


# COVID-19

## *'Red flags' on our learning journey*


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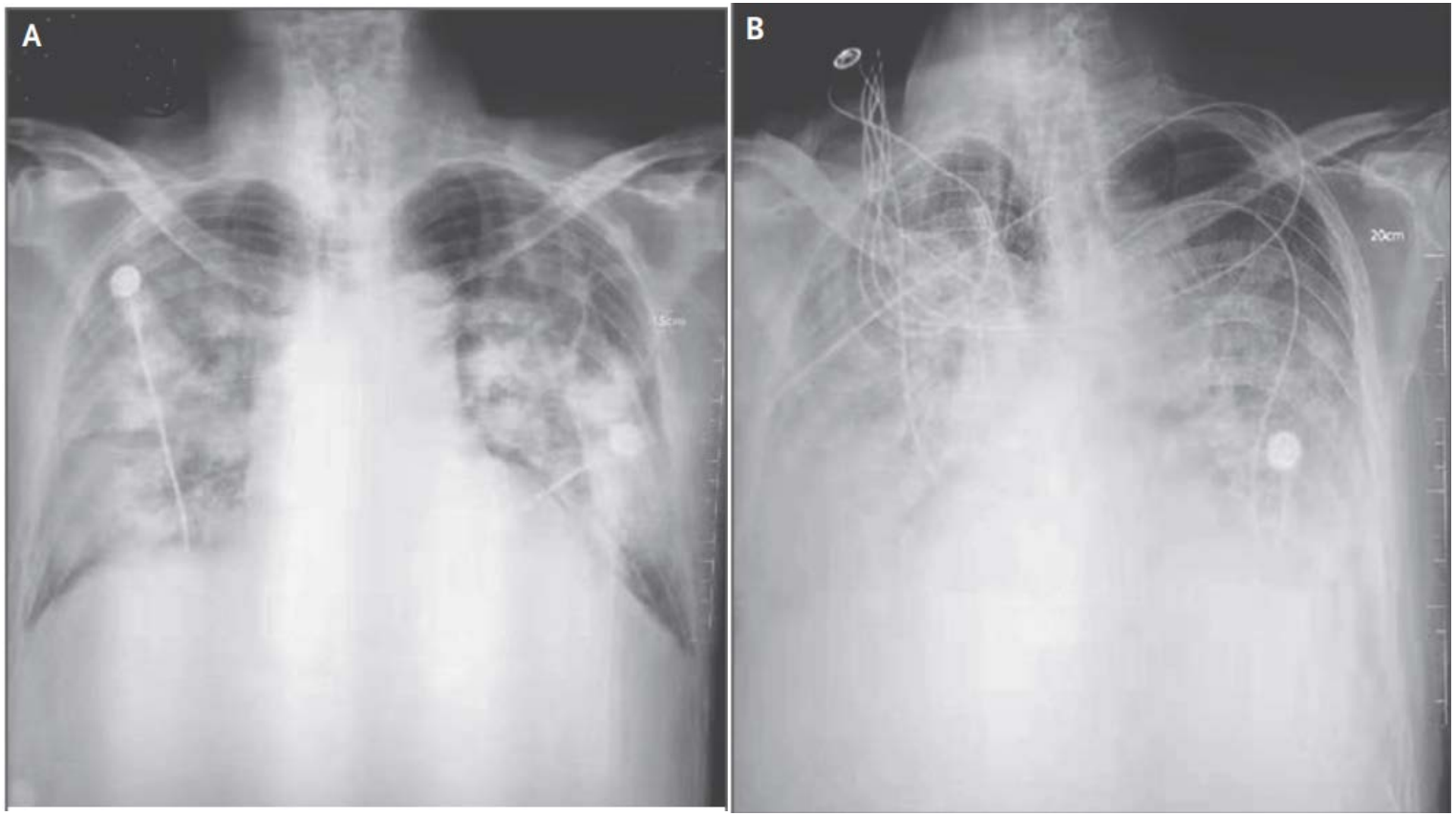
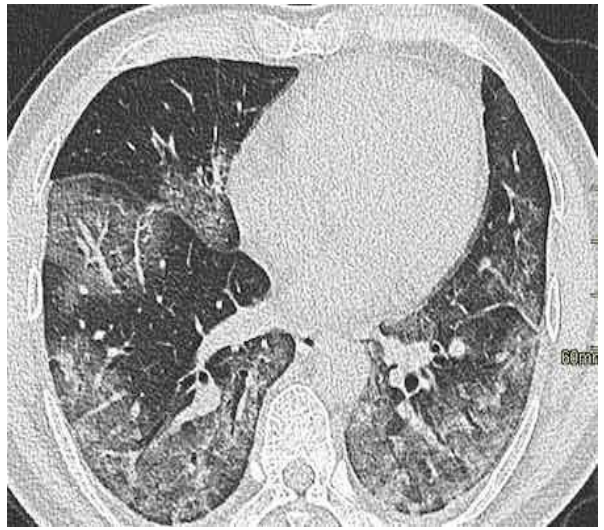
Professor of Medicine

Dept. of Viroscience
Erasmus MC

# Kliniek



JAMA | Original Investigation

# Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area

Safiya Richardson, MD, MPH; Jamie S. Hirsch, MD, MA, MSB; Mangala Narasimhan, DO; James M. Crawford, MD, PhD; Thomas McGinn, MD, MPH; Karina W. Davidson, PhD, MASc; and the Northwell COVID-19 Research Consortium

## Key Points

**Question** What are the characteristics, clinical presentation, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19) in the US?

