality of hospitalised patients for COVID-19

3. The hospitalisation rate for chronic non-covid diseases

4. Number of COVID-19 cases stratified by age

5. Number of COVID-19 cases with STEMI/NSTEMI

6. Number of COVID-19 cases with COPD

7. Number of COVID-19 cases with diabetes

8. Number of COVID-19 cases with multiple pathologies or social assistance frailties

9. The infection rate in the assisted population

PROCESS MEASURES for GENERAL PRACTITIONERS

1. Number of triage forms filled in

2. Number of cases reported to the local Public Health unit
3. Percentage of activations of the special units of care continuity

4. Number of drug prescriptions (COVID-19 therapeutic protocol)

5. Percentage of patients with co-morbidities

6. Percentage of health personnel equipped and not equipped with suitable PPE

7. Number of untreated patients in adequate level of care

8. Percentage of personnel trained for emergency management
Patients undergoing hemodialysis have a high risk of developing COVID-19 infection due to old age, multimorbidity or immunosuppression. Furthermore, the need for frequent access to Dialysis Centres, using transport systems that are often shared with other patients, and staying in closed and crowded environments for the entire duration of the treatment, can increase the risk of infection.

COVID-19 confirmed, suspected, or under investigation patients should have separate access, rooms and staff.

For other outpatient services, we recommend compliance with the outpatient section in the General Recommendations and Recommendations for cancer and immunosuppressed patients, and:

1. Ask patients to always inform the hemodialysis facility in advance by telephone in the event of symptoms onset, before attending the facility.

2. Optimise transports to haemodialysis: encourage patients to use their own means, and space appointments sufficiently to avoid crowds in the waiting room. Ask patients to wait in the car and advise them not to arrive early. Eliminate multiple transports and organise single transports; sanitise vehicles after transporting affected or suspected patients.

3. Arrival at the haemodialysis centre: the patient, accompanied to the centre by staff, must wear a surgical mask; seats must be spaced at least 1 meter apart, in the waiting room; access to the changing room must be restricted.

4. Before entering the haemodialysis room, patients must be screened by a structured interview on symptoms and contacts (see Table 5 in Appendix), body temperature and peripheral O2 saturation measurement. Patients with body temperature ≥37.5°C and/or oxygen saturation ≤96% are identified as possibly infected.

5. If screening does not reveal situations to be investigated, the patient should be accompanied to the dialysis room. If, on the other hand, the screening interview or the parameters suggest a possible infection, then the following options can arise:
PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK

a. haemodialysis that is essential: perform the haemodialysis session in isolation, as if the patient was Covid-19 positive in the designated room for suspected cases. At the end of the session, refer the patient according to the pre-established in-hospital clinical pathway. If possible, carry out urgent swabs and blood tests at the beginning of the haemodialysis session.

b. haemodialysis that can be delayed: refer the patient according to the pre-established in-hospital clinical pathway.

6. During haemodialysis session: nursing staff must verify that, in the presence of coughing or sneezing, that disposable handkerchiefs are used with a subsequent change of gloves and masks, that no signs and/or symptoms referable to a fever arise, and that the patient does not remove his/her PPEs.

7. In case of a person with a proven COVID-19 infection: perform dialysis in the designated room, organised as follows: a nursing assistant supports the designated room staff without taking direct care of patients. Each healthcare worker who works in the room to wear appropriate PPE in the filter area. The patient will be provided with PPEs and accompanied by transport staff, wearing PPE, right into the room. The doctor on call defines the dialysis therapy. Once the dialysis session has been completed, and the parameters and clinical conditions of the patient have been detected, the patient is discharged.

8. Give preference, if possible, for home dialysis for new patients.

9. In case of illness, pay attention to any required dose adjustments for drugs used to treat infection in patients with reduced kidney function.

10. Given the constant contact of these patients with the healthcare services, evaluate screening for Covid-19 (both by serological tests with and by swabs) of haemodialysis patients and operators at the beginning of the epidemic periodically, based on the local epidemiological situation.

11. Check for the presence of any asymptomatic infections among the staff regularly.
20. RECOMMENDATIONS FOR OPHTALMOLOGY

Increased exposure due to close examinations and aerosol generation procedures (AGP) and the large number of patients evaluated daily was probably the leading cause of the high mortality reported in Ophthalmology healthcare workers during the original outbreak in Wuhan, China (91). Although the frequency of ocular involvement in COVID-19 is not high, operators are still exposed to droplets and micro-droplets (92).

It is crucial to take the following actions:

1. Select which services to perform according to local epidemiology, identifying the procedures burdened by the most significant risks and providing the most effective protective devices.
   For example, during phase 1 of the emergency, it is recommended to ensure evaluations for acute glaucoma, very high uncontrolled intraocular pressure > 40 mmHg, wet active age-related macular degeneration, proliferative diabetic retinopathy, occlusion central vein retinal ischemic (CVRO), acute retinal detachments (macular on, macular off <4 weeks), retinopathy of prematurity (screening and treatment), severe active uveitis, endophthalmitis, ocular and adnexal oncology, trauma and infections.

2. Suspend non-urgent care (91).

3. Undertake scrupulous disinfection practices, protective plastic shields for slit lamp, reduction or elimination of patient conversations during slit-lamp examination are recommended when evaluating asymptomatic patients without risk factors for COVID-19. Limit the time spent with the patient under the slit lamp, and consider, on a case-by-case basis, whether ophthalmic investigations, such as ocular imaging, are critical to decision making (92).

4. To examine visual acuity without being hindered by the glasses' fogging, ask the patient to wash their spectacles with soapy water (the soapy water acts as a surfactant film reducing the surface tension and preventing the phenomena of fogging) immediately before putting on the mask (93).

