



## I. Medizinische Klinik und Poliklinik

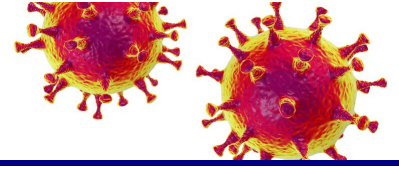
# Immunosuppression and COVID-19: The Hamburg experience

PD Dr. med. Julian Schulze zur Wiesch  
1. Medical Department University Medical

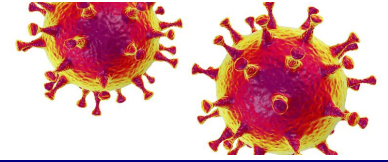


Universitätsklinikum  
Hamburg-Eppendorf

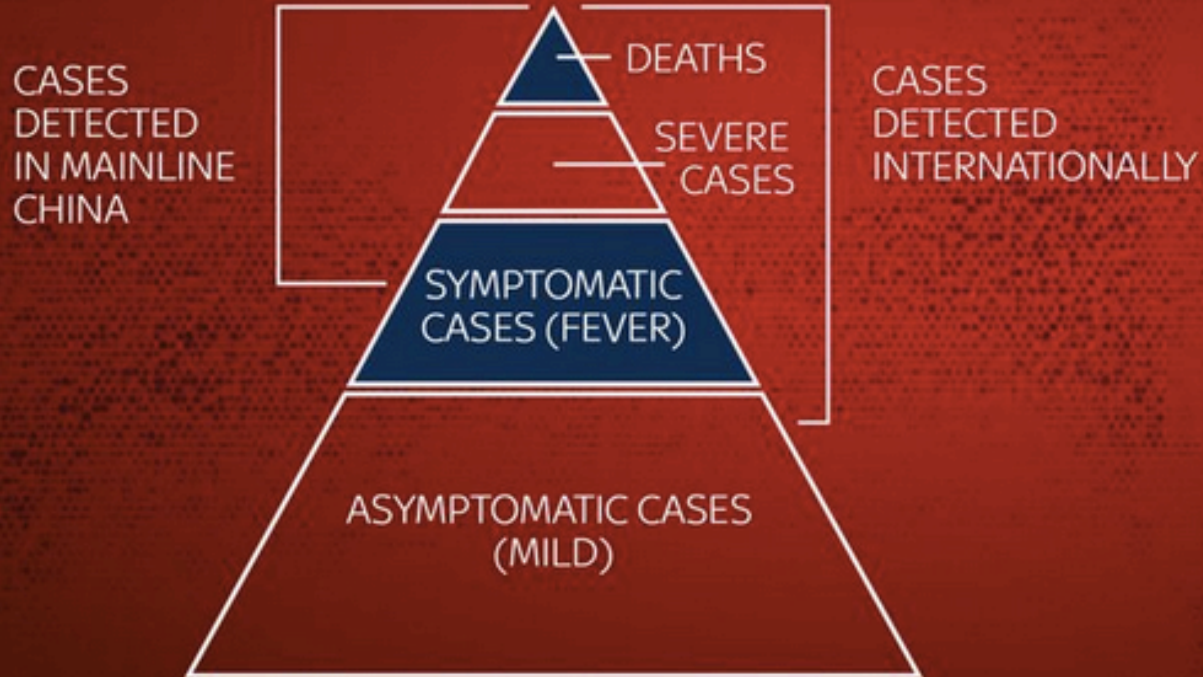
Our hearts go out to all of the COVID-19 patients, their families and their providers!