**Findings** In this case series that included 5700 patients hospitalized with COVID-19 in the New York City area, the most common comorbidities were hypertension, obesity, and diabetes. Among patients who were discharged or died (n = 2634), 14.2% were treated in the intensive care unit, 12.2% received invasive mechanical ventilation, 3.2% were treated with kidney replacement therapy, and 21% died.

**Meaning** This study provides characteristics and early outcomes of patients hospitalized with COVID-19 in the New York City area.

| Comorbidities | |
|---|---|
| Total No. | 5700 |
| Cancer | 320 (6) |
| Cardiovascular disease | |
| Hypertension | 3026 (56.6) |
| Coronary artery disease | 595 (11.1) |
| Congestive heart failure | 371 (6.9) |
| Chronic respiratory disease | |
| Asthma | 479 (9) |
| Chronic obstructive pulmonary disease | 287 (5.4) |
| Obstructive sleep apnea | 154 (2.9) |
| Immunosuppression | |
| HIV | 43 (0.8) |
| History of solid organ transplant | 55 (1) |
| Kidney disease | |
| Chronic[c] | 268 (5) |
| End-stage[d] | 186 (3.5) |
| Liver disease | |
| Cirrhosis | 19 (0.4) |
| Chronic | |
| Hepatitis B | 8 (0.1) |
| Hepatitis C | 3 (0.1) |
| Metabolic disease | |
| Obesity (BMI ≥30) | 1737 (41.7) |
| No. | 4170 |
| Morbid obesity (BMI ≥35) | 791 (19.0) |
| No. | 4170 |
| Diabetes[e] | 1808 (33.8) |

Table 1. Baseline Characteristics of Patients Hospitalized With COVID-19 (continued)

| | No. (%) |
|---|---|
| Never smoker | 3009 (84.4) |
| No. | 3567 |
| Comorbidities[f] | |
| None | 350 (6.1) |
| 1 | 359 (6.3) |
| >1 | 4991 (88) |
| Total, median (IQR) | 4 (2-8) |
| Charlson Comorbidity Index score, median (IQR)[g] | 4 (2-6) |

5700 hospitalized patients

Co-morbidity
- Hypertension 56%
- Obesity 41.7%
- Diabetes 33.8%

ICU treatment 14.2%

Mortality 21%

# De kliniek

## Op de ICU twee phenotypes

Review > Respir Physiol Neurobiol. 2020 Aug;279:103455. doi: 10.1016/j.resp.2020.103455. Epub 2020 May 11.

**Distinct phenotypes require distinct respiratory management strategies in severe COVID-19**

Chiara Robba [1], Denise Battaglini [2], Lorenzo Ball [3], Nicolo' Patroniti [4], Maurizio Loconte [5], Iole Brunetti [6], Antonio Vena [7], Daniele Roberto Giacobbe [8], Matteo Bassetti [9], Patricia Rieken Macedo Rocco [10], Paolo Pelosi [11]

- [Hyper]-inflammatoir phenotype

Beeld van een viro-sepsis

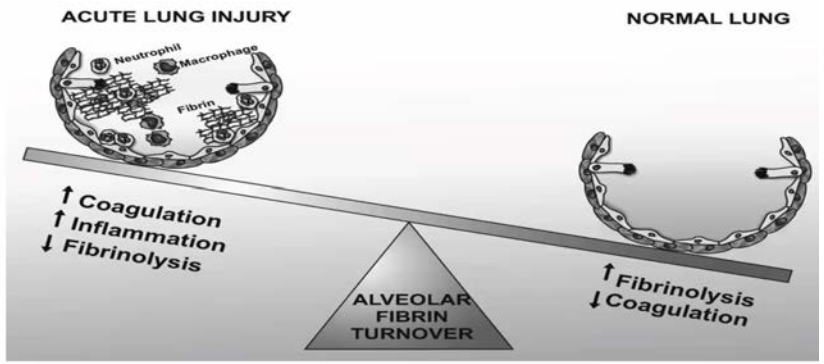
- Hypercoagualibiliteit phenotype

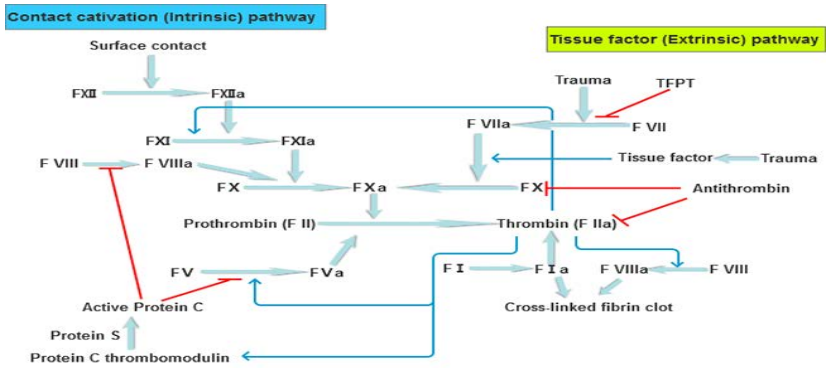
+/- 50% ptn op ICU longembolie/ intrinsieke stolling long

