# COVID-19-Update und Nachsorge


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### Krankenhaus Nord – Klinik Floridsdorf

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# Interessenskonflikte

## Vortrags- und/oder Konsulentenhonorare in den letzten 3 Jahren:

- Astra Zeneca
- Boehringer Ingelheim
- Chiesi
- Menarini
- Novartis
- Roche

# Agenda

## Update:

Risikofaktoren
Diagnose
Therapie

## Nachsorge:

Pulmonale und extrapulmonale Manifestationen

# Agenda

**Update:**

**Risikofaktoren**
**Diagnose**
**Therapie**

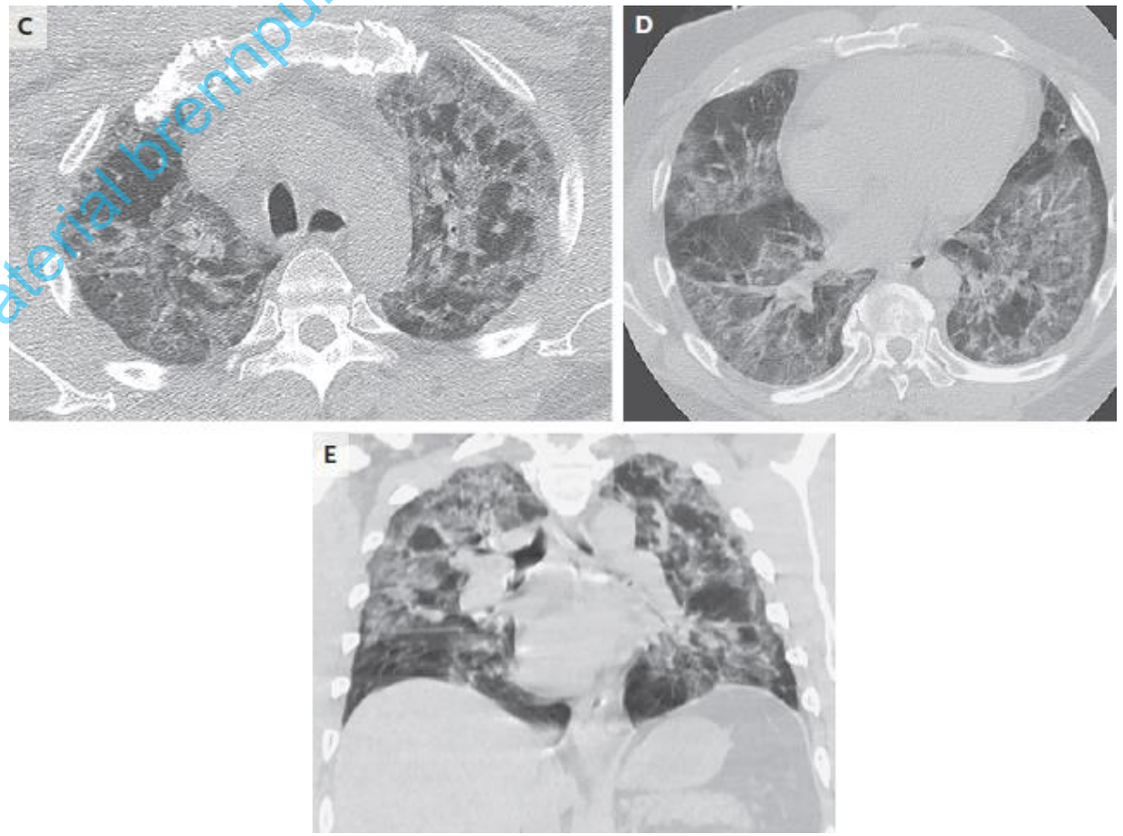
**Nachsorge:**

**Pulmonale und extrapulmonale Manifestationen**

# Risikofaktoren einer schweren oder tödlichen Covid-19 Infektion

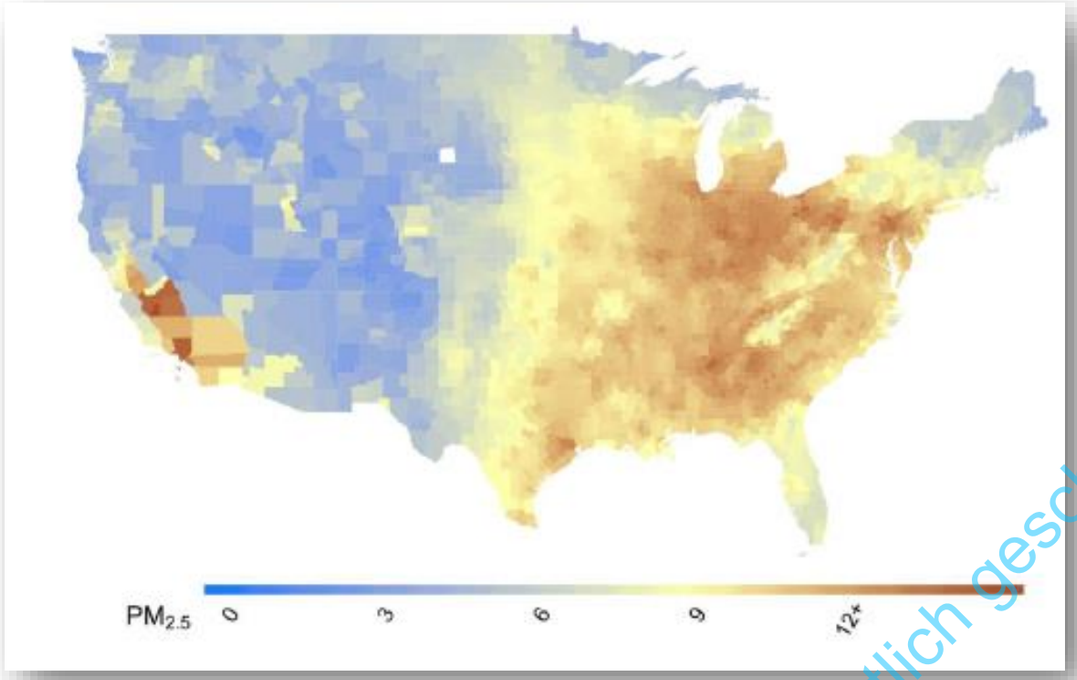
- Alter > 60a
- Komorbiditäten
  - KHK
  - COPD
  - Hypertonie
  - Diabetes
- Klinik der respiratorischen Erschöpfung
- CRP > 30 mg/L
- D-Dimer, Troponin, IL-6

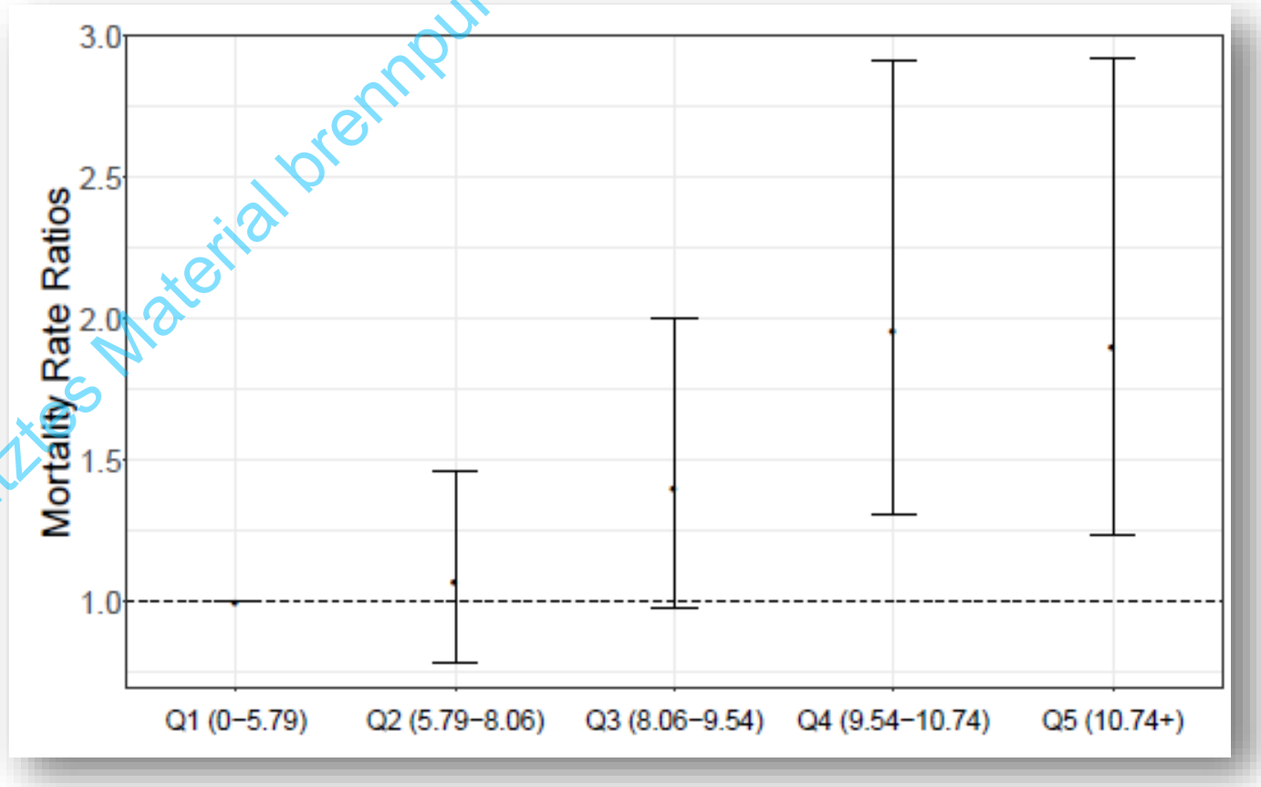
Deng SQ, JCM 2020; Zhou F, Lancet Respir Med 2020
Yang X, Lancet Respir Med 2020