**Let's tackle this in a united way!**

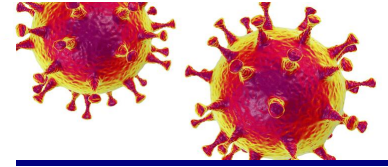


## MAJORITY OF CASES ARE MILD AND HARDLY DETECTED

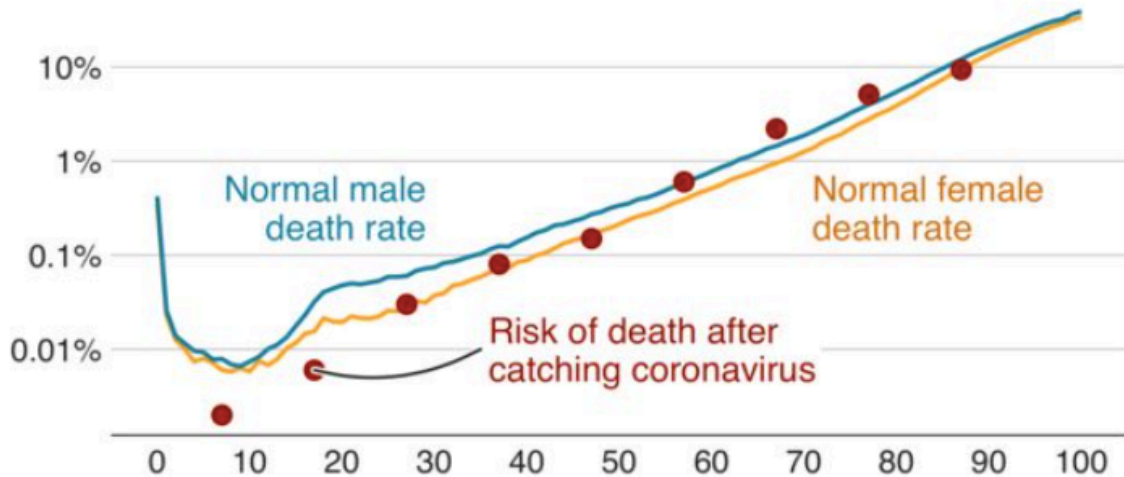


SOURCE:  
IMPERIAL  
COLLEGE  
LONDON

# Risk of dying if you get coronavirus v normal annual risk



Risk of dying each year by age (GB)



Log scale used to see differences in rates at younger ages

Source: Prof. Sir David Spiegelhalter, ONS, Imperial College London

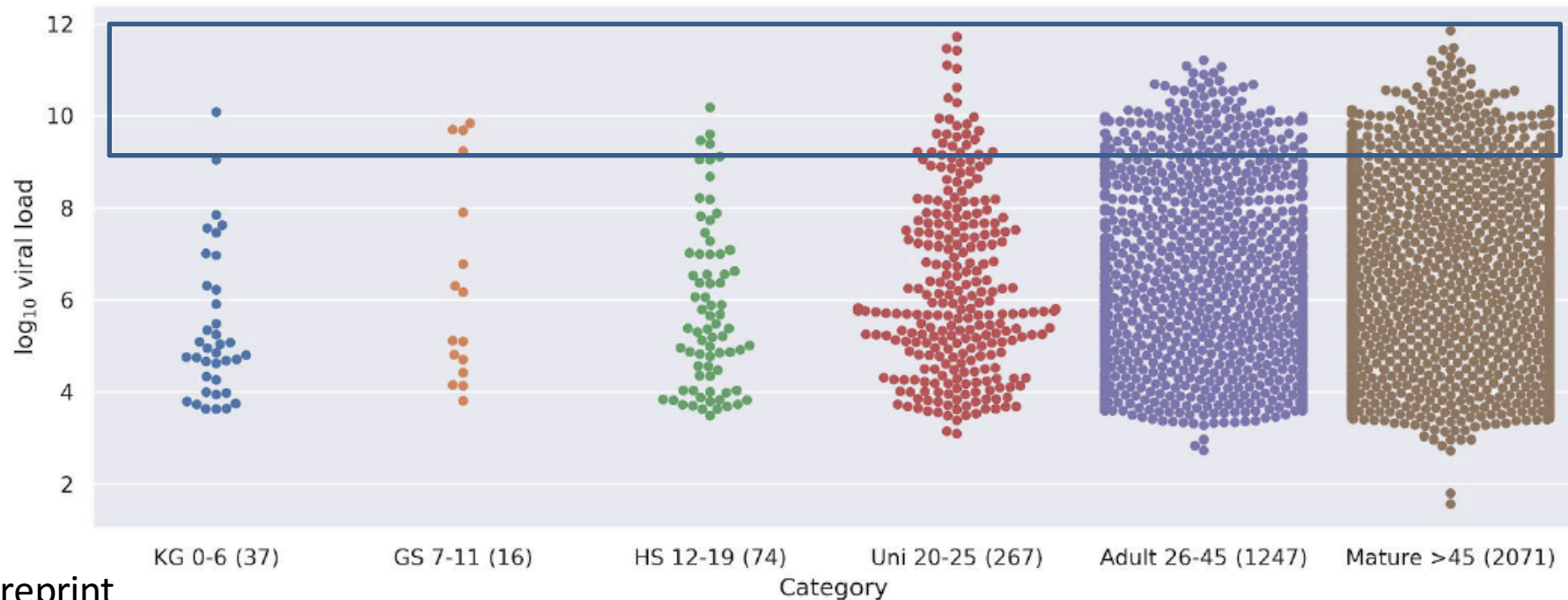


For example, an average person aged 40 has around a one-in-1,000 risk of not making it to their next birthday and an almost identical risk of not surviving a coronavirus infection. That means your risk of dying is effectively doubled from what it was if you are infected.