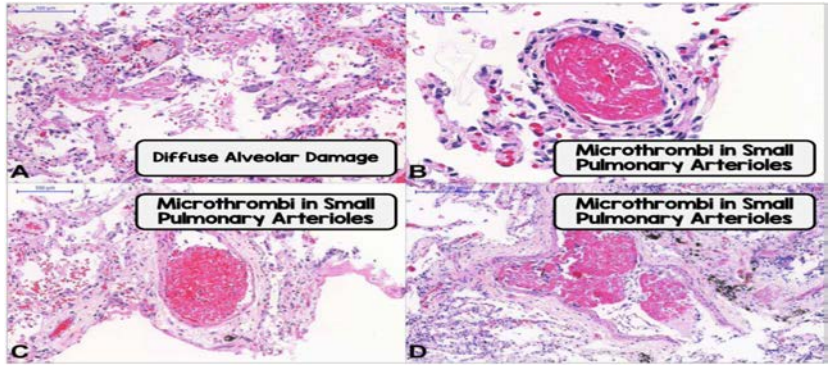
# COVID-19 and coagulopathy

DutchCOVID & Thrombosis Coalition

*ZonMW & Thrombosestichting Nederland*




Coagulation system evolved as an effector pathway of the immune system

The endpoint of inflammation is thrombosis

Treat the underlying infection/ inflammatory process

# Behandeling

- Antiviralen *[r/Remdesivir]*


ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

John H. Beigel, M.D., Kay M. Tomashek, M.D., M.P.H., Lori E. Dodd, Ph.D., Aneesh K. Mehta, M.D., Barry S. Zingman, M.D., Andre C. Kalil, M.D., M.P.H., Elizabeth Hohmann, M.D., Helen Y. Chu, M.D., M.P.H., Annie Luetkemeyer, M.D., Susan Kline, M.D., M.P.H., Diego Lopez de Castilla, M.D., M.P.H., Robert W. Finberg, M.D., et al., for the ACTT-1 Study Group Members*

- Dexamethason


September 2, 2020

**Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19**

The CoDEX Randomized Clinical Trial

Bruno M. Tomazini, MD[1,2]; Israel S. Maia, MD, MSc[3,4]; Alexandre B. Cavalcanti, MD, PhD[3,4]; et al

Author Affiliations | Article Information

JAMA. 2020;324(13):1307-1316. doi:10.1001/jama.2020.17021

- Antistolling

DutchCOVID & Thrombosis Coalition

- Plasma *[Antistoffen]*

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The NEW ENGLAND JOURNAL of MEDICINE

# Anti-virals

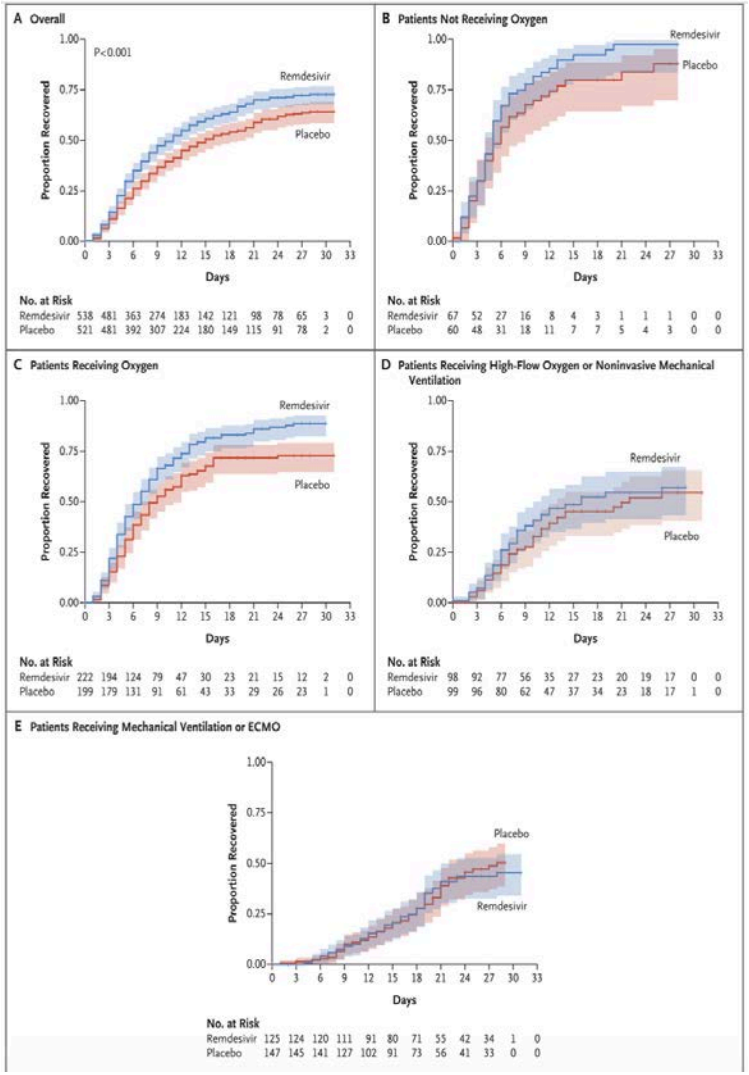
## Abstract

**Background:** Although several therapeutic agents have been evaluated for the treatment of coronavirus disease 2019 (Covid-19), none have yet been shown to be efficacious.

