

# CLINICAL MANAGEMENT FOR PATIENTS WITH PSYCHIATRIC DISORDERS AND A SARS-COV-2 INFECTION

## GUIDANCE FOR PAN-EUROPEAN RECOMMENDATIONS

COMPILED FOR THE DEPARTMENT OF PSYCHIATRY AND PSYCHOTHERAPY, UNIVERSITY HOSPITAL, LMU MUNICH:

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- Med IV, Department for Infectious Diseases (Prof. Dr. Bogner, Dr. G. Ibarra) [<http://www.klinikum.uni-muenchen.de/Medizinische-Klinik-und-Poliklinik-IV/de/Behandlungsschwerpunkte/Infektiologie/Team/aerztliches-personal/index.html>]

With consideration/citation of the following documents:

- *Covid-19 SOP*, Med III (Elham Khatamzas, Clemens Gießen-Jung)
- *COVID-19: Diagnostik und Therapie* der Stabsstelle Antibiotic Stewardship (Prof. Dr. R. Draenert)
- Documents of the Robert-Koch-Institut (RKI), STAKOB Geschäftsstelle am Robert Koch-Institut: *Hinweise zu Erkennung, Diagnostik und Therapie von Patienten mit COVID-19* [[https://www.rki.de/DE/Content/Kommissionen/Stakob/Stellungnahmen/Stellungnahme-Covid-19\\_Therapie\\_Diagnose.pdf?\\_\\_blob=publicationFile](https://www.rki.de/DE/Content/Kommissionen/Stakob/Stellungnahmen/Stellungnahme-Covid-19_Therapie_Diagnose.pdf?__blob=publicationFile)]
- Pandemic action plan of the University Hospital for Psychiatry and Psychotherapy, LMU Klinikum

## I. GENERAL INFORMATION

On 25 March 2020, the Department of Psychiatry and Psychotherapy converted one of its regular wards (C4, specialist ward for addiction disorders) into the "Psychiatric COVID-Ward". This ward officially serves for the entire University Hospital to offer care for patients primarily with psychiatric disorders suffering from comorbid covid-19.

Consequently, the Psychiatric Hospital is actively involved in the care and treatment of patients suffering from a SARS-CoV-2 induced disease.

The ward is now organized as a separate unit where patients with mental disorders and positive SARS-CoV-2 diagnosis, Covid-19- tentative diagnosis or Covid-19 diagnosis are treated.

Patients considered for treatment at the Psychiatric Hospital with a positive SARS-CoV-2 diagnosis are in particular:

- Patients **mentally instable / internistic stabile**
- Patient **mentally instable / internistic instable**
  - In mild and moderate cases, with option of transfer severe cases to an Internal Ward or an ICU Ward (medical department).
  - patients transferred to the Psychiatric Hospital in case of secondary psychiatric conditions e.g. organic psychiatric disorder due to severe infectious disease, adjustment disorders and others.

## II. CLINICAL DIAGNOSTICS

### 1. Patient Admission (suspected or confirmed SARS-CoV-2-infection)

#### Isolation

- Upon suspicion of SARS-CoV-2-infection, protection measures are immediately and stringently required and patients should be isolated.
- A Cohort of patients is not permitted.
- In case of confirmed COVID-19 infection, a cohort can be considered if RSV and Influenza A/B are ruled out.

- **CAVE:** Other hygiene related conditions are to be considered: MRSA/VRE/4-MRGN/3-MRGN. Depending on the clinical setting isolation should follow this hierarchy pattern: SARS-CoV-2 > 4-MRGN > 3-MRGN > VRE > MRSA

#### Transmission routes (CAVE! Protection measure, s.b.)

- Droplet infection
- Aerosols: no evidence, applicable under certain conditions (s.b.)
- Smear infection via contaminated surfaces not ruled out
- Feces: possible, data presently not sufficient
- Conjunctiva (eyes) as entry point
- Vertical transmission – single cases – point in time unclear
- Medical high-risk setting: Aerosol inducing processes, e.g. bronchoscopy

### Protection measures („Safety First“)

Medical staff is to reduce patient contact to an essential minimum; patient contact reserved for trained staff only:

- Stringent implementation of basic hygiene measures including hand hygiene measures
- Closing of patient room doors
- Separate patient waste disposal (infectious)
- Availability of required personal protection equipment: Protective gown (non-reusable, waterproof), disposable gloves, respiratory mask (FFP2), safety glasses resp. visor
- Staff must be trained: Video training via hospital portal
- Sick calls not permitted
- Patients and staff must wear safety masks
- Respiratory masks (FFP2) in case of direct contact to patients with SARS-CoV-2 or suspected SARS-CoV-2