5. Keep in mind that ophthalmic lenses (20 D, 90 D, 78 D, Goldmann triple mirror and super view lenses), usually used for fundus examination, cloud over, making examination impossible and that it is not possible to adopt the above expedient due to glare and reflections that would occur with diagnostic lenses. The most practical action in such cases is to uncover the nose. However, this increases contagion risk, especially if plastic
screens are not used for slit lamp. Alternatively, it is recommended that the patient wears a facial filter (FFP2-3), since its tighter fit prevents the lenses' fogging (94).

6. Due to physical proximity, during surgery and intravitreal injection, the patient and physician should wear respiratory protection appropriate to the degree of risk (93).

7. Be aware that phacoemulsification produces aqueous aerosol as it sculpts the grooves in the core. Although the risk of contagion seems minimal, it is recommended to instil a 5% povidone-iodine solution before performing cataract surgery, reducing the size of the main port to 2.2 mm (to reduce aerosol generation), allow one complete fluid exchange before the start of emulsification through an infusion/aspiration, lasting at least 6 seconds, and finally covering the eye with hydroxypropylmethylcellulose (HPMC) during the entire emulsification procedure. Although it is not an emergency procedure, it may have to be performed in the context of a more complex operation (e.g. Vitrectomy for retinal detachment) (95).
21. RECOMMENDATIONS FOR PHASE 2

Background: The shift from Phase 1 (increased and sustained transmission in the general population) to Phase 2 (reduced transmission) opened new scenarios and posed new problems in patient safety.

There are six main development lines in the second phase:

1. Epidemics monitoring for early detection of a second wave
2. Prevention and control of outbreaks
3. A safe restart of suspended healthcare activities, including:
   a. outpatient activities
   b. elective hospital admissions
   c. screening activities
4. Review of lessons learned
5. Follow-up of recovered patients
6. Vaccinations

21.1 RECOMMENDATIONS FOR EPIDEMIC MONITORING AND EARLY DETECTION OF A SECOND WAVE, PREVENTION AND CONTROL OF OUTBREAKS

1. Maintain strict surveillance and apply intensive contact tracing

2. Reinforce Public Health Department staff, with volunteers, and/or implement information technology solutions or use the ‘snowball’ method to rapidly give information

3. Enable the easy access to swabs (i.e. drive-through swabs)

4. Use systems to reduce the test turnaround time

5. Use point-of-care tests when appropriate (e.g. airports)

6. Provide clear, not ambiguous, consistent, updated, timely, multilingual information to the community

7. Raise awareness and empowerment of the general population on the use of preventive measures

8. Try to control intra-familial transmission by hosting non-hospitalised affected in dedicated facilities
PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK

9. Decongest public transports, limiting the number of trips and/or choosing alternative modes of travel

10. Adopt early and selective lockdowns in case of outbreaks

11. Anticipate and look for alternative ways to schedule "big events".

21.2 SAFE RESTART OF SUSPENDED HEALTHCARE ACTIVITIES

1. Monitor access to the hospital and other medical services (i.e. outpatient clinics) using body temperature scanning at the hospital or clinic entrance and screening interviews (see Table 5 in Appendix).

2. In case of elective hospital admission (i.e. elective surgery or pregnant women), perform oro-nasopharyngeal swab (max 5-7 days before; better 48-72h before), in addition to point 1.

3. Restrict caregivers' presence for non-professional assistance, but if their presence is required, perform an oro-nasopharyngeal swab. The same for nursing moms.

4. Create special wards to host patients requiring urgent hospital admission and waiting for swab results ("buffer wards")

5. Separate clean/unclean pathways, structurally or functionally

6. Define strategies to recover postponed outpatient or screening visits that involve verifying the persistence of the symptoms, the will of the subject and the priority of the case

21.3 REVIEW OF LESSONS LEARNED

STAFF

1. Address staff shortages in critical areas

2. Set up a staff skills and competences database

3. Enhance the skills and competencies required for emergencies

4. Protect your staff: address the physical and psychological impact

5. Re-train on PPEs and Covid-19 management
PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK

6. Arrange video-tutorial for donning/doffing and ventilators

OTHER RESOURCES

1. Restock medications, equipment and devices

2. Strengthen and reorganise primary care so that care can be provided via tele-medicine and special continuity units for Covid-19 affected individuals is provided.

3. Improve the separation between clean and unclean pathways in all healthcare facilities, structurally or at least functionally

PROCEDURES

1. Plan the hospital surge capacity for a second wave

2. Be prepared for a worst-case scenario

3. Update and standardise preventive, diagnostic and therapeutic protocols and algorithms

21.4 FOLLOW-UP OF RECOVERED PATIENTS

1. Organise a structured and integrated multidisciplinary and multi-professional follow-up, as Covid-19 is a systemic disease

2. Follow-up health teams should include: paediatricians/internists/geriatricians/infectious disease specialists, pneumologists, cardiologists, neurologists, physiatrists and physiotherapists, psychiatrists and psychologists, nutritionists, social workers, and speech therapists in case of tracheostomy

3. Give priority to patients discharged with home oxygen therapy, patients with documented pneumonia and patients with multimorbidity

4. Define the frequency of checks and follow-up duration, according to patient conditions

5. Assess general conditions, nutritional and psychological status, and ability in daily life at all appointments

6. Look for respiratory, cardiovascular, neurological, psychological sequelae
7. Perform lung imaging studies and functional breathing tests and EKG at baseline and then according to results

8. Provide further evaluations according to findings of baseline evaluation

9. Monitor immune response through serial serological tests

10. Assess criteria for immune plasma donation and refer the patient to the blood centre if indicated

21.5 VACCINATIONS

Covid-19 and vaccination have multiple relationships:
   a. Vaccination is considered the best weapon to stop the pandemic
   b. During phase 1, routine vaccinations were delayed and need to be resumed in phase 2
   c. The influenza vaccination and other vaccinations suggested for fragile patients, can reduce the pressure on healthcare during the winter months
   d. Plan and secure future Covid-19 mass vaccination