Bhatraju PK, NEJM 2020

# Long term air pollution and Covid-19 mortality in the USA



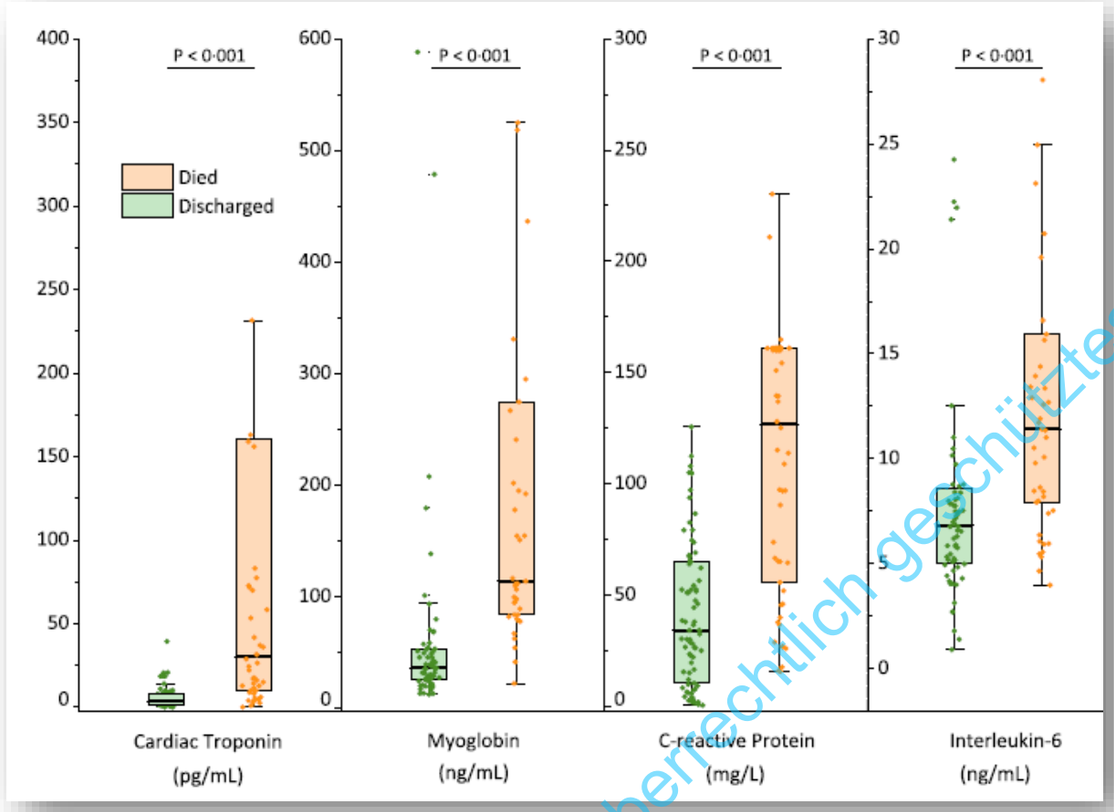



WU X, 2020

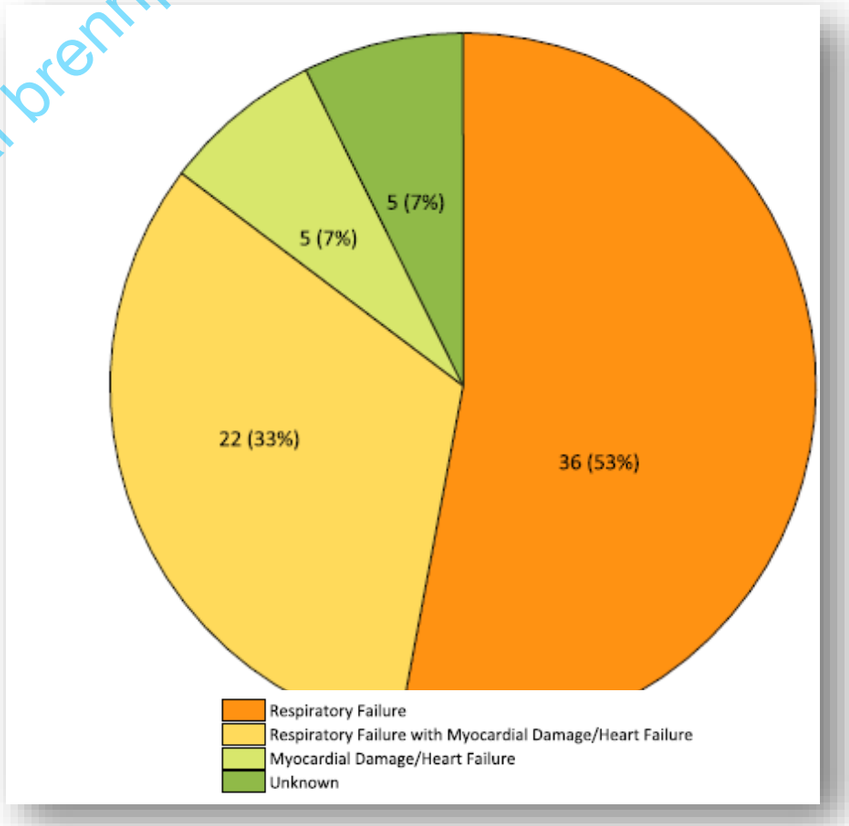
# Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China

Qiurong Ruan[1,2], Kun Yang[3], Wenxia Wang[4], Lingyu Jiang[5] and Jianxin Song[4*]

## Laboratory markers in survivors and non-survivors




## Cause of death in the ICU




Ruan Q, Intensive Care Med 2020

# Post-mortem Untersuchung von COVID-19 Patienten

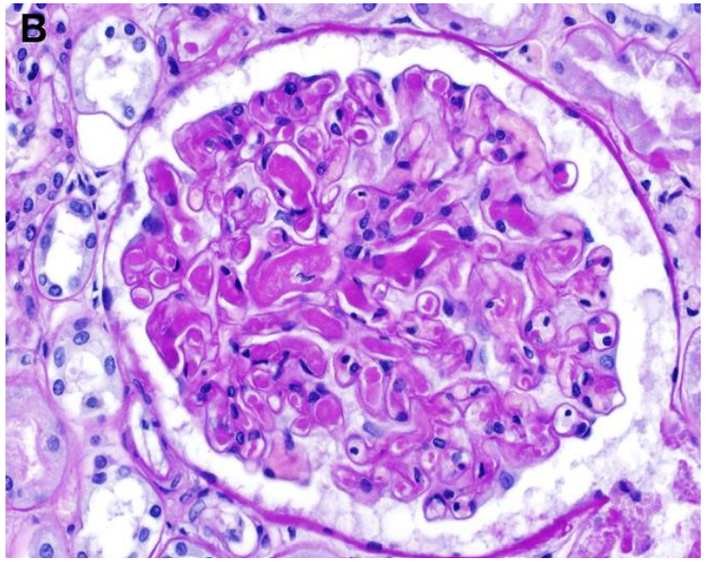
**Table 2: summary of autopsy findings**

| Organ | Diagnosis | n | % |
|---|---|---|---|
| Lung | Pulmonary capillary congestion | 21/21 | 100 |
| | Diffuse alveolar damage (DAD), exudative | 16/21 | 76 |
| | DAD, proliferative | 8/21 | 38 |
| | Reactive pneumocytes and syncytial cells | 11/21 | 52 |
| | Microthrombi of alveolar capillaries | 5/11 | 45 |
| | Bronchopneumonia, diffuse | 6/21 | 29 |
| | Bronchopneumonia, focal | 4/21 | 19 |
| | Severe mucous tracheitis | 6/21 | 29 |
| | Emphysema | 6/21 | 29 |
| | Pulmonary embolism | 4/21 | 19 |


Menter T, Histopathology 2020

# Post-mortem Untersuchung von COVID-19 Patienten

| | | | |
|---|---|---|---|
| Heart | Myocardial hypertrophy | 15/21 | 71 |
| | Senile amyloidosis | 6/21 | 29 |
| | Peracute myocardial cell necrosis | 3/21 | 14 |
| | Acute myocardial infarction | 1/21 | 5 |
| | | | |
| Kidney | Acute tubular damage | 14/15 | 93 |
| | Disseminated intravascular coagulation | 3/17 | 18 |
| | Hypertensive nephropathy | 2/17 | 12 |
| | Diabetic nephropathy | 2/17 | 12 |
| | | | |
| Liver | Steatosis | 7/17 | 33 |
| | Shock necrosis | 5/17 | |
| | ASH/NASH | 3/17 | 24 |



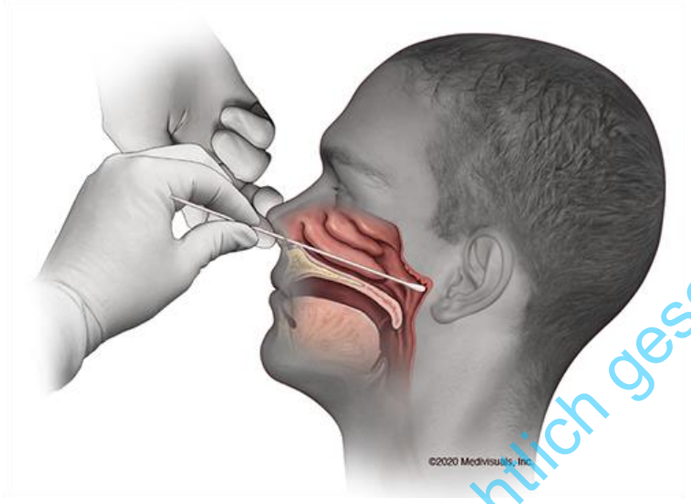

B: Kidney displaying disseminated intravascular coagulation

Menter T, Histopathology 2020

# RT-PCR ist Gold-Standard in der Diagnostik

## Early phase

**Nasopharyngeal swab**




https://health.ucdavis.edu/coronavirus/coronavirus-testing.html

## Late phase

**Induced sputum, tracheal aspirate, lavage**

https://pt.halyardhealth.com/solutions/respiratory-health/halyard-mini-bal-sampling-catheter

# Sars-CoV-2: Reinfektion oder Neuinfektion?

**172 Covid-19 Patienten mit 2 x negativen Testergebnis zum Entlassungszeitpunkt aus dem Krankenhaus**

↓

**25 Pat. (14%) mit positiver RT-PCR in der Nachsorge**

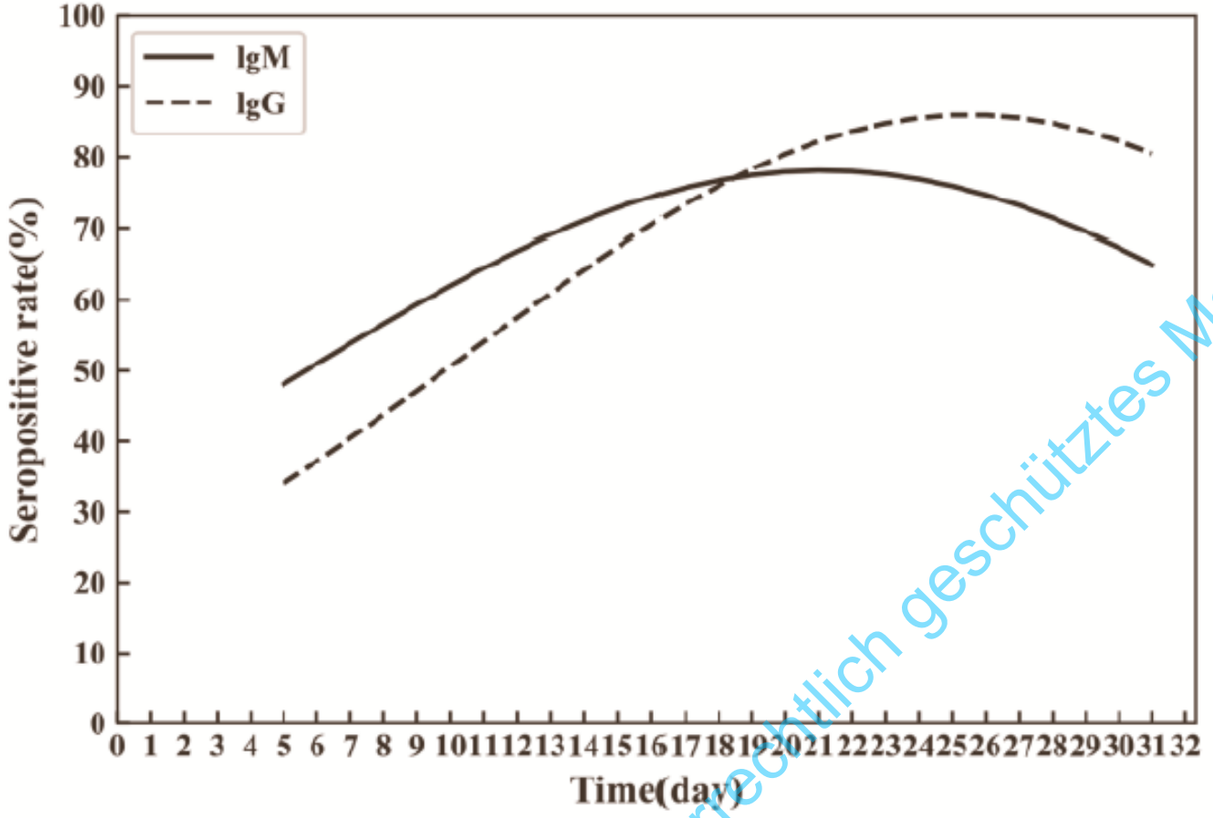
↓

**Kein Unterschied in den Charakteristika zwischen Patientengruppen bei Aufnahme oder Entlassung**


https://patientengagementhit.com/features/patient-engagement-strategies-for-post-discharge-follow-up-care