# An analysis of SARS-CoV-2 viral load by patient age

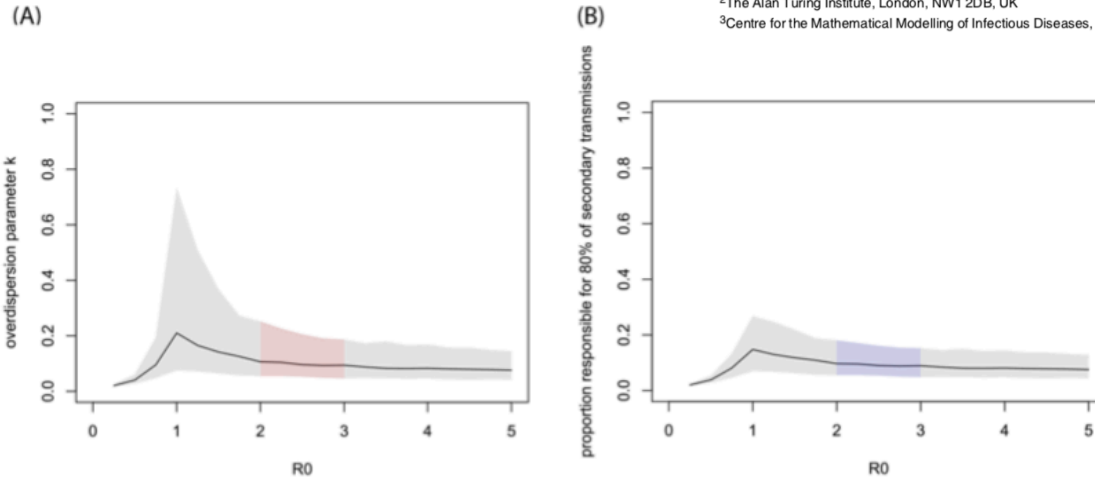
Terry C. Jones<sup>1,2</sup>, Barbara Mühlemann<sup>1,3</sup>, Talitha Veith<sup>1,3</sup>, Marta Zuchowski<sup>4</sup>, Jörg Hofmann<sup>4</sup>, Angela Stein<sup>4</sup>, Anke Edelmann<sup>4</sup>, Victor Max Corman<sup>1,3</sup>, Christian Drosten<sup>1,3</sup>

**B**



## Results

Our estimation suggested substantial overdispersion ( $k \ll 1$ ) in the offspring distribution of COVID-19 (Figure 1A and Figure 2). Within the current consensus range of  $R_0$  (2–3),  $k$  was estimated to be around 0.1 (median estimate 0.1; 95% CrI: 0.05–0.2 for  $R_0 = 2.5$ ). For the  $R_0$  values of 2–3, the estimates suggested that 80% of secondary transmissions may have been caused by a small fraction of infectious individuals (~10%; Figure 1B).



**Figure 1. MCMC estimates given assumed  $R_0$  values.** (A) Estimated overdispersion parameter for various basic reproduction number  $R_0$ . (B) The proportion of infected individuals responsible for 80% of the total secondary transmissions ( $p_{80\%}$ ). The black lines show the median estimates given fixed  $R_0$  values and the grey shaded areas indicate 95% CrIs. The regions corresponding to the likely range of  $R_0$  (2–3) are indicated by colour.

RESEARCH ARTICLE

**Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China** [version 1; peer review: 1 approved, 1 approved with reservations]

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- - Superspreader ?

## Wave of infections hits German cancer ward

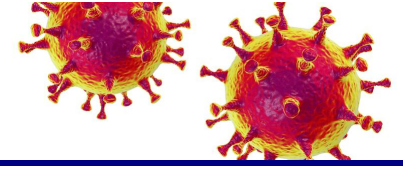
From CNN's Nadine Schmidt in Berlin

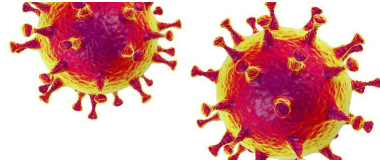


An exterior view shows the The University Medical Center Hamburg-Eppendorf in Hain 1818. Shutterstock

A cancer ward in a German hospital has been hit by an outbreak of coronavirus cases.