So, we recommend:

1. Use the resumption of suspended vaccinations and the influenza vaccination campaign as a simulation of future Covid-19 mass vaccination

2. Identify large ventilated spaces, with multiple access points, to receive thousands of people

3. Prepare procedures for supply, distribution, and storage, according to the vaccine characteristics

4. Define the priority list of people to be vaccinated

5. Recruit and train new personnel to administer vaccines

6. Establish a partnership with voluntary associations to support the vaccination process

7. Provide home vaccination for non-transportable people

8. Identify critical steps in the vaccination process and provide recommendations
22. RECOMMENDATIONS FOR HEALTHCARE STUDENTS INTERNSHIPS

1. Wear clothes that can be washed at high temperatures to reduce the risk of home contamination as much as possible

2. Stagger entrances in the locker room and the training departments

3. Avoid gatherings in the locker rooms, allow simultaneous access to a select number of students to maintain a distance of 1-2 meters when changing clothes

4. While waiting to enter the hospital, locker room or ward, wear a mask and keep a physical distance

5. Sanitise your hands before entering the locker room

6. Create a clear unclean/clean separation inside your locker and use separate bags to store professional and non-professional footwear

7. If disposable uniforms are not available, change your uniform every day or at least every 3/5 days and use only the hospital laundry service for washing. Do not wash the uniform at home.

8. Assign students only to clean wards with low-risk Covid-19 patients and assign them the care of 2-3 negative patients

9. Provide students with the appropriate PPEs and train them to use them correctly

10. Do not enter the common areas with the PPEs used for patient care

11. Change PPEs (gown, mask) if torn, wet or dirty

12. Change your gloves between each patient, sanitising hands before and after

13. Sanitise eye protection if reusable, change it for single-use

14. Avoid group breaks and especially when removing the mask to have a snack or smoke. Preferably take individual breaks without leaving the ward

15. Avoid the use of permanent and semi-permanent jewellery and nail polish
16. Instruct students on the behaviours to follow in case of symptoms suggestive of Covid-19 or the procedure to follow in case of contact with a confirmed Covid-19 patient.

17. During the internship, avoid contagion occasions linked to non-essential events (e.g. participation in parties, concerts, etc.).
It is important to measure the impact of our actions. We include some measures that may be of use.

### Outcome measures

Outcome measures should be collected to support the monitoring of effective provider (hospital) epidemic/pandemic response including the capacity to adequately treat patients with other common severe conditions like heart attacks, strokes, trauma, COPD to assure that the health of the public is protected to the fullest extent possible.

1. The hospitalisation rate for COVID-19 (indirect outcome measure of the territory).
2. The in-hospital Mortality rate of patients hospitalised for COVID-19.
3. Average Length of Stay of COVID-19 patients.
4. Percentage of COVID-19 patients admitted to ICU.
5. The in-hospital mortality rate of NO-COVID-19 patients hospitalised for AMI.
7. The in-hospital mortality rate of NO-COVID-19 patients hospitalised for COPD.
8. Percentage of NO-COVID-19 hospitalised patients that acquired COVID during the hospitalisation.
9. The COVID-19 infection rate among staff
10. Survival rates

Where possible, indicators 1-7 should be stratified by age groups.

Additionally, the proposed outcome measures should be used and interpreted with great caution if used to benchmarking care quality between providers. In this case, consistent data definitions should be adopted, and measures from 1 to 7 should be adjusted for potential confounding factors (i.e. patient case-mix) to draw meaningful and correct comparisons among providers.

### Process Measures (some examples)

1. Length of Stay
2. The average length of stay in ICU of infected
3. The average length of stay in hospital
4. Percentage of infected admitted to ICU
5. Percentage of people with co-morbidities
6. Profiles
   a. Age
   b. Gender
c. Ethnicity
d. Co-morbidity

7. Percentage of staff with and without the correct equipment
8. Number of patients not treated with the appropriate level of care
9. Percentage of staff trained
10. Number of tests performed to hospital staff

Balancing measures

1. Staff infection rate
2. Staff mortality rate
3. Staff well being
4. Illness and sickness rates
5. Mental illness
### 24. APPENDIX

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<thead>
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<th>Serious adverse effects</th>
<th>Lopinavir / Ritonavir</th>
<th>Darunavir / cobicistat</th>
<th>Chloroquine</th>
<th>Hydroxychloroquine</th>
<th>Tocilizumab</th>
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<tbody>
<tr>
<td>Hypersensitivity reaction, angioedema</td>
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<tr>
<td>Stevens-Johnson syndrome / Toxic epidermal necrolysis / Erythema multiforme</td>
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<td>QT prolongation &amp; Torsade de Pointes</td>
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<td>AV block, PR prolongation</td>
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<td>Hyperglycemia, hypertriglyceridemia</td>
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<td>Renal failure</td>
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<td>Anemia, leukopenia, neutropenia</td>
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<td>Pancreatitis</td>
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<td>Hepatotoxicity</td>
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<td>Anorexia, hypercholesterolaemia, hypertriglyceridemia</td>
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<td>Renal failure</td>
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<td>Stevens-Johnson syndrome (rarely)</td>
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<td>QT prolongation &amp; Torsades de Pointes</td>
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<td>Reduction in seizure threshold</td>
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<td>Anaphylaxis or anaphylactoid reaction</td>
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<td>Neuromuscular impairment</td>
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<td>Neuropsychiatric disorders (potential to increase delirium)</td>
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<td>Pan cytopenia, neutropenia, thrombocytopenia, aplastic anemia</td>
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<td>Hepatitis</td>
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<td>Hypoglycemia</td>
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<td>QT prolongation</td>
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<td>Cardiomyopathy</td>
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<td>Muscle asthenia</td>
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<td>Retinal or visual field alterations</td>
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<td>Skin reactions</td>
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<td>Interstitial pneumonia</td>
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<td>Infections</td>
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<td>Leukopenia, neutropenia, hypofibrinogenaemia</td>
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<td>Upper respiratory infections</td>
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<td>Herpes simplex and zoster</td>
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<td>Oral ulcerations</td>
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<td>Complicated diverticulitis</td>
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<tr>
<td>Hepatotoxicity</td>
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</table>
# PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK

