



ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

COVID-19 global pandemic: where are we now?

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GEMS/Corona-Commissariaat

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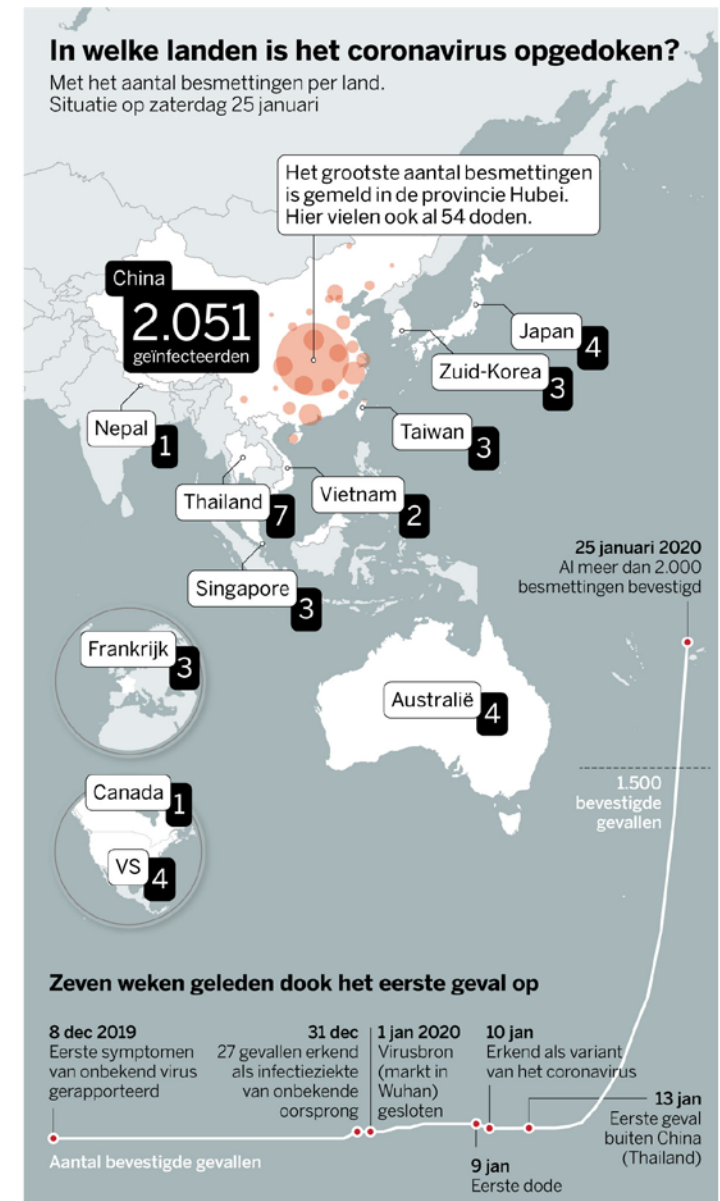
 **Hilde De Clerck**
January 4 at 12:22 PM · 🌐

😷 😷 Corona?!!



BLOOMBERG.COM
China Pneumonia Outbreak Spurs WHO Action as Mystery Lingers
A mysterious lung infection in the central Chinese city of Wuhan is being monitored by the World Health Organization.