## **2. Case history and initial medical examination**

- Case history, considering possible expositions
- Comorbidities (risk factors!)
- Health care proxy and patient's provision
- Contact data of authorised persons, relatives
- Somatic examination, especially vital parameters (heart rate/bpm, RR, SpO<sub>2</sub>, respiratory rate)

### **CAVE:** Risk factors for severe course of disease:

- Aged persons (≥ 50 years, > 80 years: mortality >15%), smokers.
- Pre-existing illnesses: Cardiovascular system (e.g. coronary heart disease and primary HTN); pulmonary disorders (e.g. asthma, chronic bronchitis); chronic hepatitis; diabetes mellitus; cancer; immune suppression

## **3. Clinical symptoms**

### Initial symptomatic

- **Fever (88%)**
- **Unproductive/dry cough (68%)**
- Indisposition/exhaustion (38%)
- Dyspnoea (19%)
- Gastrointestinal symptoms (nausea, vomiting, diarrhoea) (5%)
- Changes of taste or smell

[Documents of the Robert-Koch-Institut (RKI)]

Further symptoms: headache and limb pain, anorexia, weight loss, swelling of lymph nodes, apathy, fatigue, somnolence, confusion

### Stages of disease

1. Replicative phase: Viral replication in throat area. Duration: several days. Relatively mild symptoms due to direct viral cytopathic effect and innate immune response.
2. Adaptive immune response: Frequently reduced virus load. Less frequently aberrant immune response with tissue damage and rapid clinical worsening.

### Course of disease

- Incubation period: 5–6 days (range 1 to 14 days)
- 80% mild to moderate: patients with or without pneumonia, without dyspnoea, with SpO<sub>2</sub> ≥ 90 % pulmonary infiltrates in less than half of the lung
- 14% severe with dyspnoea, BF: > 30/min, SpO<sub>2</sub> <90 %, or pulmonary infiltration in more than half of the lung, yet not life-threatening
- 6% critical to life-threatening with respiratory failure, septic shock or multiple organ failure

[Huang et al. Lancet 2020. 6736:30183-30185]

## **4. Laboratory examinations**

Lab samples upon admission: Diff. BC, CRP, procalcitonin (PCT), IL6, kidney and liver values, Troponin T, pro-BNP, immunoglobulin, lymphocyte subpopulation, LDH, ferritin, coagulation, D-Dimer, lactate, beta-HCG in female patients at childbearing age

Daily Lab samples: according to clinical symptomatic, important for course of disease: PCT, IL6, D-Dimer, ferritin, Diff-BB, liver values, troponin T

### Typical changes

- Leukopenia, lymphopenia: frequently, thrombocytopenia (mild) in up to 35%, **eosinopenia** in up to 52%
- CRP-increase (61-86%) (>10; mostly between 10-20)
- LDH-increase (27-75%)
- PCT-increase (24%, esp. ICU-Patients)
- AST/ALT-increase (4-22%)
- Troponin-increases

[Wu et al. JAMA. 2020: doi:10.1001/jama.2020.2648]

**CAVE:** Cardiomyopathy with troponin-increase: Predictor for increased mortality, especially if troponin increases continuously from day 4. Troponin control is strongly recommended! Troponin-increases seem to be connected to a COVID-19-associated cardiomyopathy rather than a myocardial infarction.

## **5. Medical Imaging**

In conventional chest X-ray, changes are visible in 50-60 % of patients. In CT examinations, however, changes are visible in approx. 85% of cases as ground glass opacity (GGO), bilateral, less frequently unilateral infiltration (14-25%), or increase of interstitial markings [Documents of the Robert-Koch-Institut (RKI)].

**CT-Thorax** (non-contrast): at admission and for further assessment of course of disease in case of clinical worsening. Long-range indication advisable! Higher sensitivity compared to chest X-ray: abnormal in >60%, CT abnormal in >85% Typical changes: GGO; bilateral, less frequently unilateral infiltration (14-25%), possibly increase of interstitial markings