## Common adverse reactions:
- Nausea / vomiting, diarrhea
- Insomnia, anxiety
- Headache
- Rash
- Muscle Pain

## Contraindicated in:
- Cardiac disease (ischemic heart disease, cardiomyopathy, structural heart disease, QT prolongation)
- Liver failure (class C Child-Pugh)
- Haemophilia
- Porphyria
- G6PD deficiency
- Epilepsy
- Heart failure
- Recent myocardial infarction
- Porphyria
- Retinopathy
- Maculopathies
- Children <6a <31 Kg

## Monitoring:
- Transaminases
- Kidney function
- Serial complete blood count
- QT interval
- Blood count, glycemia, QT interval
- Cholesterol, blood count, transaminases

## Contraindications:
- Hypertension
- Headache
- Skin reactions
- Conjunctivitis
- Hypercholesterolemia
- Abdominal pain, gastritis
- Cough, dyspnea

## Adverse reactions:
- Nausea / vomiting, diarrhea
- Insomnia, anxiety
- Headache
- Rash
- Muscle Pain
- Nausea / vomiting, diarrhea, abdominal pain
- Visual disturbance, headache
- Extrapyramidal symptoms
- Nausea / vomiting, diarrhea, abdominal pain
- Visual disturbance, headache
- Extrapyramidal symptoms
- Rash
- Muscle Pain
- Nausea / vomiting, diarrhea, abdominal pain
- Visual disturbance, headache
- Extrapyramidal symptoms
- Visual disturbance, headache
- Extrapyramidal symptoms
- Skin rash, itching
- Extrapyramidal symptoms
- Hypertension
- Headache
- Skin reactions
- Conjunctivitis
- Hypercholesterolemia
- Abdominal pain, gastritis
- Cough, dyspnea

## Monitoring:
- Transaminases
- Kidney function
- Serial complete blood count
- QT interval
- Blood count, glycemia, QT interval
- Cholesterol, blood count, transaminases
### TABLE 1 - Chloroquine and hydroxy-chloroquine: main drug interactions

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>INTERACTIONS</th>
</tr>
</thead>
</table>
| Chloroquine | Antacids based on aluminum, calcium and magnesium and kaolin can reduce their absorption  
In association with:  
- Corticosteroids accentuation of any myopathies or cardiomyopathies  
- Phenybutazone can induce exfoliative dermatitis  
- Isoniazid, Amiodarone, Carbamazepine, Phenytoin, Phenothiazide, Ketoconazole and MAO inhibitors (Mono-Amino-Oxidase Inhibitors) risk of hepatotoxicity  
- Mefloquine and bupropion risk of convulsions  
- Metronidazole possible dystonic reactions  
- Penicillamine serious haematological or renal adverse events  
- Pyrimethamine / sulfadoxineskin reactions  
- Effects of chloroquine on other drugs:  
  - Ampicillin reduced absorption (administer at least 2 hours after chloroquine)  
  - Class IA and III antiarrhythmics, Tricyclic antidepressants, Antipsychotics increased risk of ventricular arrhythmia  
  - Antiepileptic antagonism on anticonvulsant effects  
  - Cyclosporine increase in plasma concentration  
  - Digoxin increase in plasma concentration and relative toxicity  
  - Methotrexate potentiation of the action  
  - Neostigmine and Pyridostigmine antagonism of the effects  
    - Vaccines antibody response reduction ONLY with rabies vaccine |
PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK

Hydroxychloroquine

In association with:
- Phenylbutazone can induce exfoliative dermatitis
- Isoniazid, Amiodarone, Carbamazepine, Phenytoin, Phenothiazide, Ketoconazole and MAO inhibitors (Mono-Amino-Oxidase Inhibitors) can cause hepatotoxicity

Effects of hydroxychloroquine on other drugs
- Antiepileptics antagonism on anticonvulsant effects
- Cyclosporine increased plasma concentrations
- Digoxin increased plasma concentration and relative toxicity
- Insulin and Antidiabetics potentiation of hypoglycemic effects

TABLE 2 - LOPINAVIR/RITONAVIR: Main interactions and recommendations

<table>
<thead>
<tr>
<th>Coadministered Drug</th>
<th>Mechanism of interaction</th>
<th>Clinical Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>RETROVIRAL AGENTS: Nucleoside reverse transcriptase inhibitors (NRTIs), Non-nucleoside reverse transcriptase inhibitors (NNRTIs), HIV CCR5 antagonist, Integrase inhibitor, Inhibitors of HIV protease</td>
<td></td>
<td>Specialist advice, dose adjustment is not required in most cases. Co-administration with other HIV protease inhibitors (PIs), according to current guidelines, is not recommended.</td>
</tr>
<tr>
<td>Antacids</td>
<td></td>
<td>No contraindications</td>
</tr>
<tr>
<td>Alpha antagonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALFUZOSIN</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated (hypotension)</td>
</tr>
<tr>
<td>Analgesic Drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FENTANYL</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Close monitoring (risk of respiratory)</td>
</tr>
<tr>
<td>Antianginal Drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RANOLAZINE</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>
### Antiarrhythmics

<table>
<thead>
<tr>
<th>Antiarrhythmics</th>
<th>Effect</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMIODARONE, DRONEDARONE</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated (arrhythmia)</td>
</tr>
<tr>
<td>DIGOXIN</td>
<td>Increased concentration (P-gp inhibition)</td>
<td>Plasma level monitoring</td>
</tr>
<tr>
<td>BEPRIDIL, SYSTEMIC LIDOCAINE, QUINIDINE</td>
<td>Increased concentration</td>
<td>Plasma level monitoring</td>
</tr>
</tbody>
</table>