**Methods:** We conducted a double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults hospitalized with Covid-19 with evidence of lower respiratory tract involvement. Patients were randomly assigned to receive either remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) or placebo for up to 10 days. The primary outcome was the time to recovery, defined by either discharge from the hospital or hospitalization for infection-control purposes only.

**Results:** A total of 1063 patients underwent randomization. The data and safety monitoring board recommended early unblinding of the results on the basis of findings from an analysis that showed shortened time to recovery in the remdesivir group. Preliminary results from the 1059 patients (538 assigned to remdesivir and 521 to placebo) with data available after randomization indicated that those who received remdesivir had a median recovery time of 11 days (95% confidence interval [CI], 9 to 12), as compared with 15 days (95% CI, 13 to 19) in those who received placebo (rate ratio for recovery, 1.32; 95% CI, 1.12 to 1.55; P<0.001). The Kaplan-Meier estimates of mortality by 14 days were 7.1% with remdesivir and 11.9% with placebo (hazard ratio for death, 0.70; 95% CI, 0.47 to 1.04). Serious adverse events were reported for 114 of the 541 patients in the remdesivir group who underwent randomization (21.1%) and 141 of the 522 patients in the placebo group who underwent randomization (27.0%).

**Conclusions:** Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with Covid-19 and evidence of lower respiratory tract infection. (Funded by the National Institute of Allergy and Infectious Diseases and others; ACCT-1 ClinicalTrials.gov number, NCT04280705.).




Cumulative recovery estimates are shown in the overall population (Panel A), in patients with a baseline score of 4 on the ordinal scale (not receiving oxygen; Panel B), in those with a baseline score of 5 (receiving oxygen; Panel C), in those with a baseline score of 6 (receiving high-flow oxygen or noninvasive mechanical ventilation; Panel D), and in those with a baseline score of 7 (receiving mechanical ventilation or ECMO; Panel E).

Table 1. Demographic and Clinical Characteristics at Baseline.*

| Characteristic | All (N=1063) | Remdesivir (N=541) | Placebo (N=522) |
|---|---|---|---|
| Age — yr | 58.9±15.0 | 58.6±14.6 | 59.2±15.4 |
| Male sex — no. (%) | 684 (64.3) | 352 (65.1) | 332 (63.6) |
| Race or ethnic group — no. (%)† | | | |
| American Indian or Alaska Native | 7 (0.7) | 4 (0.7) | 3 (0.6) |
| Asian | 134 (12.6) | 77 (14.2) | 57 (10.9) |
| Black or African American | 219 (20.6) | 108 (20.0) | 111 (21.3) |
| White | 565 (53.2) | 279 (51.6) | 286 (54.8) |
| Hispanic or Latino — no. (%) | 249 (23.4) | 132 (24.4) | 117 (22.4) |
| Median time (IQR) from symptom onset to randomization — days‡ | 9 (6–12) | 9 (6–12) | 9 (7–13) |
| No. of coexisting conditions — no. /total no. (%)‡ | | | |
| None | 193/920 (21.0) | 91/467 (19.5) | 102/453 (22.5) |
| One | 248/920 (27.0) | 131/467 (28.1) | 117/453 (25.8) |
| Two or more | 479/920 (52.1) | 245/467 (52.5) | 234/453 (51.7) |
| Coexisting conditions — no./total no. (%) | | | |
| Hypertension | 460/928 (49.6) | 231/469 (49.3) | 229/459 (49.9) |
| Obesity | 342/925 (37.0) | 177/469 (37.7) | 165/456 (36.2) |
| Type 2 diabetes | 275/927 (29.7) | 144/470 (30.6) | 131/457 (28.7) |
| Score on ordinal scale — no. (%) | | | |
| 4. Hospitalized, not requiring supplemental oxygen, requiring ongoing medical care (Covid-19–related or otherwise) | 127 (11.9) | 67 (12.4) | 60 (11.5) |
| 5. Hospitalized, requiring supplemental oxygen | 421 (39.6) | 222 (41.0) | 199 (38.1) |
| 6. Hospitalized, receiving noninvasive ventilation or high-flow oxygen devices | 197 (18.5) | 98 (18.1) | 99 (19.0) |
| 7. Hospitalized, receiving invasive mechanical ventilation or ECMO | 272 (25.6) | 125 (23.1) | 147 (28.2) |
| Baseline score missing | 46 (4.3) | 29 (5.4) | 17 (3.3) |

# Dexamethason

September 2, 2020

## Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19

### The CoDEX Randomized Clinical Trial

Bruno M. Tomazini, MD[1,2]; Israel S. Maia, MD, MSc[3,4]; Alexandre B. Cavalcanti, MD, PhD[3,4]; et al

≫ Author Affiliations | Article Information

*JAMA*. 2020;324(13):1307-1316. doi:10.1001/jama.2020.17021

## Conclusions

In patients with COVID-19 and moderate or severe ARDS, use of intravenous dexamethasone plus standard care, compared with standard care alone, resulted in a statistically significant increase increase in the number of ventilator-free days (days alive and free of mechanical ventilation) over 28 days.