Yuan J, CID 2020

# Antikörper-Testung bei Covid-19




**85 RT-PCR positive COVID Patienten**

↓

**77% Sensitivität**

**100% Spezifität**

**100% PPV**

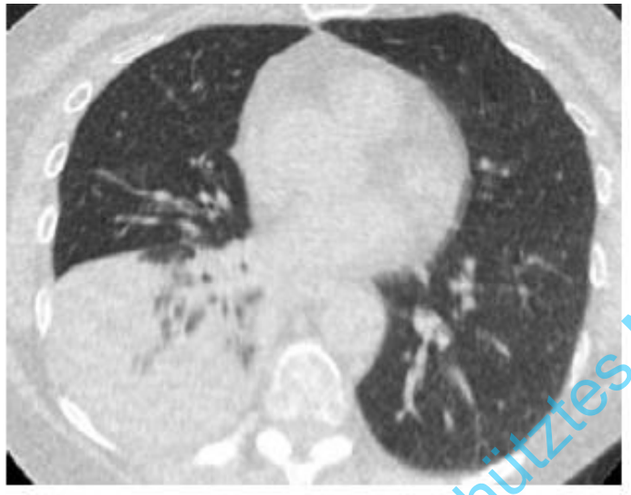
**80%NPV**

Xiang F, CID 2020

# CO-RADS – A categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation

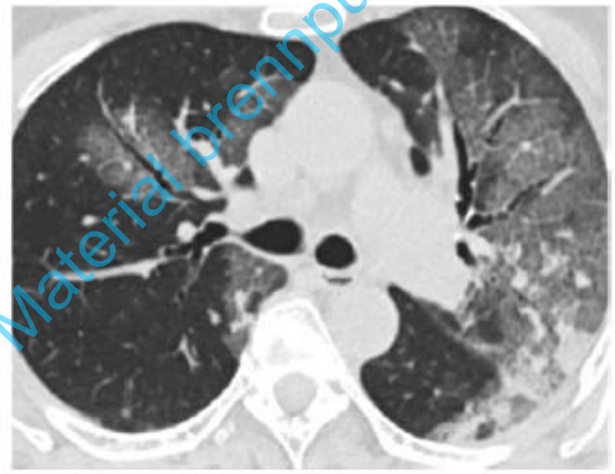
## CO-RADS 2 Score

a **Chronische Bronchitis**
**Tree in bud**
↓
**COVID negativ**

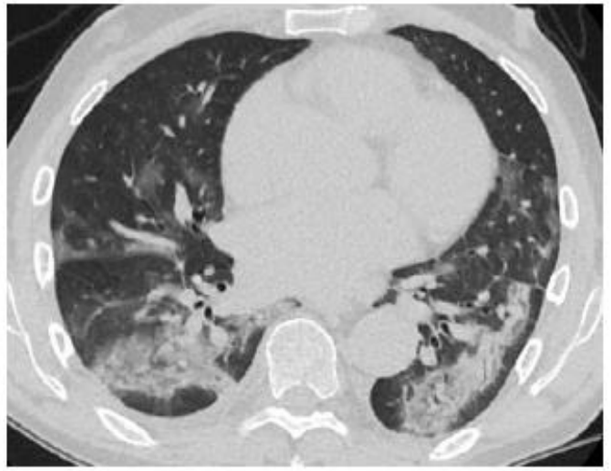


b **Konsolidierung**
**Lobärpneumonie**
↓
**COVID negativ**

## CO-RADS 5 Score



c **GGOs + Konsolidierung**
**Verdickung der Septen**
↓
**COVID positiv**



d **GGOs + Konsolidierung**
**Subpleural, multifocal**
↓
**COVID positiv**

Luyt CE, Chest 2012

# Management der mild und moderat verlaufenden Covid Erkrankung

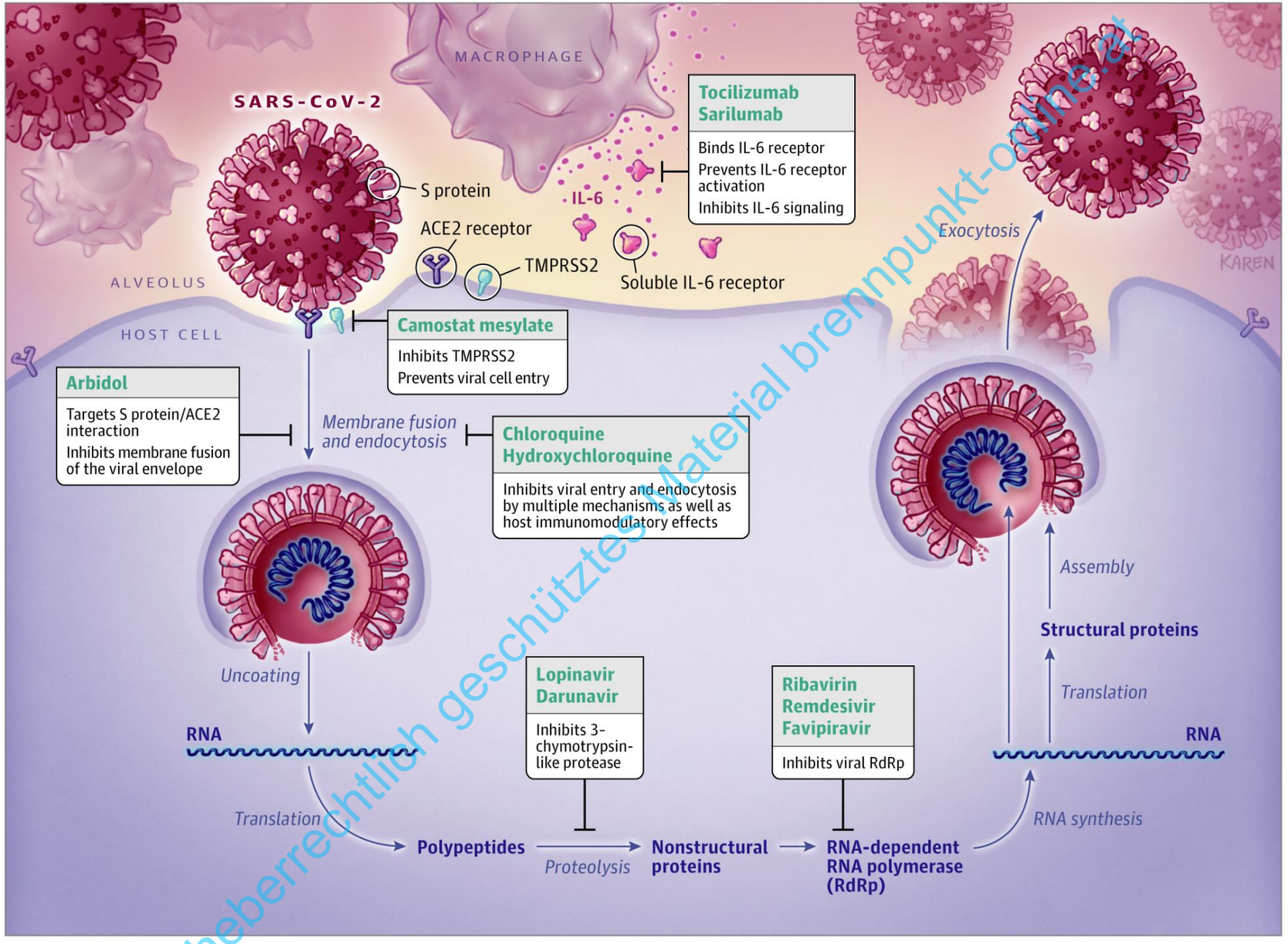
KEY CLINICAL POINTS

## MILD OR MODERATE COVID-19

- Covid-19 (the illness caused by SARS-CoV-2) has a range of clinical manifestations, including cough, fever, malaise, myalgias, gastrointestinal symptoms, and anosmia.
- Diagnosis of Covid-19 is usually based on detection of SARS-CoV-2 by PCR testing of a nasopharyngeal swab or other specimen.
- Evaluation and management of Covid-19 depends on the severity of the disease; patients with mild disease typically recover at home.
- Patients with moderate or severe Covid-19 are usually hospitalized for observation and supportive care.
- There are no proven therapies for Covid-19; thus, referral of patients to clinical trials is critical.
- Infection control and prevention efforts center on personal protective equipment for health care workers, social distancing, and testing.



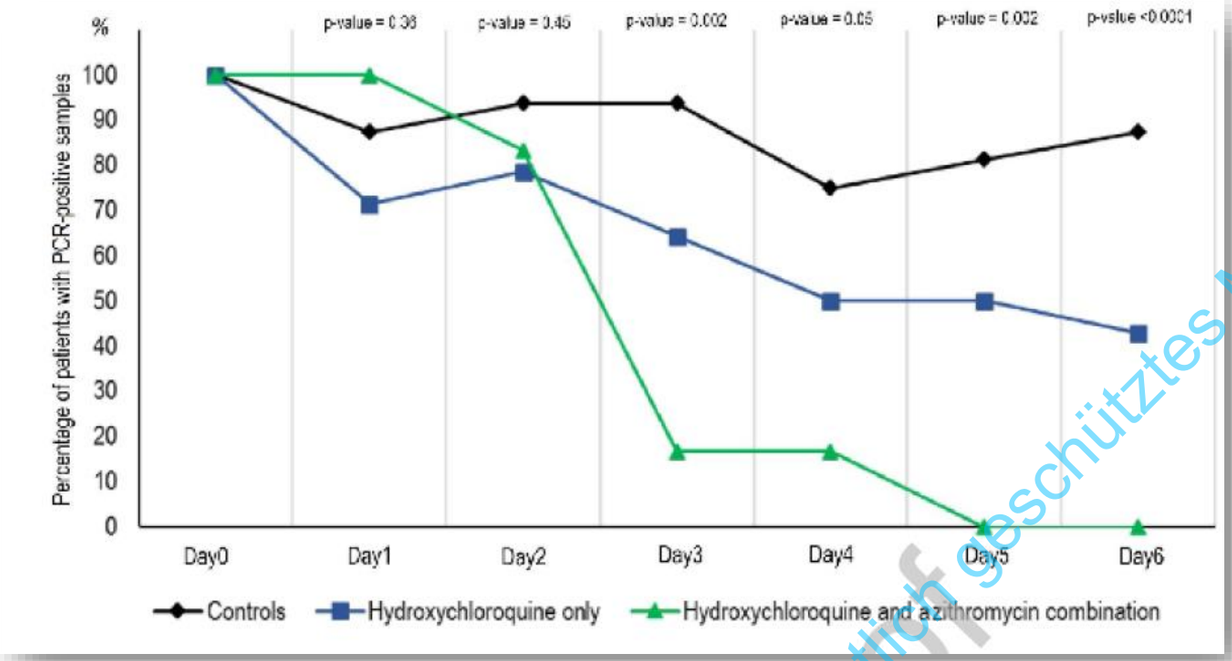
Gandhi RT, NEJM 2020






JAMA 2020

# Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open label non-randomized clinical trial




**CAVE:**

**"Untreated patients from another center and cases refusing the protocol were included as controls"**

Gautret P, Int J Antimicrob Agents 2020

# Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19

**Table 2. Associations between Hydroxychloroquine Use and the Composite End Point of Intubation or Death in the Crude Analysis, Multivariable Analysis, and Propensity-Score Analyses.**

| Analysis | Intubation or Death |
|---|---|
| No. of events/no. of patients at risk (%) | |
| Hydroxychloroquine | 262/811 (32.3) |
| No hydroxychloroquine | 84/565 (14.9) |
| Crude analysis — hazard ratio (95% CI) | 2.37 (1.84–3.02) |
| Multivariable analysis — hazard ratio (95% CI)* | 1.00 (0.76–1.32) |
| Propensity-score analyses — hazard ratio (95% CI) | |
| With inverse probability weighting† | 1.04 (0.82–1.32) |
| With matching‡ | 0.98 (0.73–1.31) |
| Adjusted for propensity score§ | 0.97 (0.74–1.28) |