### Antibiotics

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Effect</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLARITHROMYCIN</td>
<td>Moderate increase of under-curve area (CYP3A inhibition)</td>
<td>Dose reduction in kidney failure (CrCL&lt;30 ml/min); attention in patients with impaired liver and kidney function</td>
</tr>
</tbody>
</table>

### Antineoplastics

<table>
<thead>
<tr>
<th>Antineoplastics</th>
<th>Effect</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialist Advice</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Anticoagulants

<table>
<thead>
<tr>
<th>Anticoagulants</th>
<th>Effect</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>WARFARIN</td>
<td>CYP2C9 induction</td>
<td>INR monitoring</td>
</tr>
<tr>
<td>RIVAROXABAN</td>
<td>AUC: ↑ 153%, Cmax: ↑ 55% (CYP3A and P-gp inhibition)</td>
<td>Contraindicated (bleeding)</td>
</tr>
<tr>
<td>VORAPAXAR</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>

### Antiepileptic

<table>
<thead>
<tr>
<th>Antiepileptic</th>
<th>Effect</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHENYTOIN</td>
<td>Concentrazioni diminuite (induzione del CYP2C9 e del CYP2C19)</td>
<td>Plasma level monitoring</td>
</tr>
<tr>
<td>CARBAMAZEPINE, PHENOBARBITAL</td>
<td>Increased Carbamazepine concentration (CYP3A inhibition); reduced Lopinavir concentration (CYP3A induction)</td>
<td>Plasma level monitoring</td>
</tr>
</tbody>
</table>

### Antidepressants and anxiolytics
**PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Effect</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TRAZODONE</strong></td>
<td>AUC: ↑ 2.4 times</td>
<td>Dose reduction</td>
</tr>
<tr>
<td>Antifungals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KETOCONAZOLE</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Dose reduction</td>
</tr>
<tr>
<td>Antigout</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COLCHICINE</td>
<td>AUC: ↑ 3-times; Cmax: ↑ 1.8-times (CYP3A and/or P-gp inhibition)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Antihistamines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASTEMIZOLE, TERFENADINE</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated (severe arrhythmias)</td>
</tr>
<tr>
<td>Anti Infectives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusidic Acid</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated (rhabdomyolysis)</td>
</tr>
<tr>
<td>Antimycobacterial agents</td>
<td></td>
<td>Specialist Advice</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIDAZOLAM</td>
<td>Oral administration: AUC: ↑ 13-times parenteral administration: AUC: ↑ 4-times (CYP3A inhibition)</td>
<td>Oral administration contraindicated; close monitoring for parenteral administration</td>
</tr>
<tr>
<td>Beta2 agonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SALMETEROL</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated (severe cardiovascular event and arrhythmias)</td>
</tr>
<tr>
<td>Calcium Channel Blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FELODIPINE, NIFEDIPINE, NICARDIPINE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications</td>
<td>Interaction Description</td>
<td>Recommendation</td>
</tr>
<tr>
<td>----------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td>Steroids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEXAMETHASONE</td>
<td>Reduction of Lopinavir concentrations (CYP3A induction)</td>
<td>Clinical monitoring of anti-viral activity</td>
</tr>
<tr>
<td>Phosphodiesterase inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVANAFIL, SILDENAFIL</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Ergot Alkaloids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIHYDROERGOTAMINE AND OTHERS</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Intestinal Prokinetics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CISAPRIDE</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Direct anti-HCV agents</td>
<td>Increased plasma concentration (combined mechanisms)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>HCV protease inhibitors</td>
<td></td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Immunosuppressors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CICLOSPORINE</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Plasma level monitoring</td>
</tr>
<tr>
<td>Statins</td>
<td></td>
<td>Contraindicated; fluvastatin and pravastatin tolerated</td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>METHADONE</td>
<td>Decrease in concentration</td>
<td>Plasma level monitoring</td>
</tr>
<tr>
<td>Contraceptives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethinylestradiol</td>
<td>Decrease in concentration</td>
<td>Use additional contraceptive methods</td>
</tr>
</tbody>
</table>

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### Hormone Replacement Therapy (HRT)

| Levothyroxine | Potential interactions not well documented | TSH monitoring during the first month from the beginning and/or from the end of the treatment |

### TABLE 3 - DARUNAVIR/COBICISTAT: Main interactions and recommendations

<table>
<thead>
<tr>
<th>Co-administered drug</th>
<th>Interaction mechanism</th>
<th>Clinical recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-retroviral agents (HIV)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibitors of the strand transfer of integrase, inhibitors nucleoside / nucleotide HIV reverse transcriptase inhibitors (NRTIs)</td>
<td></td>
<td>Specialist advice, no dose adjustment necessary, except for Emtricitabine / tenofovir alafenamide</td>
</tr>
<tr>
<td>Non-nucleoside / nucleotide inhibitors of HIV reverse transcriptase (NNRTI)</td>
<td></td>
<td>Specialist advice, non-recommended co-administration RILPIVIRINE, the increase of which is not considered relevant, is an exception</td>
</tr>
<tr>
<td>CCR5 Antagonists</td>
<td></td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>MAVAVIROC</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Specialist advice for dose adjustment</td>
</tr>
<tr>
<td>Al / M or calcium carbonate based antacids</td>
<td></td>
<td>No dose adjustment</td>
</tr>
<tr>
<td>Alpha antagonists</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Patient Safety Recommendations for COVID-19 Pandemic Outbreak