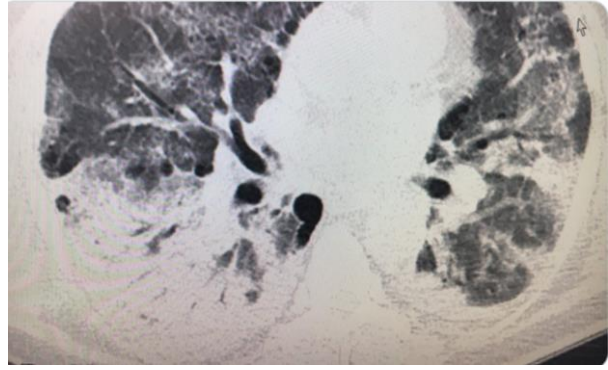
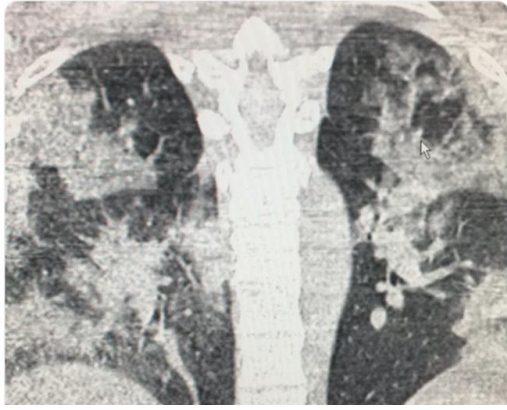


Fig.: CT-Lung: 85 % of cases: GGO, bilateral infiltrations, increase of interstitial markings

## 6. Virological examinations

PCR: the most sensitive of the non-invasive methods

- PCR from **deep nasal/throat swab**: Sensitive in first week (replicative phase in throat area). In case of negative test result but maintaining clinical suspicion, a second test is advisable.
- 2. Sample: lower respiratory passages, e.g. tracheobronchial secretion (extraction, no BAL) or **sputum**: In case of detection of pulmonic infiltrated sputum >> nasal/throat swab (progressive disease). In case of typical clinical picture (and CT) and negative PCR, isolation should be maintained and test repeated.
- Influenza A/B and RSV (quick test)
- In case of clinical suspicion: Sputum bacteriology + mycoplasma + Sputum for extensive PCR
- Legionella urinary antigen test
- Organ- or bone marrow transplanted/immune suppressed patients (TNF-Inhibition): EBV/CMV-PCR, Adeno-PCR
- Aspergillus antigen and Beta-Glucan in case of clinical suspicion
- Blood cultures in case of fever and before empirical antibiotics

## 7. Diagnosis

- Specific: viral pneumonia or
- Unspecific: acute respiratory symptom of any severity
- Lab diagnosis: direct pathogen detection: sample isolation (culture) or nucleic acid detection (e.g. PCR)
- Epidemiological confirmation: epidemiological link with proved infection
- Occurrence of two or more pneumonias in one medical institution with probable or suspected epidemiological link, even without direct pathogen detection

### ➤ Diagnostic criteria:

Diagnosis Covid-19: - positive PCR for SARS-CoV-2 (independent on material)

Suspected. Covid-19: - typical clinical symptoms  
 - typical CT-changes  
 - Eosinopenia

## 9. Coding of diagnoses (ICD-10)

- Psychiatric diagnosis/diagnoses first (ICD 10, Chapter F)
- Covid-19: emergency code U07.1!
- Pneumonia: J12.8 (other viral pneumonia) plus U07.1!
- SARS: U04.9 plus U07.1!
- In case of cough, fever without confirmed pneumonia: B43.2 plus U07.1!
- Coding of all other diagnoses

## III. Treatment strategies in Psychiatry

The treatment follows the severity of the illness and consists mainly of supportive measures. In cases of aggravation, severe or critical courses an internistic respectively intensive care monitoring (transfer!) is to be ensued. The treatment of the psychiatric disorder should be maintained as good as or resumed as soon as possible

### Criteria for inpatient treatment/inpatient admission indication (Covid-Ward C4):

- Medical assessment (psychiatric diagnosis)
  - Temperature > 38°C
  - BF > 20/min, reduced SpO<sub>2</sub> at room temperature
  - RR < 90mmHg
  - Disorientation
  - Comorbidities
- **CAVE:** Treatment at the Psychiatric Hospital is followed in close consultation with the internal medical unit (internistic supervision)

### 1. General treatment measures

- Top priority: Hygiene measures and instant isolation!
- **Symptomatic** treatment:
  - *Moderate volume loading for circulatory stabilisation; restrictive* volume management – seek negative fluid balance: consider worsening of oxygenation
  - *Antipyretic medication:* (paracetamol, ibuprofen (WHO has lifted its warning of ibuprofen application in COVID-19 patients))
  - *Respiratory therapy:* respiratory exercise, expectorating, NaCl-Inhalation