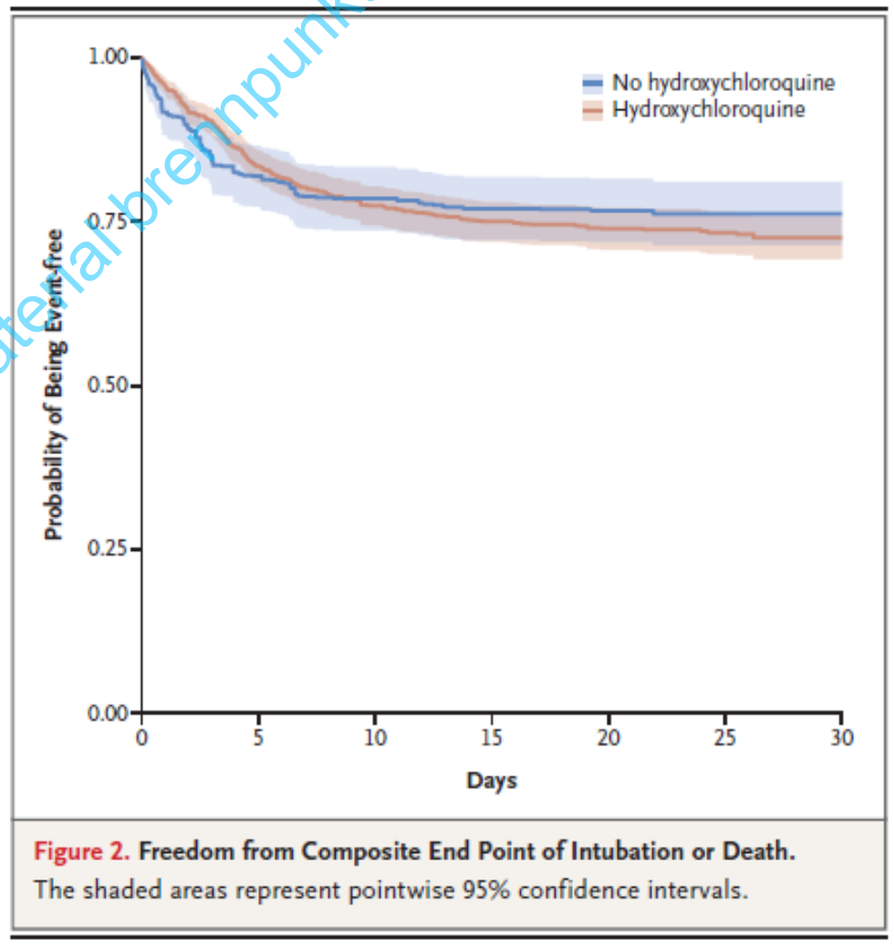
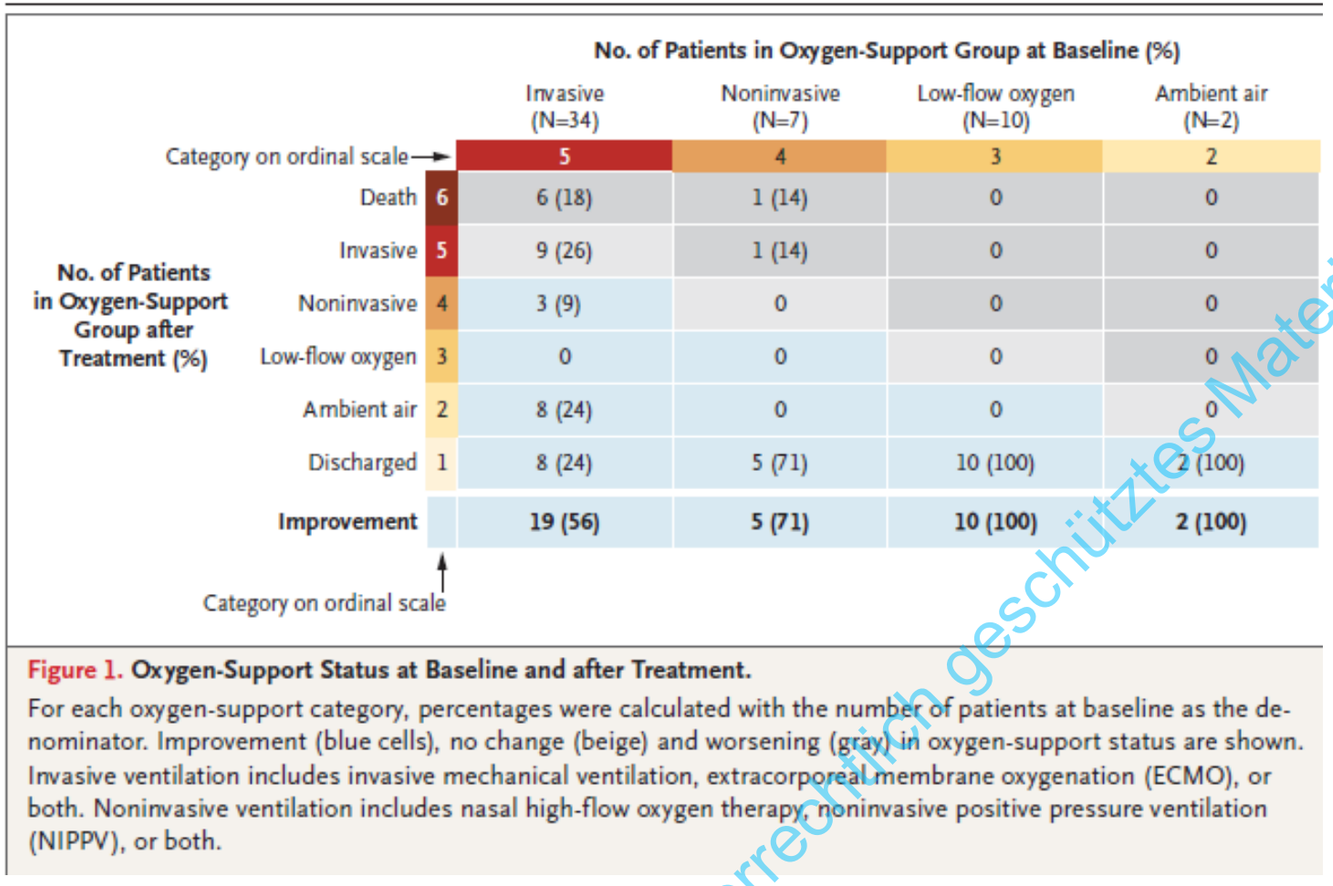



**Figure 2. Freedom from Composite End Point of Intubation or Death.**
The shaded areas represent pointwise 95% confidence intervals.

Kein statistisch signifikanter Unterschied wenn für folgende Faktoren korrigiert: Alter, Geschlecht, BMI, Vorerkrankungen, und Dauermedikation

Geleris J, NEJM 2020

# Compassionate use of Remdesivir for severe Covid-19



| No. of Patients in Oxygen-Support Group after Treatment (%) | | No. of Patients in Oxygen-Support Group at Baseline (%) | | | |
|---|---|---|---|---|---|
| | | Invasive (N=34) | Noninvasive (N=7) | Low-flow oxygen (N=10) | Ambient air (N=2) |
| Category on ordinal scale → | | 5 | 4 | 3 | 2 |
| Death | 6 | 6 (18) | 1 (14) | 0 | 0 |
| Invasive | 5 | 9 (26) | 1 (14) | 0 | 0 |
| Noninvasive | 4 | 3 (9) | 0 | 0 | 0 |
| Low-flow oxygen | 3 | 0 | 0 | 0 | 0 |
| Ambient air | 2 | 8 (24) | 0 | 0 | 0 |
| Discharged | 1 | 8 (24) | 5 (71) | 10 (100) | 2 (100) |
| **Improvement** | | **19 (56)** | **5 (71)** | **10 (100)** | **2 (100)** |

Category on ordinal scale ↑

**Figure 1. Oxygen-Support Status at Baseline and after Treatment.**

For each oxygen-support category, percentages were calculated with the number of patients at baseline as the denominator. Improvement (blue cells), no change (beige) and worsening (gray) in oxygen-support status are shown. Invasive ventilation includes invasive mechanical ventilation, extracorporeal membrane oxygenation (ECMO), or both. Noninvasive ventilation includes nasal high-flow oxygen therapy, noninvasive positive pressure ventilation (NIPPV), or both.

**53 patients (median age 64yrs) with SpO2 < 94% on room air or receiving O2 supplementation**

**median symptom days before antiviral treatment 12 days**

↓

**10 days Remdesivir i.v.**

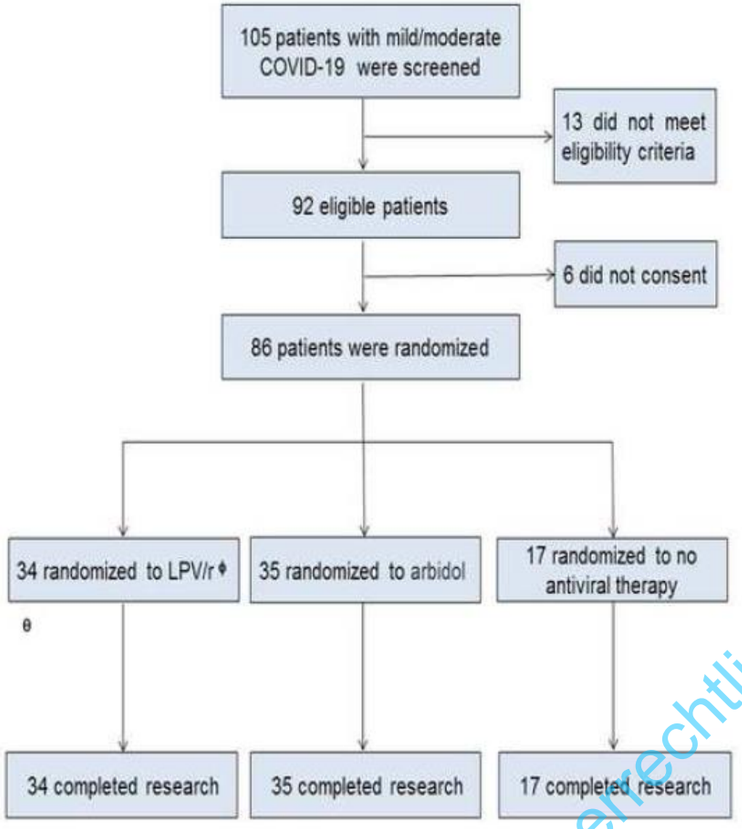
**(200mg day 1, followed by 100mg daily)**

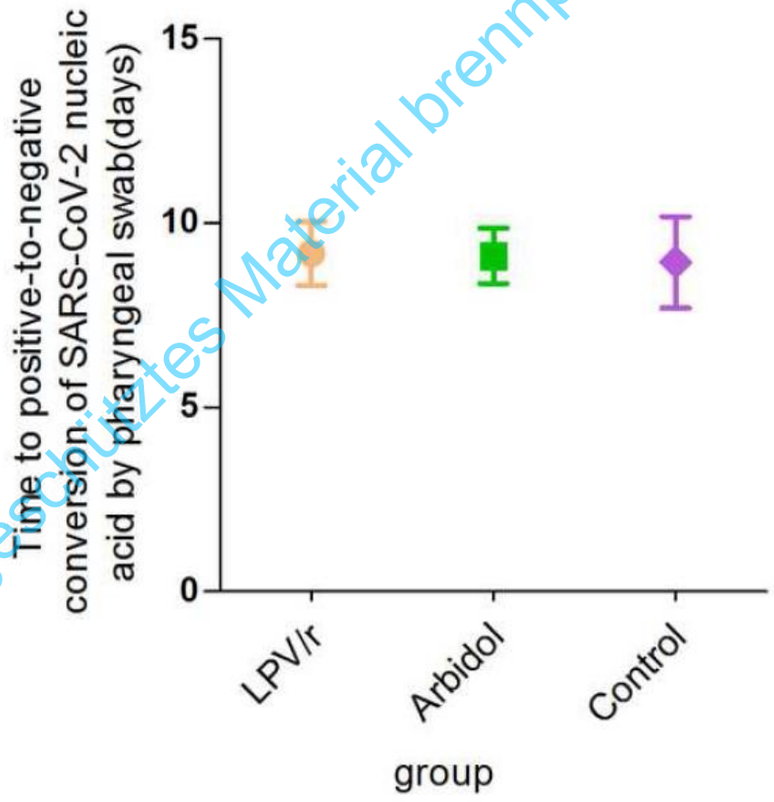
↓

**68% improvement in oxygen support**

Grein J, NEJM 2020

# Efficacy and safety of lopinavir/ritonavir or arbidol in mild/moderate COVID-19: exploratory randomized controlled trial