NOS

# Afweerremmer geeft ziekste covid-19-patiënten betere kansen

19 novemebr 2020

De onderzoekers kunnen nog niet zeggen hoeveel minder sterfte er optreedt in de groep die tocilizumab kreeg en de controlegroep die het niet kreeg. Ook is nog niet duidelijk hoeveel korter de patiënten uit de tocilizumab-groep op de IC lagen en aan apparaten die hun vitale functies overnamen.

Ernstig zieke covid-19-patiënten die behandeld worden met de afweerremmer tocilizumab hebben bijna twee keer zoveel kans op een beter verloop van hun ziekte als patiënten die het middel niet krijgen. Dat is gemeten op basis van overleving van de ziekenhuisopname én van de duur van de beademing en andere ondersteuning van organen die ze nodig hadden op de intensive care.

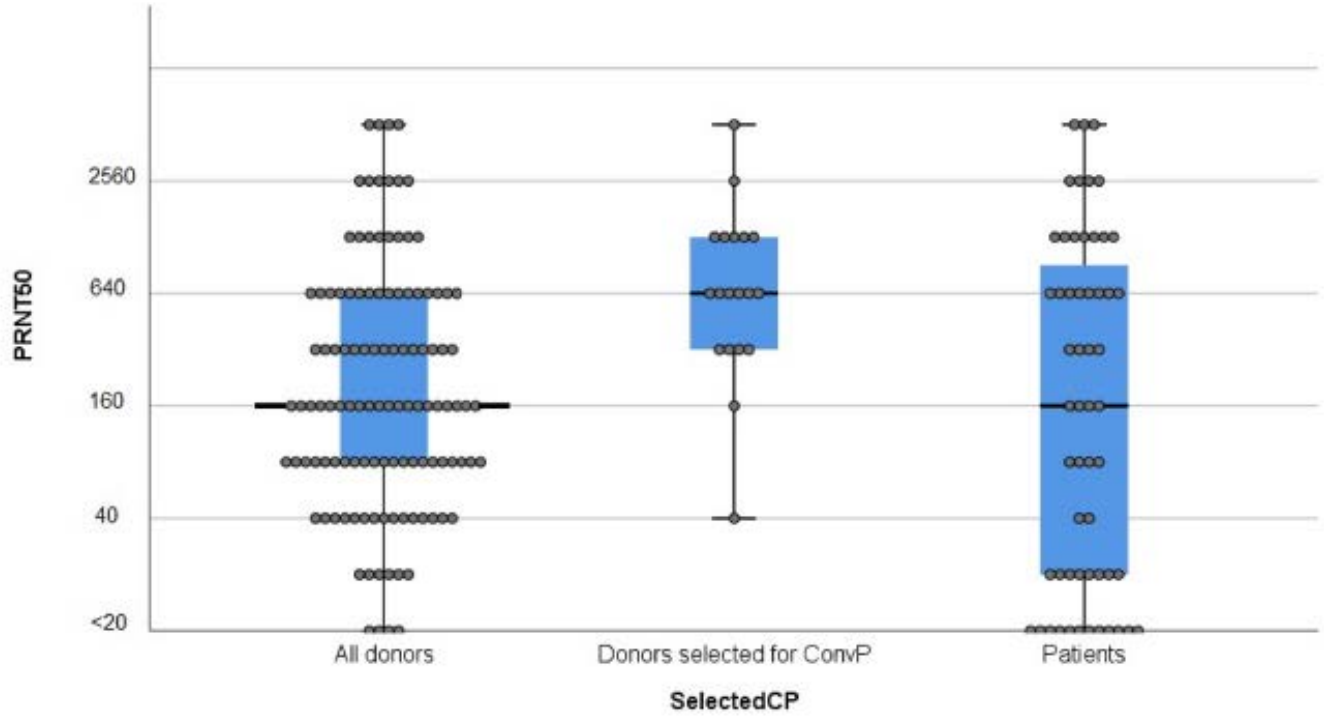
# Reconvalescent plasma [antibodies]

- Antibodies from donors for prophylaxis and/or treatment ?

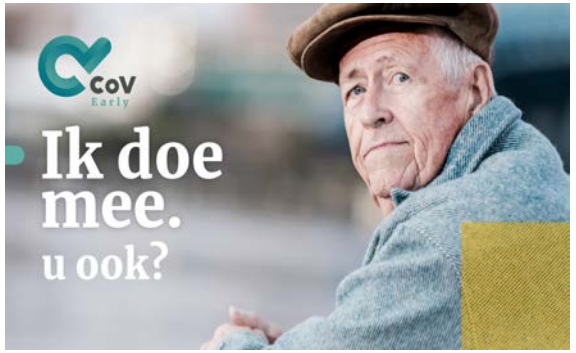
- Risk for antibody dependent enhancement ??

# Treatment study
## *Patients*
### *Convalescent-plasma-for-COVID (ConCOVID) study*

(Gharbharan et al., medRxiv 2020.07.01.20139857; doi: https://doi.org/10.1101/2020.07.01.20139857 )



# CoV-Early studie




- Bewezen COVID19 infectie

***Inclusie criteria***

Patient die nog geen 7d ziek is en minstens 50 jaar oud komt misschien in aanmerking.