Around 20 patients and 20 employees tested positive for Covid-19 at the University Medical Centre Hamburg-Eppendorf (UKE) last week, the hospital confirmed to CNN on Wednesday.





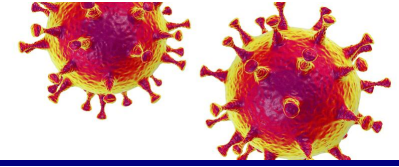
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## Implications of SARS-CoV-2 Infection and COVID-19 Crisis on Clinical Cancer Care: Report of the University Cancer Center Hamburg

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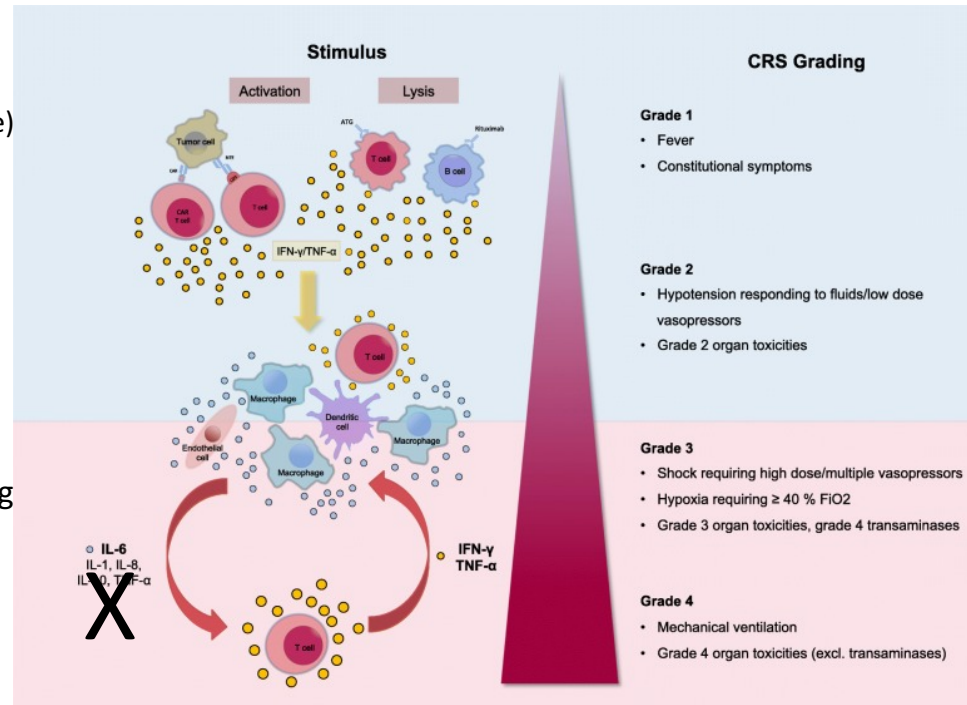


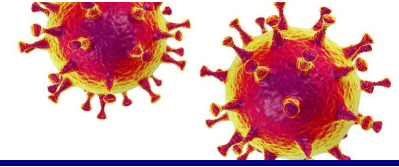
## CRS - Pathomechanism

Stages:

1. Replicative Phase
2. Phase of the (adaptive) immune response

„This progression may explain the clinical phenomenon wherein patients are relatively OK for several days, but then suddenly deteriorate when they enter the adaptive immunity stage“ (e.g. Young et al. 3/3/2020)