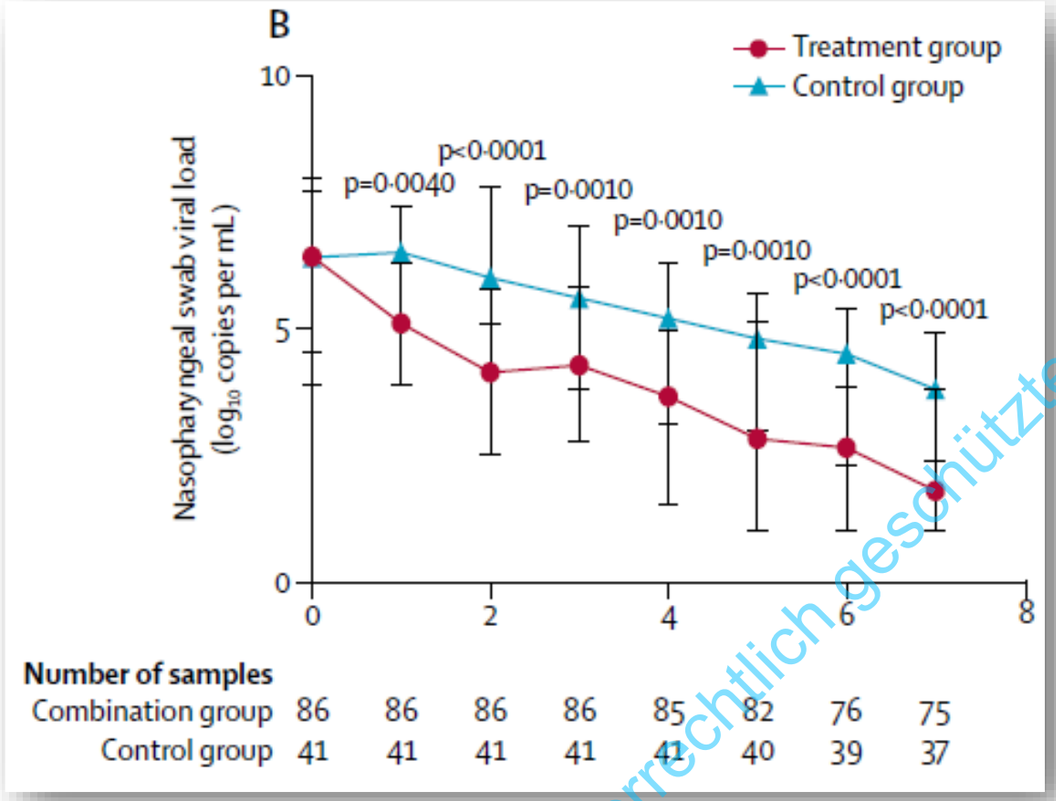



**No difference in symptoms or Chest CT at days 7 or 14**

Li Y, Cell 2020

# Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial




**Konversion von PCR positiv zu negativ:**

**7 Tage für Triple-Therapie**

**12 Tage für Lopinavir-Ritonavir**

**P = 0.001**

**Aufenthaltsdauer im Krankenhaus´:**

**9 Tage für Triple-Therapie**

**14.5 Tage für Lopinavir-Ritonavir**

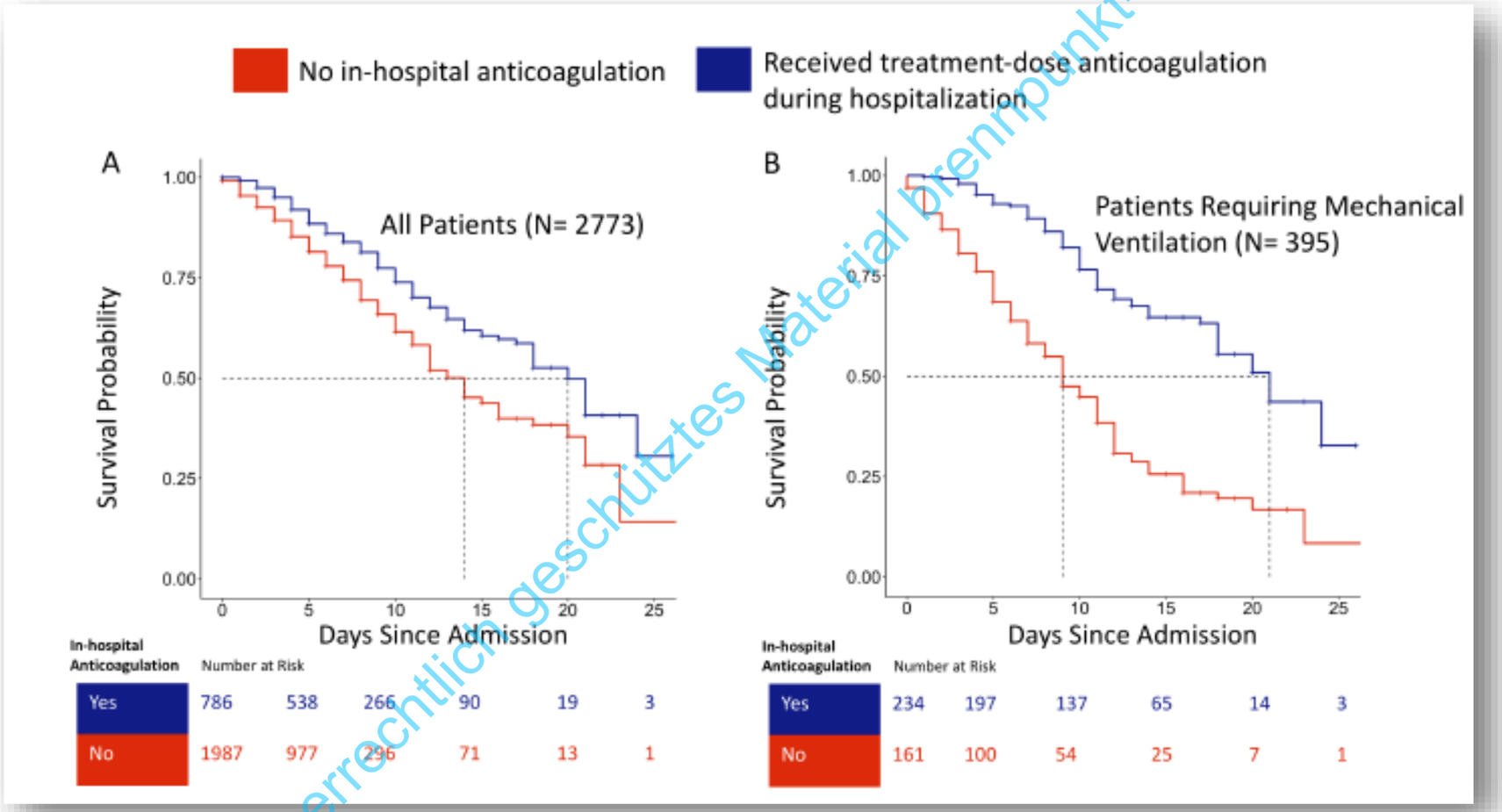
**P = 0.016**

**Outcome besser wenn**

**Therapie innerhalb von 7d vor Symptombeginn**

Hung IFN, Lancet 2020

# Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19






Paranjpe I, JACC 2020

# Agenda

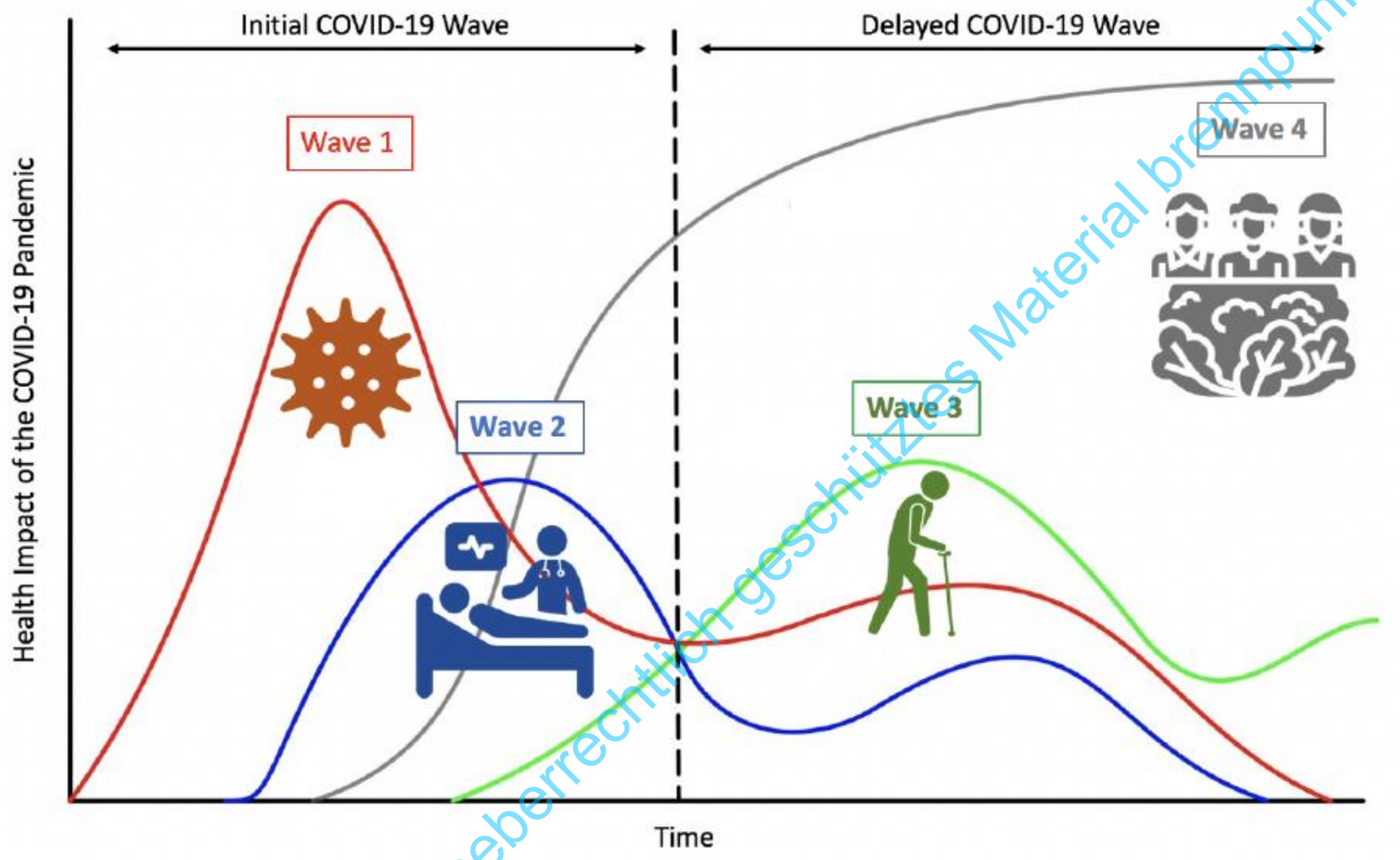
**Update:**

Risikofaktoren
Diagnose
Therapie