70j of ouder : Patient kan altijd meedoen

50-69 en man: Kan altijd meedoen

50-69 en vrouw: Alleen indien ook bepaalde comorbiditeit

covearly.study@erasmusmc.nl of b.rijnders@erasmusmc.nl

- < 7 dagen klachten

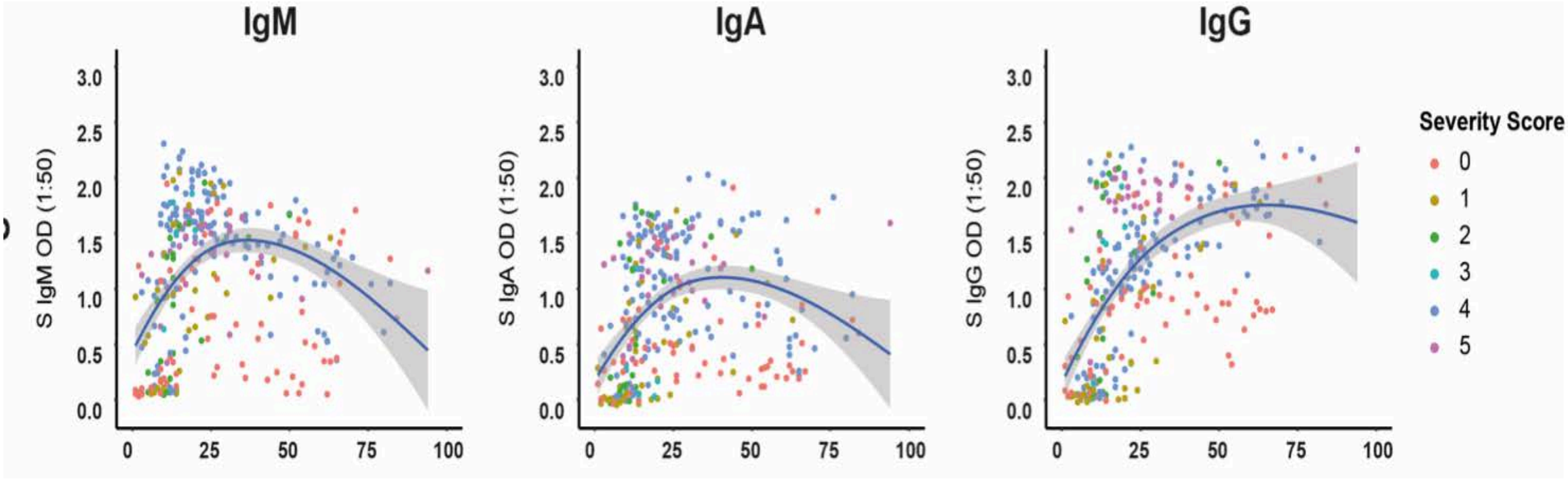
- Plasma therapie

# Antistoffen, hoe zit het nu?


- Duur bescherming [waning immunity] -> voorspellende waarde antistoftiters?
- Testen antistoffen in klinische setting zinvol of niet?
- Herd immunity, hoe zit dat?

# Longitudinal evaluation and decline of antibody responses in SARS-CoV-2 infection

## Longevity of the Ab response




->
time

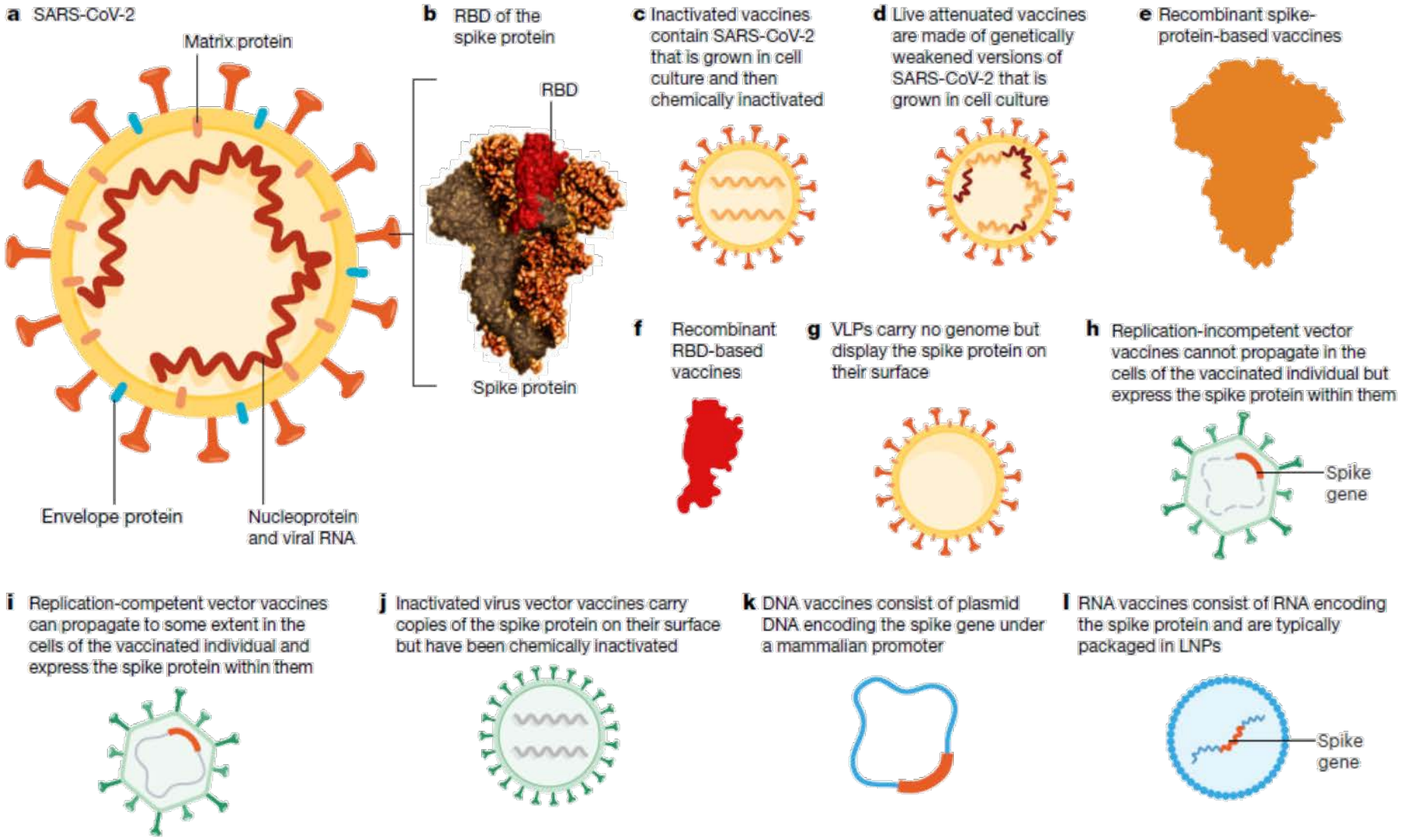
Jeffrey Seow et al
medRxiv preprint doi: https://doi.org/10.1101/2020.07.09.20148429