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Effect on Metabolism</th>
<th>Contraindications/Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alfuzosin</strong></td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated (hypotension)</td>
</tr>
<tr>
<td><strong>Al Fentanyl</strong></td>
<td>Increased concentration (inhibition of CYP3A4)</td>
<td>Dose reduction and monitoring (respiratory depression risk)</td>
</tr>
<tr>
<td><strong>Antianginal / Tymic Antiaries</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Amiodarone, Dronedarone Chinidina, Bepridile, Ivrabradina, Ranolazina</strong></td>
<td>Increased concentration (inhibition of CYP3A and/or CYP2D6)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td><strong>Dysopyramide, Flecainide, Systemic Lidocaine, Mexiletine, Propaphenone</strong></td>
<td>Increased concentration (inhibition of CYP3A and/or CYP2D6)</td>
<td>Caution and monitoring</td>
</tr>
<tr>
<td><strong>Digoxin</strong></td>
<td>Increased concentration (P-glycoprotein inhibition)</td>
<td>Dose titration and accurate monitoring of drug concentration</td>
</tr>
<tr>
<td><strong>Antibiotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clarithromycin</strong></td>
<td>Increased AUC (CYP3A inhibition)</td>
<td>Caution and dose adjustment in patients with renal impairment (CrCL &lt;30 ml/min)</td>
</tr>
<tr>
<td><strong>Anticoagulants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Warfarin</strong></td>
<td>Theoretical mechanism of alteration of plasma concentrations</td>
<td>INR monitoring</td>
</tr>
<tr>
<td><strong>Apixaban, Edoxaban, Rivaroxaban</strong></td>
<td>Increased plasma concentrations</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Co-administered drug</td>
<td>Interaction mechanism</td>
<td>Clinical recommendations</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------</td>
<td>-------------------------</td>
</tr>
</tbody>
</table>
| antiemetics          |                       |                         | 64
<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Action</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOMPERIDONE</td>
<td>Not studied</td>
<td>contraindicated</td>
</tr>
<tr>
<td>Antifungals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CLOTRIMAZOLO, FLUCONAZOLO, ITRACONAZOLO, ISAUVUCONAZOLO, POSACONAZOLO</td>
<td>Increased concentration (inhibition of CYP3A and/or P-gp)</td>
<td>Caution, clinical monitoring and dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Voriconazole contraindicated</td>
</tr>
<tr>
<td>Antigout</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colchicine</td>
<td>Increased concentration (inhibition of P-gp and/or CYP3A4)</td>
<td>Dosage reduction, contraindicated in the presence of hepatic or renal impairment</td>
</tr>
<tr>
<td>H2 receptor antagonists</td>
<td></td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>Antimycobacterials</td>
<td></td>
<td>Specialized evaluation, tendentially contraindicated</td>
</tr>
<tr>
<td>Antipsychotics/Neuroleptics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PERFENAZINA, Risperidone, Tioridazina</td>
<td>Increased plasma concentrations (inhibition of CYP3A, CYP2D6 and/or P-gp)</td>
<td>Dose reduction and clinical monitoring</td>
</tr>
<tr>
<td>Lurasidone, Pimozide, Sertindolo, Quetiapina</td>
<td></td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Anticancer</td>
<td>Theoretical mechanism of concentration increase (CYP3A inhibition)</td>
<td>Specialist evaluation, extreme caution</td>
</tr>
<tr>
<td>Beta2 agonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Effect Description</td>
<td>Recommendation</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>---------------------------------------</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated (serious cardiovascular adverse events, arrhythmias)</td>
</tr>
<tr>
<td><strong>Beta blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carvedilol, Metoprolol, Timolol</td>
<td>Plasma concentrations increased (CYP3A inhibition)</td>
<td>Dose reduction and clinical monitoring</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipina, Diltiazem, Felodipina, Nifedipina, Nicardipina, Verapamil</td>
<td>Increased concentration (inhibition of CYP3A and / or CYP2D6)</td>
<td>Dose reduction and clinical monitoring</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Reduction of Darunavir and / or cobicistat concentrations (CYP3A induction)</td>
<td>Caution</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td></td>
<td>No dose adjustment</td>
</tr>
<tr>
<td>Inhibitors of phosphodiesterase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tadalafil, Sildenafil</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Antivirals direct action against HCV (inhibitors NS3-4A protease)</td>
<td>Increased plasma concentrations (combination of mechanisms)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Endothelial receptor antagonists (Bosentan)</td>
<td>Increased concentration (theoretical consideration)</td>
<td>Contraindicated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------------------------------------------------</td>
<td>-----------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>immunosuppressant</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYCLOSPORINE</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Monitoring of drug levels</td>
</tr>
<tr>
<td>everolimus</td>
<td></td>
<td>contraindicated</td>
</tr>
<tr>
<td><strong>Narcotics, Opioids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>METHADONE</td>
<td>Increased concentration (theoretical consideration)</td>
<td>Monitoring of drug levels</td>
</tr>
<tr>
<td>Buprenorphine / naloxone</td>
<td>Increased concentration (theoretical consideration)</td>
<td>Clinical monitoring</td>
</tr>
<tr>
<td>FENTANYL, OXYCODONE, TRAMADOL</td>
<td>Increased concentration (theoretical consideration)</td>
<td>Clinical monitoring</td>
</tr>
<tr>
<td>Opioid antagonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NALOXEGOL</td>
<td>Not studied</td>
<td>contraindicated</td>
</tr>
<tr>
<td><strong>Sedatives / hypnotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUSPIRONE, CLORAZEPAM, DIAZEPAM, ESTAZOLAM, FLURAZEPAM, ZOLPIDEM</td>
<td>Increased concentration (CYP3A inhibition)</td>
<td>Caution, dose reduction and clinical monitoring</td>
</tr>
<tr>
<td>MIDAZOLAM (PARENTERAL)</td>
<td></td>
<td>Only in intensive care.</td>
</tr>
<tr>
<td>MIDAZOLAM (ORAL)</td>
<td></td>
<td>contraindicated</td>
</tr>
</tbody>
</table>
### Urological drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Caution</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FESOTERODINA, SOLIFENACINA</strong></td>
<td>Not and clever or</td>
<td>Caution, dose reduction and clinical monitoring</td>
</tr>
<tr>
<td><strong>DAPOXETINE</strong></td>
<td>Not and clever or</td>
<td>contraindicated</td>
</tr>
</tbody>
</table>