### 2. Supportive Therapy

- DVT prophylaxis (Clexane 40mg, if no confidence interval and no oral anticoagulation)
- Intermit PPI if not urgently indicated (Ulcer? GIB? GERD?)
- Continue antihypertensives (ACE-Inhibitors, neither intermission nor new administration initiation of AT1-blockers - s.b.)
- Breathing exercises, physical mobilisation by nursing staff if possible, Thera-Band®, physiotherapy
- Nutrition, especially in patients with disease related anorexia

### 3. Administration of oxygen

O<sub>2</sub>-administration: preferably cautious (infectiousness could possibly increase by aerosol formation in O<sub>2</sub>-administration); only in distinct dyspnoea, after clinical symptomatic

- Aim: SpO<sub>2</sub> 90-95% at BF <20/min
- O<sub>2</sub>-administration if SpO<sub>2</sub> <92% (no later than 90%)
- Nasal, mask, High-flow as needed (CAVE: increased aerosol formation)

- **CAVE:** silent hypoxemia: persisting BF > 20/min; O<sub>2</sub> demand ≥ 4 l/min, seek transfer to ICU; patients with sudden deterioration or persistent BF >30/min a timely fasting is advisable

#### Special issues:

##### – Antibiotics

Only in suspected bacterial superinfection – Signs: clinical worsening, sudden CRP increase, leukocytosis

##### Procedure:

- Take several blood samples (aerobic + anaerobic)
- Consider sputum culture
- Check lab parameters (CRP, PCT, BB)

##### Calculated antibiotic therapy:

- As per guideline: community acquired pneumonia
- Amoxi/Clav 3 x 875/125 mg p.o. or Amp/Sulb 3 x 3 gr i.v. ± Azithro 1 x 500 mg i.v.
- Consider combination of azithromycin or moxifloxacin (CAVE interactions and QTc interval). Azithromycin and other macrolide antibiotics (additional immune modulatory effects) can be preferably administered in COVID-19 patients with pulmonary involvement)

- **CAVE:** prophylactic administration of antibiotics without reference to bacterial infection is not recommended
- In Patients with suspected bacterial superinfection and/or septic course, a calculated antibiotic therapy should be initiated, in case of sepsis within half an hour. In case without detection of pathogens and standard procalcitonine the antibiotic therapy should be terminated within 48 hours. [Documents of the Robert-Koch-Institut (RKI)]

##### – Corticosteroids

- No corticosteroid administration without distinct indication

##### – Antiviral therapy

- Currently there is no confirmed effective antiviral therapy available
- Uncomplicated phase: (inpatient or outpatient): no antiviral therapy
- Preferred treatment in clinical studies and under careful consideration of risk-benefit balance as well as in ICU settings

##### – ACE-Inhibitors

- Continue ACE-Inhibitors and angiotensin receptor blockers but refrain from new administration initiation

#### – Characteristics of Psychopharmaca

- *Lithium*: In case of high fever: sufficient intake of fluids, distributed throughout the day. In case of additional vomiting/diarrhoea: dose adjustment, as needed intermission of lithium treatment for 24 hours
- *Clozapine*: (agranulocytosis): initial continuation of clozapine (treatment success of psychotic disorder not to be hazarded by discontinuation or dose reduction, check blood count regularly
  - *In case of bacterial superinfection: calculated antibiotic treatment (s.a.), close consultation with the internal medical unit*
  - **CAVE**: Patients are strictly quarantined and are often incommunicado. This situation involves an additional and considerable psychosocial burden especially for patients with mental disorders, which can lead to further worsening of symptoms as well as decompensation. Therefore, continuous psychotherapeutic and psychosocial therapy options should be maintained. This can be accomplished by medical, psychological and psychosocial staff as well as by tele-medical methods, such as video or telephone consulting.

#### IV. Course of disease

##### Early warning indicators for severe course of disease

In the treatment of patients with Covid-19 at the Psychiatric Hospital, severe and critical cases must be detected at an early stage.

- Detection and treatment of probable complications at the earliest possible stage
- Prevention of secondary infections
- Early administration of oxygen
- Timely contacting of Internal Ward

##### Predictors for a severe course of disease

- Progressive reduction of lymphocyte count in peripheral blood
- Steady increase of pro-inflammatory cytokine, e.g. IL-6 and CRP
- Steady increase of lactate values
- Steady increase of pathological changes in the lungs within a very short period of time
- Worsening of hypoxaemia under standard oxygen therapy
- **Sepsis**: T: > 38 ° or < 36 °C; HF > 90/min, BF > 20/min or PaCO<sub>2</sub> < 32 mm Hg, leucocytes > 12 000 or < 4000/mm<sup>3</sup> or > 10% immature forms