# Sneltesten

*belangrijke vragen vooraf*

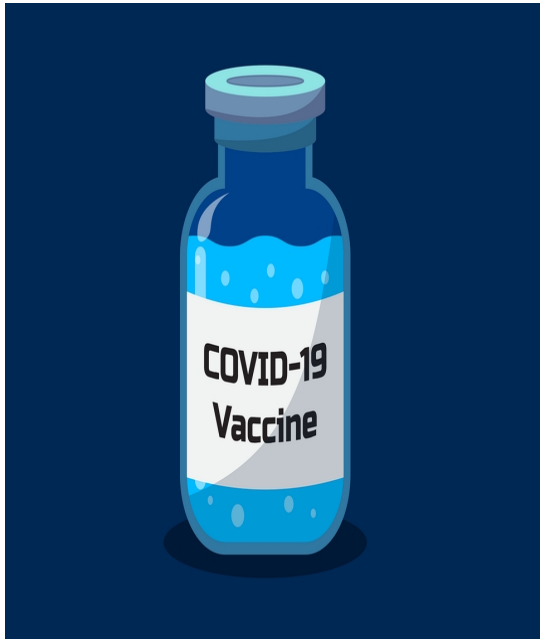

- Test eigenschappen *[validatie van de test]*
- Test eigenschappen *[sensitiviteit, specificiteit]?*
- Wanneer wordt test afgenomen in beloop van de klachten?