### CONTRACEPTIVES

<table>
<thead>
<tr>
<th>Drug</th>
<th>Caution</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>drospirenone</strong></td>
<td>Alteration of plasma concentrations</td>
<td>Use additional methods of contraception</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitoring for possible hypokalaemia</td>
</tr>
<tr>
<td><strong>Statins and other hypo-lipidemic agents (Lomitapide)</strong></td>
<td></td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>

---

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## TABLE 4 – Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Lapinavir / Ritonavir</th>
<th>Darunavir / cobicistat</th>
<th>Chloroquine</th>
<th>Hydroxychloroquine</th>
<th>Tolicizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serious adverse effects</strong></td>
<td>• Hypersensitivity reaction, angioedema</td>
<td>• QT prolongation &amp; Torsade de Pointes</td>
<td>• QT prolongation</td>
<td>• Hypoglycemia</td>
<td>• Interstitial pneumonia</td>
</tr>
<tr>
<td></td>
<td>• Stevens-Johnson syndrome / Toxic epidermal necrolysis / Erythema multiforme</td>
<td>• Anorexia, hypercholesterolemia, hypertyrlglyc eridemia</td>
<td>• Torsades de Pointes</td>
<td>• QT prolongation</td>
<td>• Leukopenia</td>
</tr>
<tr>
<td></td>
<td>• QT prolongation</td>
<td>• Renal failure</td>
<td>• Reductio n in seizure threshold Anaphylaxis or anaphylactoid reaction</td>
<td>• Cardio myopathy</td>
<td>• Neutropenia</td>
</tr>
<tr>
<td></td>
<td>• AV block, PR prolongation</td>
<td>• Stevens-Johnson syndrome (rarely)</td>
<td>• Neuromuscular impairment</td>
<td>• Muscle asthenia</td>
<td>• Hypofibrinogenemia</td>
</tr>
<tr>
<td></td>
<td>• Hyperglycemia, hypertriglyceridemia</td>
<td>• QT prolongation</td>
<td>• Skin reactions</td>
<td>• Retinal or visual field alterations</td>
<td>• Upper respiratory infections</td>
</tr>
<tr>
<td></td>
<td>• Renal failure</td>
<td>• Neurapsychiatric disorders (potential to increase delirium)</td>
<td>• Hypoglycemia</td>
<td>• Fever</td>
<td>• Herpes simplex and zoster</td>
</tr>
<tr>
<td></td>
<td>• Anemia, leukopenia, neutropenia</td>
<td>• Pancreatit is</td>
<td>• Pancytopenia, neutropenia, thrombo cytopeni a, aplastic anemia</td>
<td>• Skin reactions</td>
<td>• Oral ulcerations</td>
</tr>
<tr>
<td></td>
<td>• Pancreatit is</td>
<td>• Hepatitis</td>
<td>• Hepatitis</td>
<td>• Complicat ed diverticulitis</td>
<td>• Hepatotoxicity</td>
</tr>
</tbody>
</table>
## Patient Safety Recommendations for COVID-19 Pandemic Outbreak

| Common adverse reactions: | • Nausea / vomiting, diarrhea
• Insomnia, anxiety
• Headache
• Rash
• Muscle Pain |
|--------------------------|---------------------------------------------------------------|
|                          | • Nausea / vomiting, diarrhea
• Insomnia, anxiety
• Headache
• Rash
• Muscle Pain |
|                          | • Nausea / vomiting, diarrhea
• Insomnia, abdominal pain
• Visual disturbance, headache
• Extrapyramidal symptoms |
|                          | • Nausea / vomiting, diarrhea
• Insomnia, abdominal pain
• Visual disturbance, headache
• Extrapyramidal symptoms |
|                          | • Hypertension
• Headache
• Skin reactions
• Conjunctivitis
• Hypercholesterolemia
• Abdominal pain, gastritis
• Cough, dyspnea |

| Contraindicated in: | • Cardiac disease (ischemic heart disease, cardiomyopathy, structural heart disease, QT prolongation)
• Liver disease |
|---------------------|---------------------------------------------------------------|
|                     | • Liver failure (class C Child-Pugh)
• Haemophilia |
|                     | • Porphyria
• G6PD deficiency
• Epilepsy
• Heart failure
• Recent myocardial infarction |
|                     | • Porphyria
• Retinopathy
• Maculopathies
• Children <6 <31 Kg |
|                     | • Administration of alive or attenuated vaccines |

| Monitoring: | • Transaminases
• Kidney function
• Serial complete blood count
• QT interval |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>• Blood count, glycemia, QT interval</td>
</tr>
<tr>
<td></td>
<td>• Cholesterol, blood count, transaminases</td>
</tr>
<tr>
<td>Acronym</td>
<td>Question</td>
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<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>S</td>
<td>Any Covid-19 symptom in the last 14 days?</td>
</tr>
<tr>
<td>C</td>
<td>Any close contact with confirmed/suspected Covid-19 subjects in the last 14 days?</td>
</tr>
<tr>
<td>I</td>
<td>Any prescription of home isolation or quarantine in the last 14 days?</td>
</tr>
<tr>
<td>S (Swab)</td>
<td>Have you had a swab for SARS-CoV2 in the last 14 days? What about the result?</td>
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</tr>
<tr>
<td>R (Return)</td>
<td>Have you come back from countries that require a control swab in the last 14 days? Have you had the swab? What about the result?</td>
</tr>
</tbody>
</table>
PLEASE NOTE:

1. **THE QUESTIONS**

   Should also be addressed to the home attendant/caregiver, who should not be admitted to the hospital, if triage is positive. In this case, the patient must also be considered a close contact if cohabiting and so managed accordingly. If the answer to the question Symptoms or Contacts is positive, refer the respondent to the attending physician for the necessary investigations.