**Nachsorge:**

**Pulmonale und extrapulmonale Manifestationen**

# Covid-19 Pandemie: Herausforderungen an das Gesundheitssystem

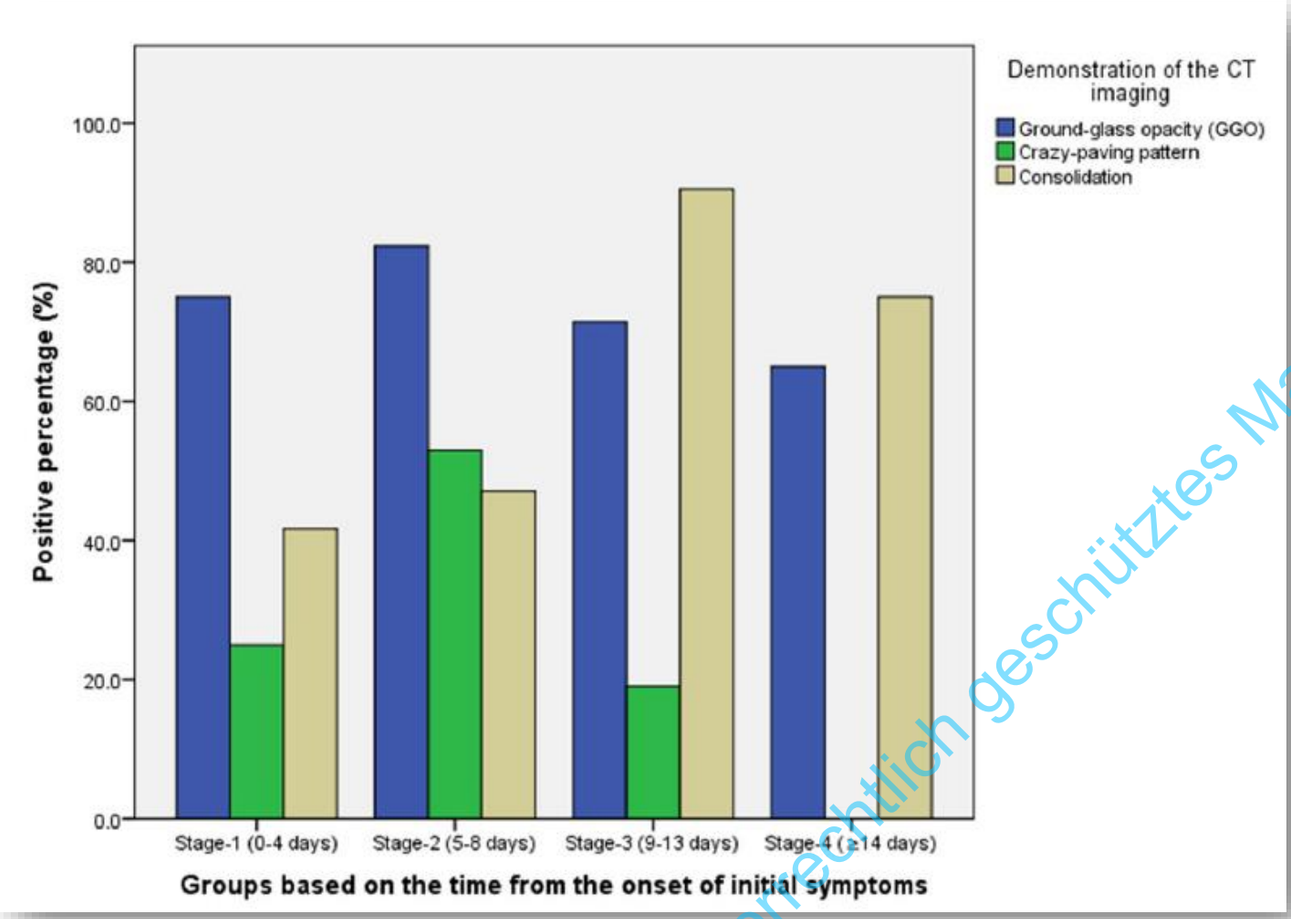



**Wave 4: Post COVID-19 Era**

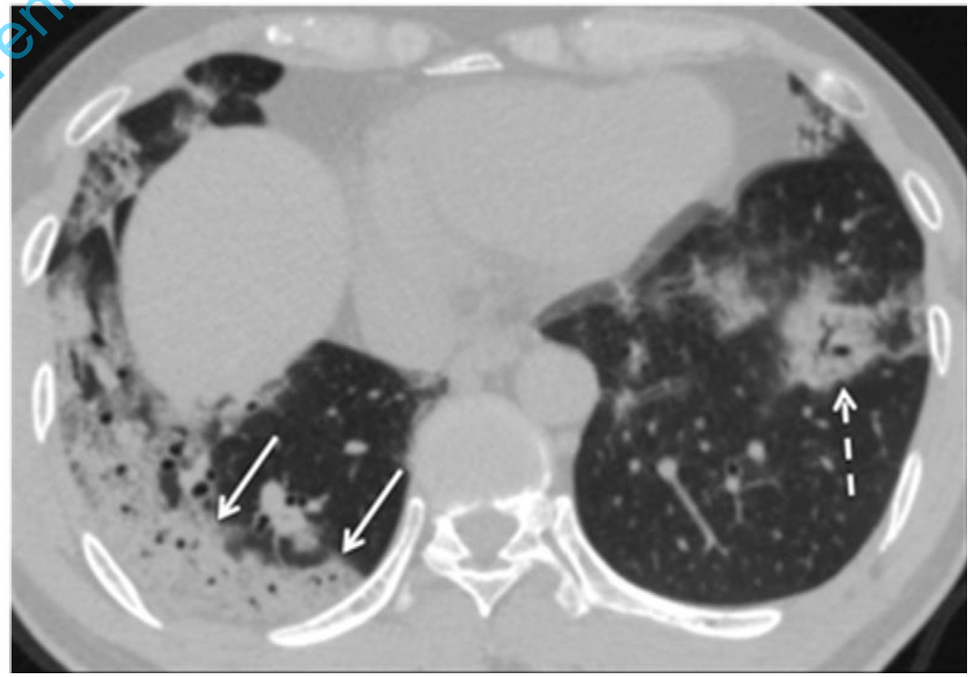
- Loss of / Sick Healthcare Workers
- Economic and Social Unrest
- Psychological Trauma
- Backlog of Patients Requiring Care

Vervoort D, Ann Thorac Surg 2020

# Chronologie radiologischer Veränderungen bei Covid-19




Pan F, Radiology 2020



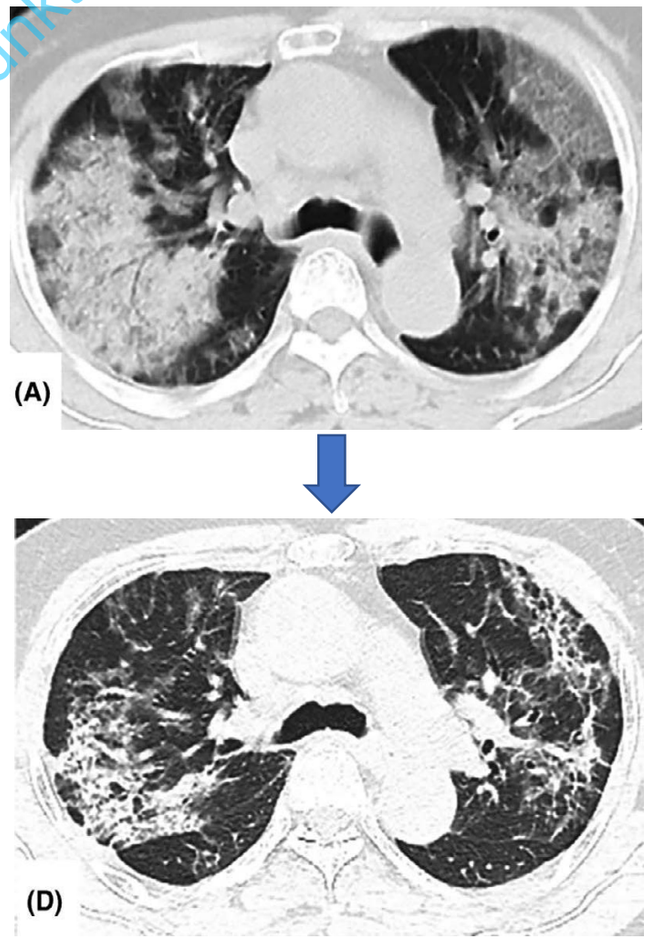
Bernheim A, Radiology 2020

# Zeitlicher Verlauf der Resolution pathologischer Befunde in der Thorax-CT post COVID-19

**Rückgang von mindestens**
**75% der intrapulmonalen Läsionen**
**in der CT nach 2 Wochen**

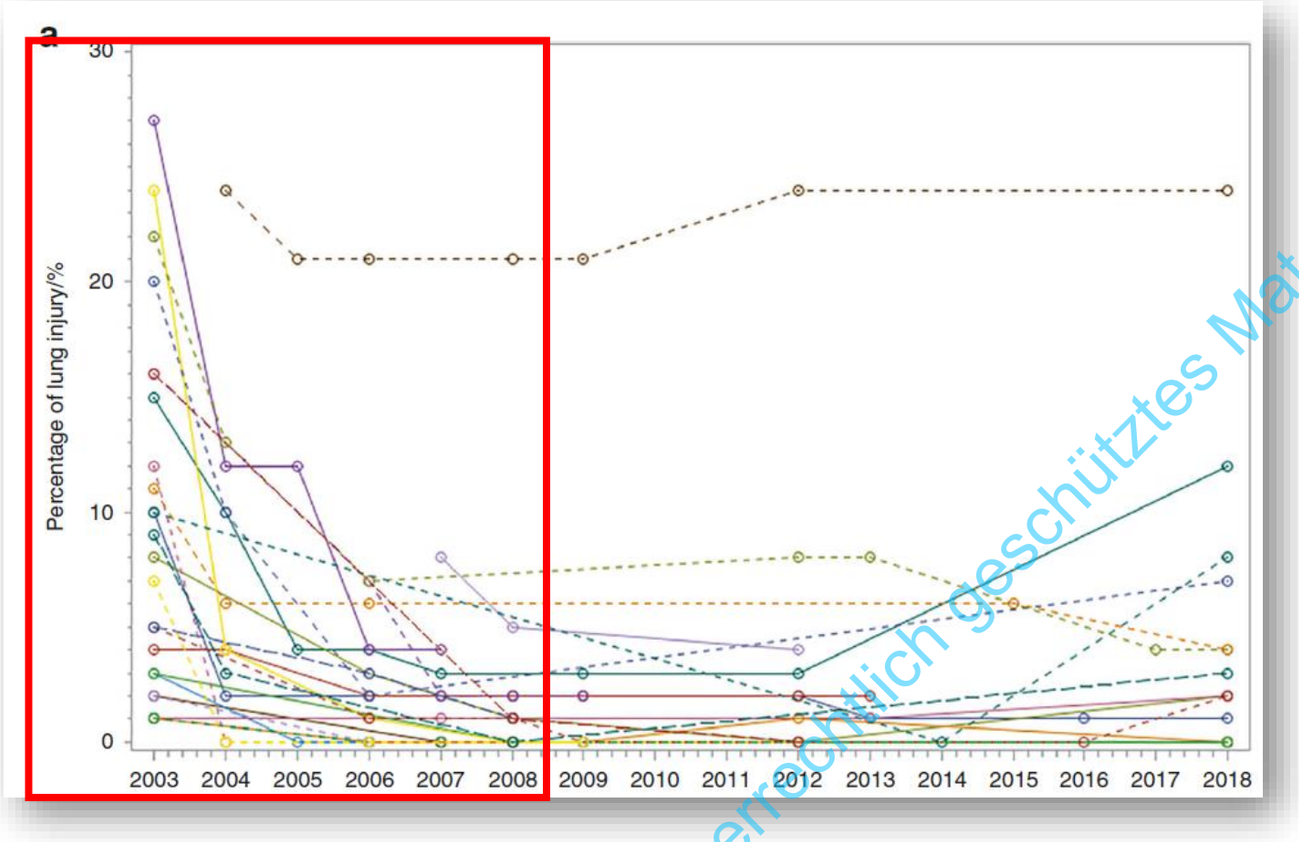
**82% der Fälle mit mild-moderaten Verlauf**
**76% der Fälle mit schweren Verlauf**