# Verschillende Corona vaccins in ontwikkeling




Florian Krammer, Nature 2020

# COVID-19 vaccin

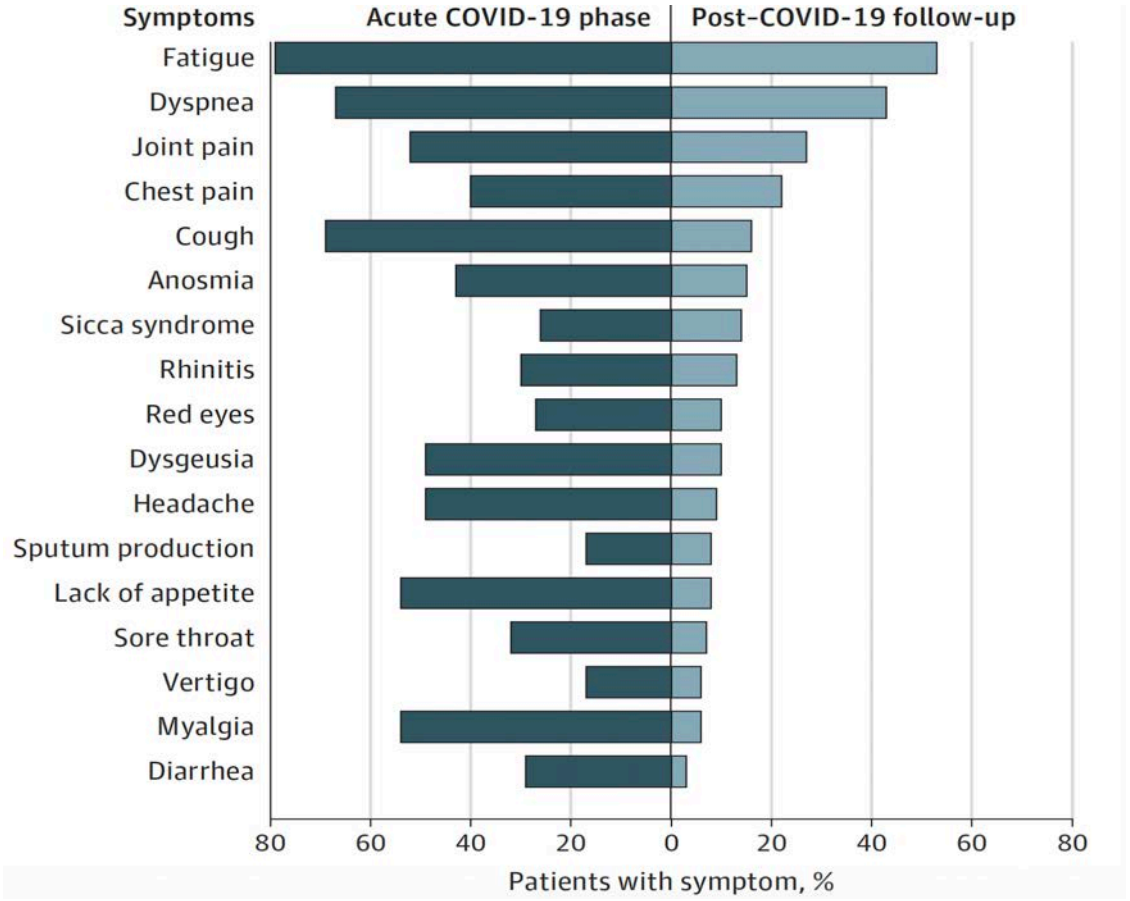



- Wanneer beschikbaar?
- Hoeveelheid beschikbare vaccins?
- Wie wordt als eerste gevaccineerd?
- Mate van bescherming *[besmetting vs ontwikkelen ziekte]*
- Duur bescherming?

# Lange termijn effecten

# Klinische symptomen in acute fase en 2 maanden follow-up in gehospitaliseerde COVID-19

Carfì A, Gemelli Against COVID-19 Post-Acute Care Study Group.
Persistent Symptoms in Patients After Acute COVID-19. *JAMA.* 2020



# Lange termijn effecten

- Pulmonaal

Restrictieve longschade

- Cardiaal

Myocarditis

- Neurologisch

Concentrarie stroornissen/ cognitieve stoornissen

- Algmeen

Vermoeidheid/ uithoudingsvermogen

# Cardiaal

> Cardiovasc Res. 2020 Aug 1;116(10):1666-1687. doi: 10.1093/cvr/cvaa106.

## COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options

Tomasz J Guzik [1 2], Saidi A Mohiddin [3 4], Anthony Dimarco [3], Vimal Patel [3], Kostas Savvatis [3], Federica M Marelli-Berg [4], Meena S Madhur [5], Maciej Tomaszewski [6], Pasquale Maffia [7 8], Fulvio D'Acquisto [9], Stuart A Nicklin [1], Ali J Marian [10], Ryszard Nosalski [1 2], Eleanor C Murray [1], Bartlomiej Guzik [11], Colin Berry [1], Rhian M Touyz [1], Reinhold Kreutz [12], Dao Wen Wang [13], David Bhella [14], Orlando Sagliocco [15], Filippo Crea [16], Emma C Thomson [7 14 17], Iain B McInnes [7]

**The most common complications include**

- Arrhythmia (atrial fibrillation, ventricular tachyarrhythmia, and ventricular fibrillation)
- Cardiac injury [elevated highly sensitive troponin I (hs-cTnI) and creatine kinase (CK) levels]
- Fulminant myocarditis
- Heart failure
- Pulmonary embolism
- Disseminated intravascular coagulation (DIC).

# Long

Review > Front Immunol. 2020 Jun 26;11:1626. doi: 10.3389/fimmu.2020.01626. eCollection 2020.

## Overview: Systemic Inflammatory Response Derived From Lung Injury Caused by SARS-CoV-2 Infection Explains Severe Outcomes in COVID-19

Rafael B Polidoro [1], Robert S Hagan [2], Roberta de Santis Santiago [3], Nathan W Schmidt [1]

- **Increased clotting tendency**

- **COVID-19 Associated Lung Injury (CALI)**

# Neurologisch

Review > J Neurol Sci. 2020 Oct 15;417:117085. doi: 10.1016/j.jns.2020.117085. Epub 2020 Aug 7.

## Neurological complications of coronavirus infection; a comparative review and lessons learned during the COVID-19 pandemic

Maryam Sharifian-Dorche [1], Philippe Huot [2], Michael Osherov [2], Dingke Wen [3], Alexander Saveriano [2], Paul S Giacomini [2], Jack P Antel [2], Ashkan Mowla [4]

225 studies on CoV infections associated neurological manifestations in human were reviewed.

The most common neurological complaints in COVID-19 were

**Anosmia, ageusia, headache and more serious complications, such as stroke, impairment of consciousness, seizures, and encephalopathy**

# Gedrag en het doorbreken van gewoonten

*behaviour and behavorial change*

Mensen creëren het risico en tegelijk hebben mensen de sleutel tot de oplossing

*People create the risk and at the same time people hold the key to the solution*

Menselijk gedrag is het sleutelwoord

*Human behavior is the keyword*




# COVID-19

*A learning journey*

VIROSCIENCE LAB
WHERE SKILLS MEET TO STUDY & PROTECT