## Patient 1

Datum/Uhrzeit	Leukozyten (Leuk) (3.8 - 11.0) Mrd/l	C-reaktives Protein (CRP) (- 5) mg/l	Interleukin 6 (IL6) (<7.0) ng/l	Ferritin (22.0 - 322.0) µg/l
27.04.20 17:16	7.0 <sup>Δ</sup>	<4 <sup>Δ</sup>	5.9 <sup>Δ</sup>	309.0 <sup>ΔD</sup>
19.04.20 20:04	9.1 <sup>Δ</sup>	<4 <sup>Δ</sup>		
06.04.20 08:00	4.7 <sup>Δ</sup>	<4 <sup>Δ</sup>	61.6 <sup>H</sup>	967.8 <sup>H</sup>
04.04.20 08:00	4.4 <sup>Δ</sup>	<4 <sup>Δ</sup>	86.5 <sup>H</sup>	1226.4 <sup>H</sup>
02.04.20 08:00	3.1 <sup>ΔL</sup>	22 <sup>H</sup>	473.9 <sup>H</sup>	1588 <sup>H</sup>
31.03.20 08:00	3.6 <sup>ΔL</sup>	189 <sup>H</sup>	1004.0 <sup>H</sup>	2277 <sup>H</sup>
* 30.03.20 07:00	7.2 <sup>Δ</sup>	253 <sup>H</sup>	117.8 <sup>H</sup>	1762 <sup>H</sup>
29.03.20 08:00	10.9 <sup>Δ</sup>	239 <sup>H</sup>	114.6 <sup>H</sup>	1456 <sup>H</sup>
27.03.20 10:37	6.2 <sup>Δ</sup>	106 <sup>H</sup>	110.0 <sup>H</sup>	1161 <sup>H</sup>
26.03.20 21:40	4.8 <sup>Δ</sup>	66 <sup>H</sup>		
21.03.20 02:42	4.8 <sup>Δ</sup>	15 <sup>H</sup>		

## Patient 2

Datum/Uhrzeit	Leukozyten (Leuk) (3.8 - 11.0) Mrd/l	C-reaktives Protein (CRP) (- 5) mg/l	Interleukin 6 (IL6) (<7.0) ng/l	Ferritin (10.0 - 291.0) µg/l
27.04.20 18:01	4.6 <sup>Δ</sup>	<4 <sup>Δ</sup>	21.0 <sup>H</sup>	212.8 <sup>ΔD</sup>
07.04.20 08:00	3.8 <sup>ΔL</sup>	8 <sup>H</sup>	115.7 <sup>H</sup>	1109.7 <sup>H</sup>
06.04.20 08:00	3.0 <sup>ΔL</sup>	28 <sup>H</sup>	530.1 <sup>H</sup>	1519.4 <sup>H</sup>
03.04.20 08:00	3.1 <sup>ΔL</sup>	124 <sup>H</sup>	758.6 <sup>H</sup>	2695.2 <sup>H</sup>
02.04.20 09:59	5.4 <sup>Δ</sup>	286 <sup>H</sup>	743.4 <sup>H</sup>	2315 <sup>H</sup>
* 01.04.20 08:00	9.1 <sup>Δ</sup>	301 <sup>H</sup>	131.5 <sup>H</sup>	1627 <sup>H</sup>
30.03.20 16:42	2.9 <sup>ΔΔL</sup>	95 <sup>H</sup>	62.4 <sup>H</sup>	1232 <sup>H</sup>
30.03.20 13:51	3.5 <sup>ΔL</sup>	96 <sup>H</sup>		1148 <sup>H</sup>

Off-label use of Tocilizumab 8 mg/Kg two patients with protracted disease course  
-patients were discharged 7 days later in excellent health

Results of controlled studies are needed-  
(Future direction? Immunomodulation + SARS-CoV2 antiviral)

[Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz](#). 2019;

62(7): 870–880.

Published online 2019 Jun 14. German. doi: [10.1007/s00103-019-02976-0](https://doi.org/10.1007/s00103-019-02976-0)

PMCID: PMC7096087

PMID: [31201446](https://pubmed.ncbi.nlm.nih.gov/31201446/)

## Management of seasonal influenza in 2017/2018 at a German tertiary-care hospital

### Abstract

**Background.** There are only few structured reports on inpatient management of a seasonal influenza epidemic.

**Objectives.** A systematic description of a seasonal influenza patient population at a German university hospital to improve risk stratification and clinical care.

**Methods.** In this monocentric, retrospective observational study of the 2017/2018 influenza season at the University Medical Center Hamburg-Eppendorf, patients with confirmed influenza infection were included.

**Results.** Of all influenza swabs performed in the emergency department, 24% ( $n = 162/676$ ) were positive. A total of 255 patients (median age 66 years) had an

influenza infection (influenza A  $n = 79$ , influenza B  $n = 176$ ); 27 (15.3%) were nosocomial infections. Of the 179 (70.2%) patients that were hospitalized, 51 (20%) received intensive medical care. Patients with subsequent need for intensive care had an elevated CRP level (69.5 mg/dl [SD 62.8] vs. 141.7 [SD 127.2] mg/dl) at the time of influenza diagnosis and more frequent infiltrates in X-ray/CT of the thorax ( $n = 43$  [33.6%] vs.  $n = 43$  [84.3%]). Antiviral therapy with oseltamivir was administered for 74 (29.0%) patients and 11 (6.1%) patients were treated with extracorporeal membrane oxygenation (ECMO). Of the 23 (9.0%) patients who died, only four of them had been

vaccinated (trivalent). Those four had an influenza B infection.