##### Criteria for transfer to an Internal Ward

- Transfer of patients with the following monitoring indications: cardiovascular monitoring, invasive RR-monitoring and/or high-flow O<sub>2</sub> therapy
- Severe clinical course, O<sub>2</sub>-saturation < 90 %, tachypnoea, BF>24, paO<sub>2</sub><70mmHg, newly emerging arrhythmias, newly emerging pericardial effusion, newly emerging heart insufficiency, pulmonary oedema, congested liver or peripheral oedema

##### Criteria for transfer to an ICU Ward

- Rapid respiratory worsening resp. indication for invasive respiration, catecholamine necessity, severe sedation



## V. FURTHER PROCEDURE

### 1. Discharge from hospital / outpatient aftercare

#### Criteria for clinical stability criteria

- Afebrile  $\geq$  3d
- Symptom onset  $\geq$  7d
- Clinical improvement of respiratory symptoms
- Continuous improvement of COVID-19 Lab parameters
- 2 negative respiratory SARS-CoV-2 PCRs at an interval of at least 24 hours

#### Or:

- Self-isolation guaranteed according to RKI directives
- Patient informed about procedures in case of worsening; patient able to follow these instructions
- Periodic aftercare treatment via telephone conducted by COVID-19 team

### 2. Discharge into isolation hotel

Patients clinically dischargeable **AND** who cannot be quarantined at home, in agreement with public health department and respective counselling. These patients can be transferred to a hotel

## CECKLIST COVID-19

Date [onset of symptoms]: \_\_\_\_\_

M	F	_____ years
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Gender/Age:

A: Signs and Symptoms [tick box]:

Date							
general (flu-like)*							
fever							
dry cough							
shortness of breath							
gastrointestinal							
Loss of smell/taste							

\* (head-) aches, loss of appetite, weight loss, fatigue, somnolence, confusion

B: Virology: SARS-CoV-2 PCR [positive/negative]:

Date				
SARS-CoV-2				
Influenza				
RSV				

C: Laboratory testing [tick box]:

Date							
Leukopenia							
Eosinopenia							
LDH > 300 U/l							

CRP > 5 mg/dl							
IL-6 > 50 pg/ml							
D-dimer >1µg/ml							
Troponin elevated							
AST/ALT elevated							
Urea > 19mg/dl (7mmol/l)							
Procalcitonin elevated							

**D: Respiratory distress: respiratory rate, SpO<sub>2</sub>, Lactate:**

<b>Date</b>							
Respiratory Rate							
SpO <sub>2</sub> w/o oxygen supply							
SpO <sub>2</sub> with	__ l O <sub>2</sub> /min						
Lactate (mmol/l)							

**E: Imaging: Chest CT:**

<b>Date</b>		
consolidative abnormalities		
ground-glass opacification		
infiltrates		

**F: CRB-65 Score:**

<b>Date</b>							
<b>Score*</b>							

\* each item scores one point:

- confusion
- urea >19mg/dL (>7mmol/L)
- respiratory rate  $\geq$ 30/min
- blood pressure  $\leq$ 60mmHg (diastolic) or  $\leq$ 90mmHg (systolic)
- age  $\geq$ 65

**G: Monitoring severity [tick box]:**

<b>Date</b>							
high LDH							
high CRP							
respiratory rate >30/min							
SpO2 <93%							
extended infiltrates							

## REFERENCES

This manual was conducted with consideration of the following documents and in cooperation with the following persons:

ABS-Team (Dr. A. Weber, Dr. J. Jung, Prof. Dr. R. Draenert)  
Zentrale Notaufnahme (Prof. Dr. med. M. Klein)  
Medizinische Klinik II (Dr. med. Stecher, Dr. med. B. Aulinger)  
Medizinische Klinik III (Prof. Dr. med. M. von Bergwelt, Prof. Dr. med. H.-J. Stemmler, PD Dr. C. Gießen-jung, Dr. med. E. Khatamzas, Dr. med. T. Herold)  
Medizinische Klinik IV (Prof. Dr. J. Bogner, Prof. H. Schulze-Koops)  
Medizinische Klinik V (Prof. Dr. med. J. Behr, PD Dr. N. Kneidinger, Dr. K. Kahnert)  
Klinik für Anästhesiologie (Prof. Dr.med. J. Briegel, PD Dr. M. Irlbeck, Dr. med. M. Zoller, Dr. med. I. Schröder)  
Max von Pettenkofer Institut (Prof. Dr. med. O. Keppler)

- Covid-19 SOP, Med III (Elham Khatamzas, Clemens Gießen-Jung)
- manual COVID-19: Diagnostik und Therapie der Stabsstelle Antibiotic Stewardship (Prof. Dr. R. Draenert)
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