Zheng C, Int J Infect Dis 2020




Zhang J, Allergy 2020

# Langzeitfolgen der SARS-Infektion

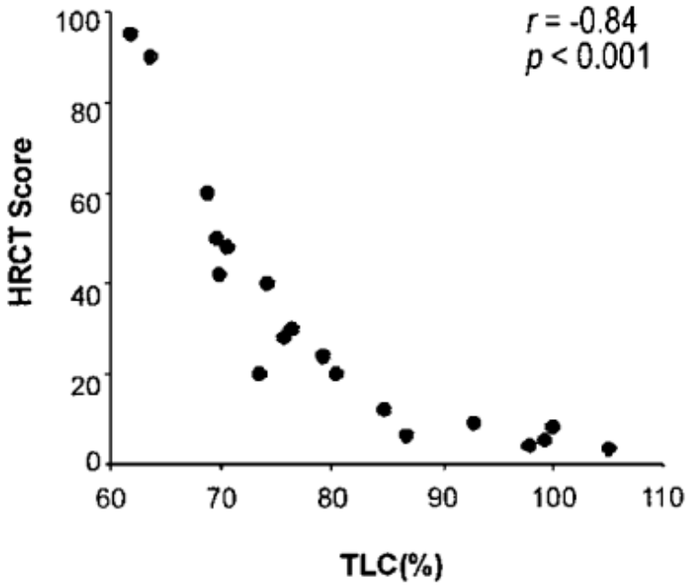


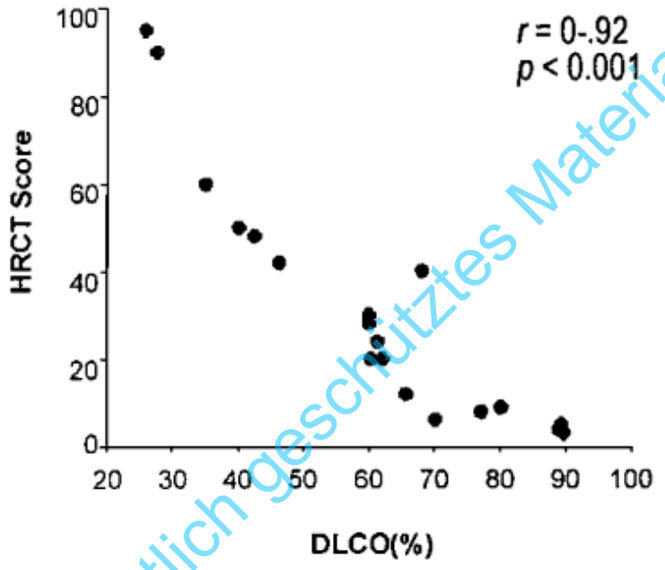

**19 Patienten, 3 Jahre nach SARS:**

- **21% mit Hinweisen für eine restriktive Ventilationsstörung**
- **35% mit eingeschränkter Diffusionskapazität**

Zhang P, Bone Res 2020

# Lungenfunktion und Thorax-CT post SARS



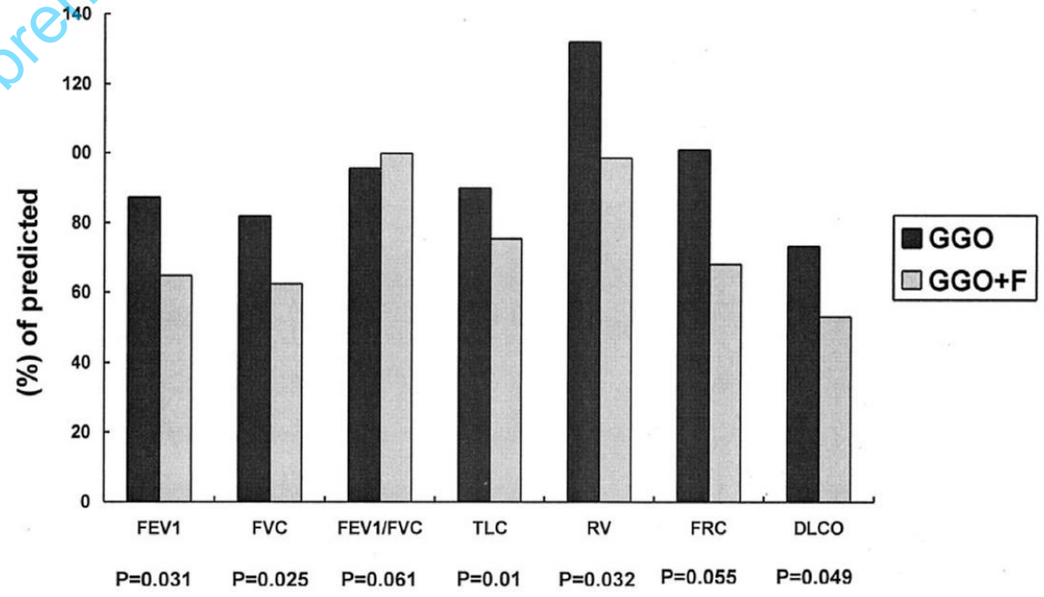




FIGURE 4. Comparison of pulmonary function measurements between the GGO and GGO+F groups.