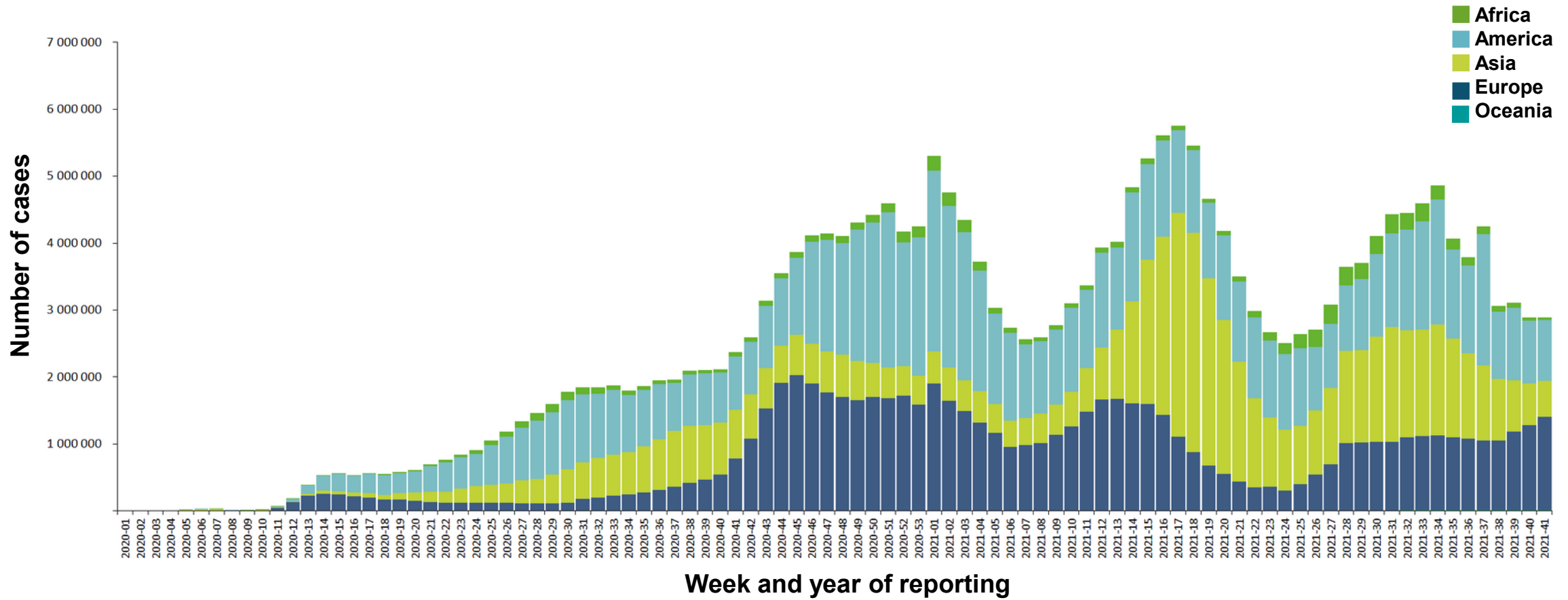
 **Jason Gale** ▶ **Global Outbreak Alert and Response Network**
January 4 at 10:17 AM · 🌐