**Conclusion.** The structured use of diagnostic tests (influenza PCR, X-ray/CT chest and CRP) and antiviral therapy (oseltamivir) as well as targeted management of admission, intensive care capacities, and an increase in vaccination rates are important for improving patient care and optimizing the use of resources during seasonal influenza epidemics.

### Keywords

Seasonal influenza · Antiviral therapy · ECMO · Influenza vaccination · CRP

Influenza-Abstriche in der ZNA des UKE Dezember 2017- April 2018		Influenzapatienten UKE n=231	
Abstriche in der ZNA n	676	Influenza Typ A n (%)	65 (28,1)
		Influenza Typ B n (%)	166 (71,9)
		Weiblich n (%)	100 (43,3)
		Alter >65 Jahren (%)	127 (55,0)
		CCI median	4
Davon positiv n	162	Immunsuppression n (%)	84 (36,4)
		Externe Übernahmen n=24	
		Influenza Typ A n (%)	14 (58,3)
		Influenza Typ B n (%)	10 (41,7)
		Weiblich n (%)	12 (50,0)
Positivrate %	24,0	Alter >65 Jahren (%)	6 (25,0)
		CCI median	3
		Immunsuppression n (%)	17 (70,8)

Ambulante Entlassung (ZNA) n=76	
Influenza Typ A n (%)	26 (34,2)
Influenza Typ B n (%)	50 (65,8)
Weiblich n (%)	39 (51,3)
Alter >65 Jahren (%)	27 (35,5)
CCI median	3
Immunsuppression n (%)	15 (19,7)

Stationäre Aufnahme n=179	
Influenza Typ A n (%)	53 (29,6)
Influenza Typ B n (%)	126 (70,4)
Weiblich n (%)	73 (40,8)
Alter >65 Jahren (%)	106 (59,2)
CCI median	4
Immunsuppression n (%)	86 (48,0)

Normalstation n=128	
Influenza Typ A n (%)	30 (23,4)
Influenza Typ B n (%)	98 (76,6)
Weiblich n (%)	51 (39,8)
Alter >65 Jahren (%)	81 (63,3)
CCI median	5
Immunsuppression n (%)	56 (43,8)

Intensivstation n=51	
Influenza Typ A n (%)	23 (45,1)
Influenza Typ B n (%)	28 (54,9)
Weiblich n (%)	22 (43,1)
Alter >65 Jahren (%)	63 (12)
CCI median (min-max)	4 (0-12)
Immunsuppression n (%)	30 (58,8)

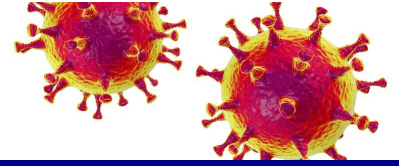
Verweildauer >7d n=66	
Influenza Typ A n (%)	15 (22,7)
Influenza Typ B n (%)	51 (77,3)
Weiblich n (%)	26 (39,4)
Alter >65 Jahren (%)	44 (66,7)
CCI median	6
Immunsuppression n (%)	27 (40,9)

Todesfälle n=2	
Influenza Typ A n (%)	0 (0)
Influenza Typ B n (%)	2 (100)
Weiblich n (%)	2 (100)
Alter >65 Jahren (%)	2 (100)
CCI median	6
Immunsuppression n (%)	0 (0)

Todesfälle n=21	
Influenza Typ A n (%)	9 (42,9)
Influenza Typ B n (%)	12 (57,1)
Weiblich n (%)	10 (47,6)
Alter >65 Jahren (%)	12 (57,1)
CCI median	4
Immunsuppression n (%)	15 (71,4)

ECMO n=11	
Influenza Typ A n (%)	8 (72,7)
Influenza Typ B n (%)	3 (27,3)
Weiblich n (%)	5 (45,5)
Alter >65 Jahren (%)	3 (27,3)
CCI median	3
Immunsuppression n (%)	8 (72,7)
Verstorben n (%)	7 (63,6)

231 influenza patients  
 36% immune suppressed  
 15,3% nosokomial infections  
 mortality 9% (71% immune suppressed)