2. **EMERGENCY ROOM**

   A "Yes" is sufficient to suspend the questions and proceed to the execution of the swab, whatever the reason for ER access is.

3. **DELIVERY OF BENEFITS**

   In the event of a Covid-19 telephone triage, unpostponable care can be scheduled as last visit/access, to reduce the risk of contaminations. In the case of a face-to-face interview, the patient is immediately isolated, and care is delivered as a priority.

4. **ENVIRONMENTAL DISINFECTION**

   At the end of any visit:
   
   a. unclean pathway: disinfect the environment and air the room;
   b. clean pathway: air the room, disinfect contact surfaces and the devices used

5. **HEALTHCARE WORKERS PERSONAL PROTECTIVE EQUIPMENT (PPE)**

   Unclean pathway: wear medium-risk or high-risk PPE if dealing with procedures that generate aerosols
   Clean pathway: wear low-risk PPE
Multimedia links

1. PHARMACOV - pharmacists against Covid-19

https://www.pharmacov.com
Control of drug interactions carried out by a group of Italian pharmacists, after registration. Free of charge.

2. VIRGILIO - VIRtual GuIde for Live Doffing

Virtual doffing assistant (Italian) - https://www.insafetyhealthcare.it/virgilio-virtual-guide-for-live-doffing/

Virtual doffing assistant (English) - https://soundcloud.com/user-384027357/sets/covid19-virtual-guides-for-doffing-ppe
25.REFERENCES


13. Rapporto Prima Linea COVID-19 assetto organizzativo gestionale dei PS/DEA nell’ambito di focolaio epidemico o pre-epidemico Available online at: https://www.simeu.it/w/articoli/leggiArticolo/334/dir


19. Ministero della Salute, All.3 Polmonite da nuovo Coronavirus in Cina Available online at: https://www.quotidianosanita.it/allegati/allegato8404255.pdf


29. Center for disease control and prevention. Interim Considerations for Infection Prevention and Control of Coronavirus Disease 2019 (COVID-19) in Inpatient Obstetric Healthcare
PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK


43. Management of the corpse with suspect, probable or confirmed COVID-19 respiratory infection – Italian interim recommendations for personnel potentially exposed to material from corpses, including body fluids, in morgue structures and during autopsy practice. Vittorio Fineschi on behalf of the Scientific Society of Hospital Legal Medicine of the National Health System (COMLAS) and Anna Sapino on behalf of the Italian Society of Anatomical Pathology and Cytology (SIAPEC), Pathologica, in press. Available online at: https://www.pathologica.it/article/view/101


47. Solon R. Providing Psychological First Aid Following a Disaster. Occup Health Saf. 2016 May;85(5):40, 42, 44. Available online at: https://ohsonline.com/Articles/2016/05/01/Providing-Psychological-First-Aid-Following-a-Disaster.aspx

48. WHO, War Trauma Foundation and World Vision International - Psychological first aid: Guide for field workers. Available online at:
https://apps.who.int/iris/bitstream/handle/10665/44615/9789241548205_eng.pdf?sequence=1&isAllowed=y


50. Raccomandazioni per situazioni di emergenza - Presidio Riabilitativo di Montalto di Fauglia - IRCCS Fondazione Stella Maris, sede amministrativa Calambrone (Pisa)


56. Cong-Ying Song et al., COVID-19 early warning score: a multi- parameter screening tool to identify highly suspected patients [pre- print] Available online at: https://www.medrxiv.org/content/10.1101/2020.03.05.20031906v1

PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK


PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK


74. Association for the Advancement of Medical Instrumentation. Liquid Barrier Performance and Classification of Protective Apparel and Drapes Intended for Use in Health Care Facilities; 2012 (ANSI/AAMI PB70:2012):6-7 (§4.2.1-4.2.3) Available online at: https://my.aami.org/aamiresources/previewfiles/pb70_1206_preview.pdf


77. Progetto per la riorganizzazione dell’attività di assistenza infermieristica, ostetrica e di supporto nelle Unità Organizzative del Policlinico S. Orsola-Malpighi. Available online at: https://www.aosp.bo.it/reparti_servizi/servinfer/materiali/Pgt_riorg_assistenza_supporto_8_04_Documento.pdf
78. Anarti, Come affrontare il Covid-19 in terapia intensiva. 9 marzo 2020 Available online at: https://www.fnopi.it/2020/03/09/aniarti-raccomandazioni-area-critica-efccna-covid-19/


PATIENT SAFETY RECOMMENDATIONS FOR COVID-19 PANDEMIC OUTBREAK

doi: 10.1136/bmj.m2980. Update in: BMJ. 2020 Sep 11;370:m3536. PMID: 32732190; PMCID: PMC7390912. Available online at: https://www.bmj.com/content/370/bmj.m2980

86. CDC. Resources for health professionals: parasites - Strongyloides [website]. Washington (DC): Centers for Disease Control and Prevention; 2020 Available online at: https://www.cdc.gov/parasites/strongyloides/health_professionals/index.html


88. Vivanti A, et al. Transplacental transmission of Sars_CoV-2 infection. 2020 Nat Commun 11, 3572 Available online at: https://doi.org/10.1038/s41467-020-17436-6


92. Chuan-bin Sun, Y.-y.W., Geng-hao Liu, Zhe Liu, Role of the eye in transmitting human coronavirus: what we know and what we do not know. Front Public Health. 2020; 8: 155. Available online at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7193031/


94. Vered Hazanchuk, How to wear a face mask without fogging your glasses. Available online at: https://www.aao.org/eye-health/tips-prevention/face-mask-foggy-glasses-coronavirus-covid