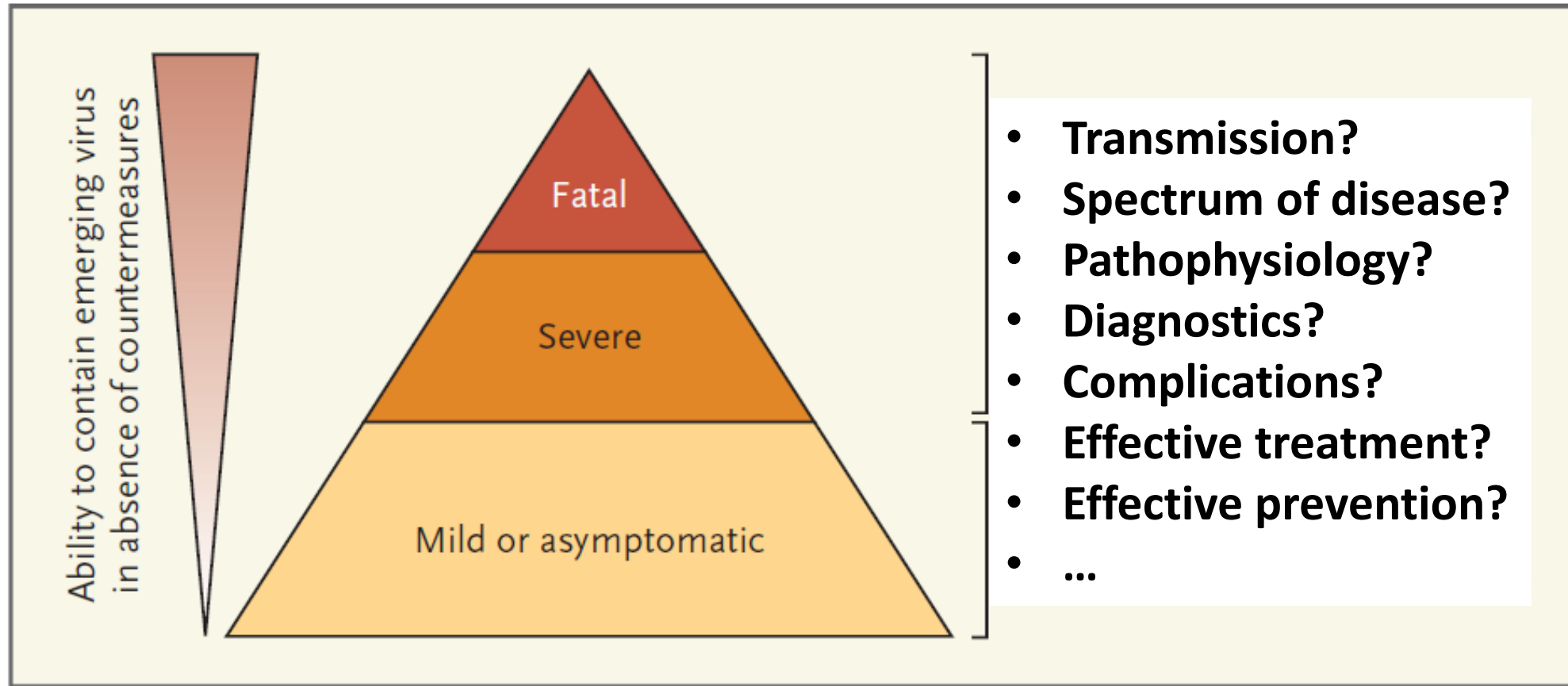
DS Infografiek | Bron: Reuters, Somagnews.com, who.int