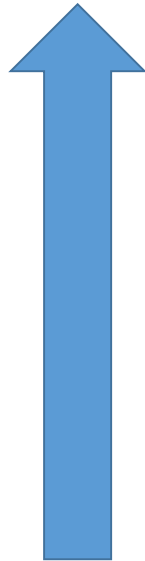


Still in hospital: 7Pts ICU, 10 ID ward

149 COVID-19 patients  
24,2% immune suppressed  
16,1% nosokomial infections  
mortality 14% (47,8% immune suppressed)

## Immuno suppression - only one of many risk factors ....

RISK for complications  
Increased mortality



**Hypertension**

**Age**

**Diabetes**

**Sex**

**BMI**

Hematologic disease

Ongoing Chemotherapy

**COPD/Lung disease**

Coronary heart disease

Heart failure

Kidney disease

Immunosuppression

Genetic factors ?

Virus strain

Size Viral inoculum

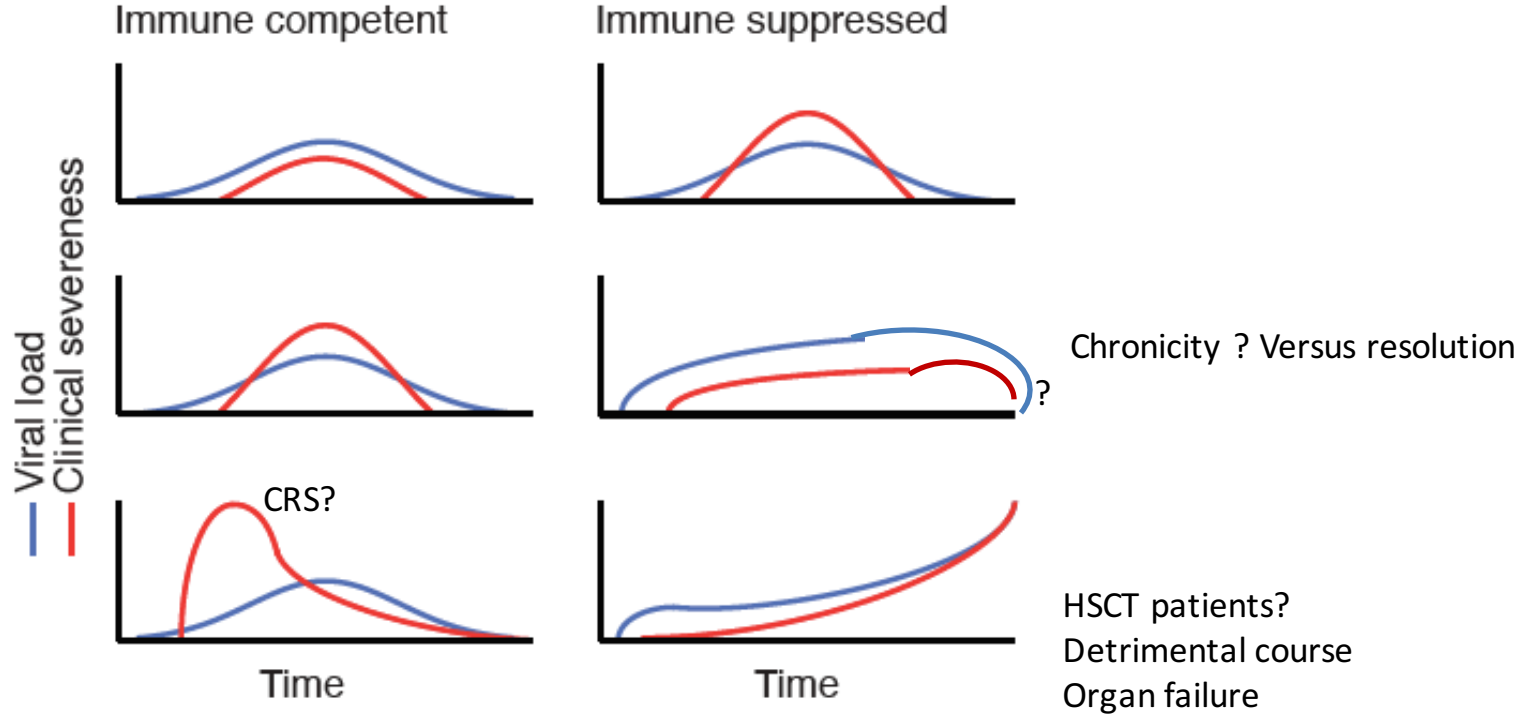
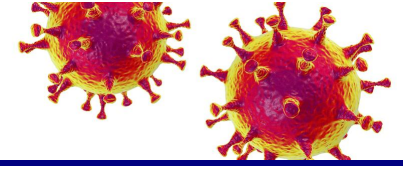
Cirrhosis