Hsu HH, Chest 2004

**GGOs, Fibrosierungen,Bronchiektastien**

Hsu HH, Chest 2004

**CT-Pathologien 12 Monate nach einer Influenza A Epidemie, H5N9**

**↓**

**41% Fibrosezeichen**

**51% GGOs**

Chen J; Sci Reports 2017

# Funktioneller Verlauf nach einem ARDS

## Influenza A Epidemie, H5N9

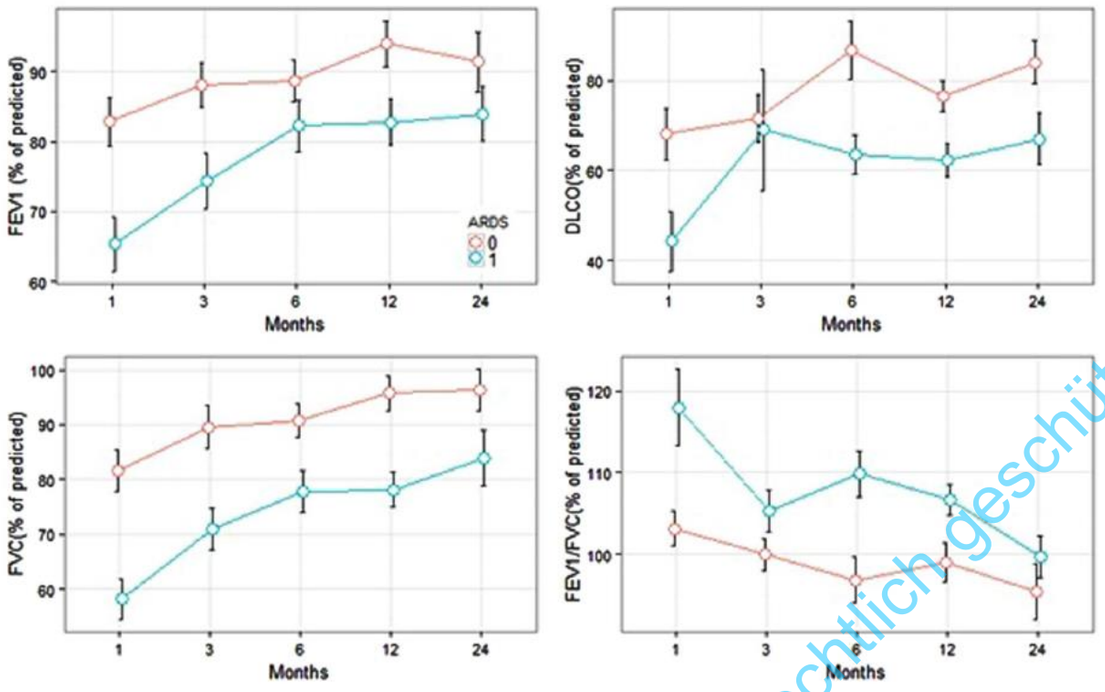



**Figure 3.** The influence of ARDS on lung function changes of the survivors with H7N9 infections during follow up.

Chen J; Sci Reports 2017

## Influenza A Epidemie, H1N1

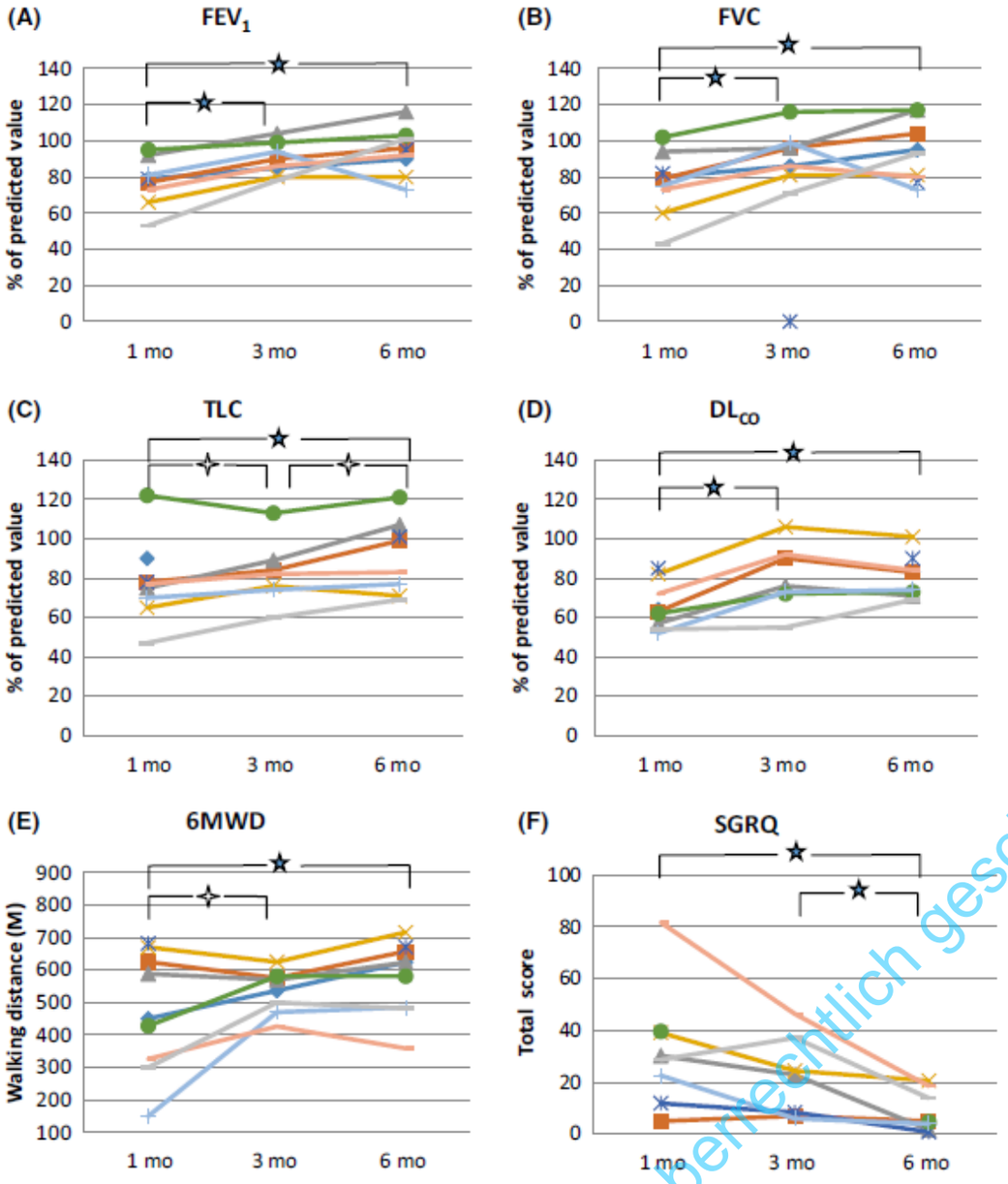
**12 Monate nach ARDS:**

**40-50% mit Belastungsdyspnoe**

**70% mit eingeschränkter DLCO**

**50% mit Angst**
**20% Risiko für PTSD**

Luyt CE, Chest 2012



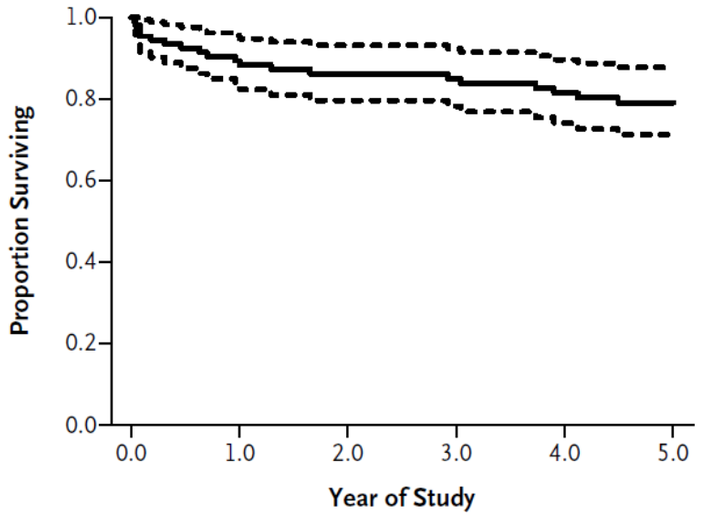

# Funktionelle Veränderungen post Influenza A H1N1 ARDS

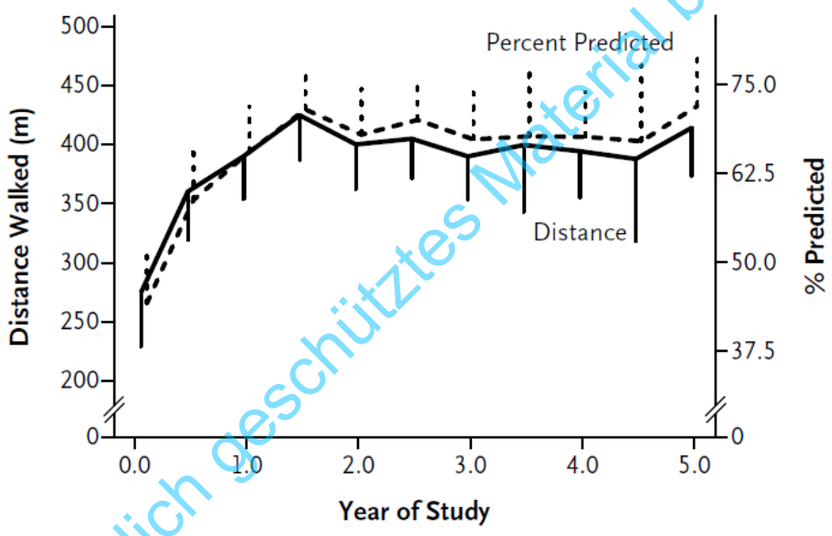
## (post Lungenrehabilitation)

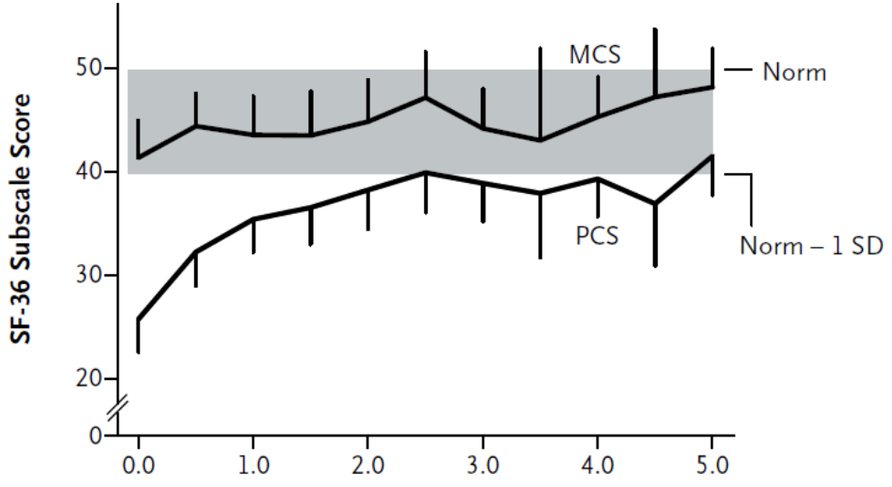
Hsieh MJ, Influenza Other Respir Vir 2018

# Langzeitdaten nach ARDS

## Survival, Gehtest, QoL




Herridge MS, NEJM 2011

# Risikofaktoren für Leistungsverlust nach akutem Lungenversagen

## ICU-Aufenthaltsdauer
## + systemische Kortisondosis

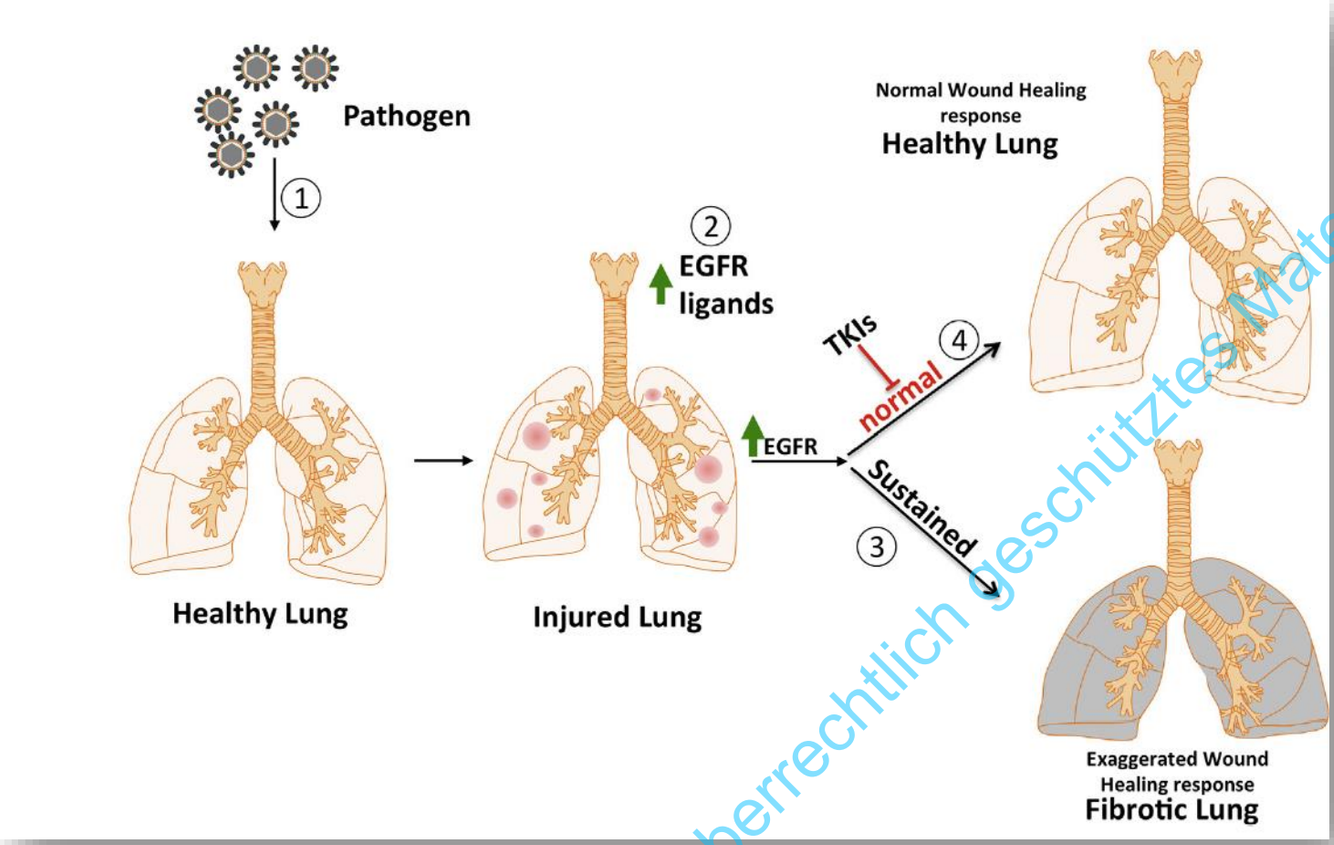
## Körperliche
## Leistungseinschränkungen

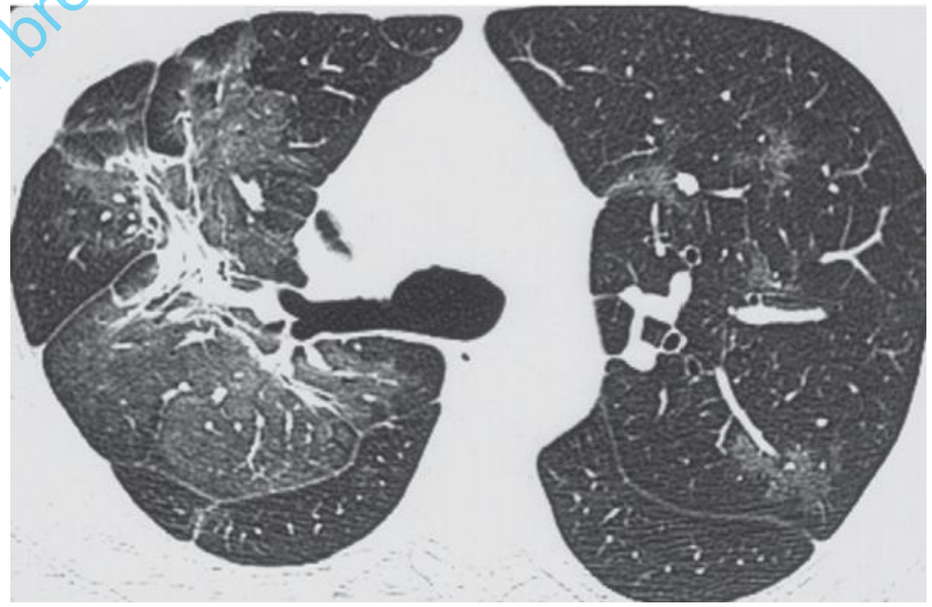


Needham DM, AJRCCM 2014

# The role of epidermal growth factor receptor (EGFR) signaling in SARS coronavirus-induced pulmonary fibrosis

Thiagarajan Venkataraman, Matthew B. Frieman*





Antiviral Res 2017

# COVID-19 Nachsorge

**Funktionsdiagnostik**
- Spirobody, DLCO, Bel.-BGA
- Ergometrie, 6-MWT

**Bildgebung**
- Thoraxröntgen
- HR-Thorax-CT

**Komorbiditäten**
- Kardiologisch, Nephro,…
- Neurologie


**Präventionsmassnahmen**
- Raucherentwöhnung
- Impfung: Influenza, Pneumo

**Rehabilitation:**
- Ambulant, Heimtraining
- Stationäre Rehab

**Psychosoziale Betreuung**