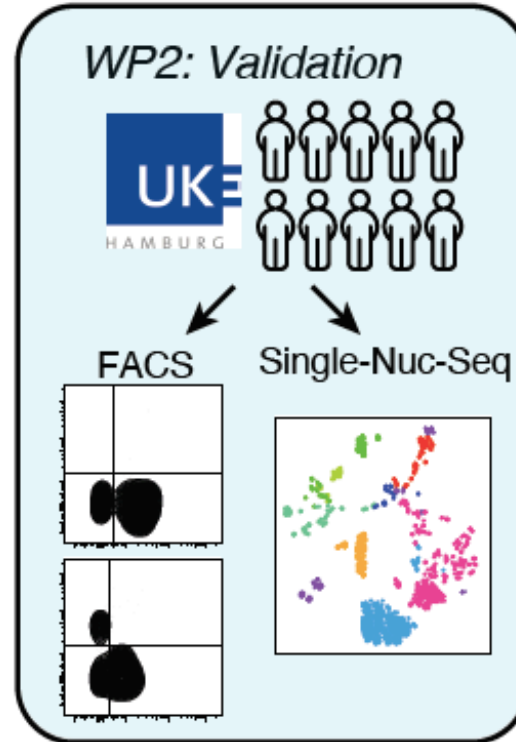
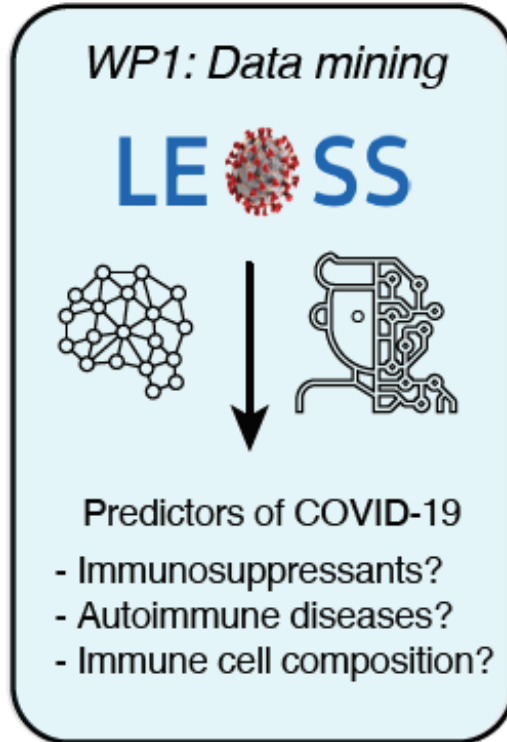
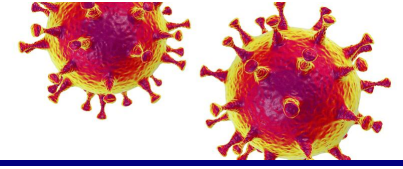
Etc..

Risk factors seem to add up

Generally mild disease course

Source: SzW -his own observations and hypothesis







# Take home messages

- **First rule: we have to calm our patients (and ourselves) - there is a lot of fear!**
  - Stay on their stable immunosuppressant medications,
  - Stay in good health (light training, sleep, food)
  - Stick to the general COVID-19 distance/hygiene rules
  - There are COVID-19 guidelines issued by the respective medical society
  - Update vaccination status
  - There is no preemptive -COVID-19 medication-
  - Do not schedule unnecessary appointments but do also not cancel necessary ones.
- **The clinical COVID-19 course of immunosuppressed course can vary greatly:**
  - Mostly benign course (some patients might have even fewer symptoms)
  - Some might have higher SARS-Cov2 PCR CT values in swabs and even viremia!
  - Sometimes longer PCR+- chronicity, relapse ? Eg swabs+ sputum+
  - In some patients no/weak/delayed Ab response develops
  - HSCT COVID-19 patients seem to have dismal outcome
  - Immunosuppressants as needed for primary disease
  - Treat COVID-19 with same with supportive treatment as immunocompetent patient
  - Interdisciplinary thinking - boards - especially before planned off-label treatment
- **Let´s be vigilant and avoid In-hospital outbreak situations**
  - Cave: Tx , cancer and HSCT wards !
  - Test, test, test
- **We need to learn much more about COVID-19 in the immunosuppressed patient.**