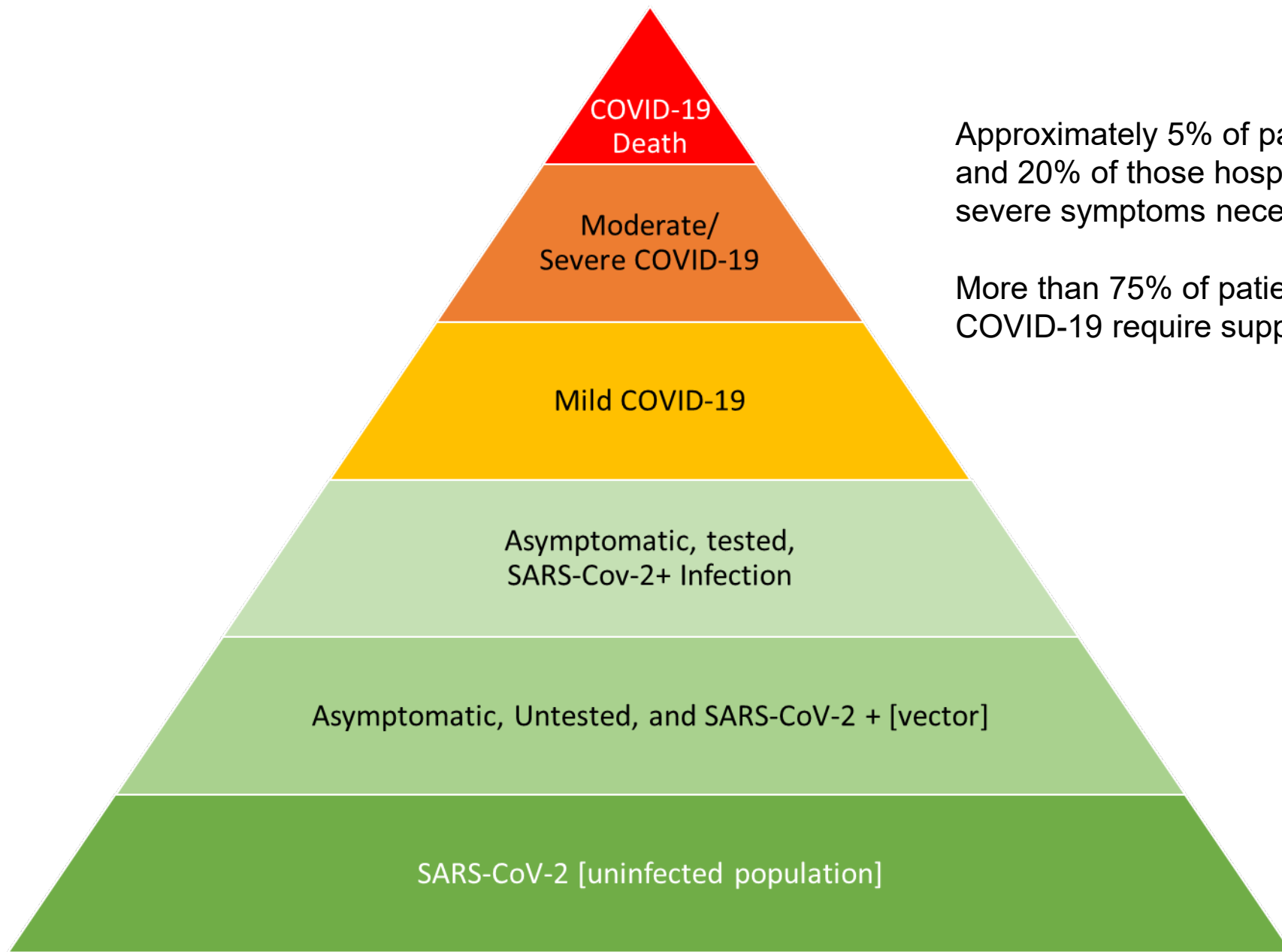


COVID-19 at a global scale



A new infectious disease was born...



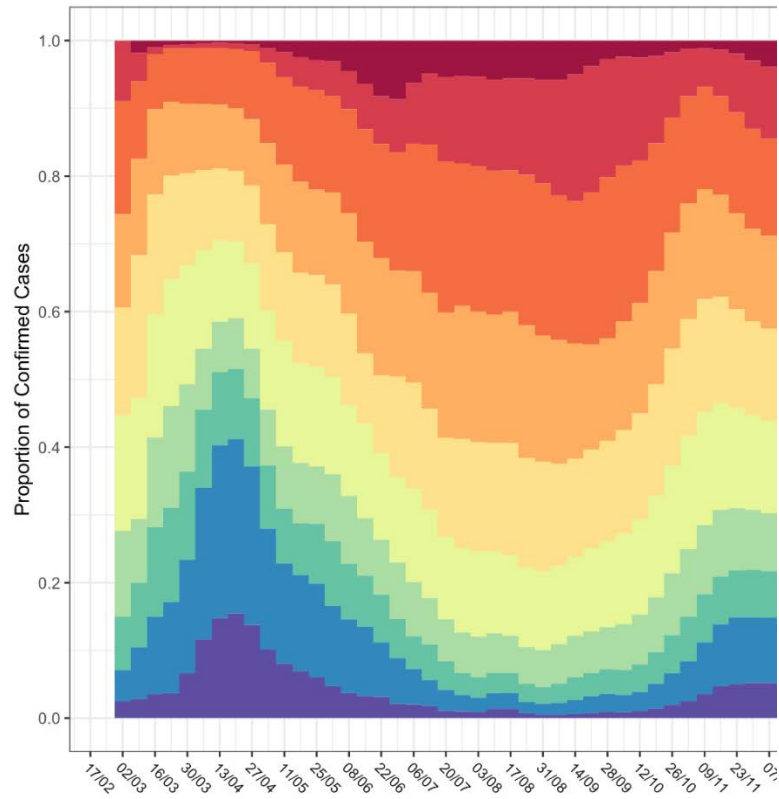


Approximately 5% of patients with COVID-19, and 20% of those hospitalized, experience severe symptoms necessitating intensive care.

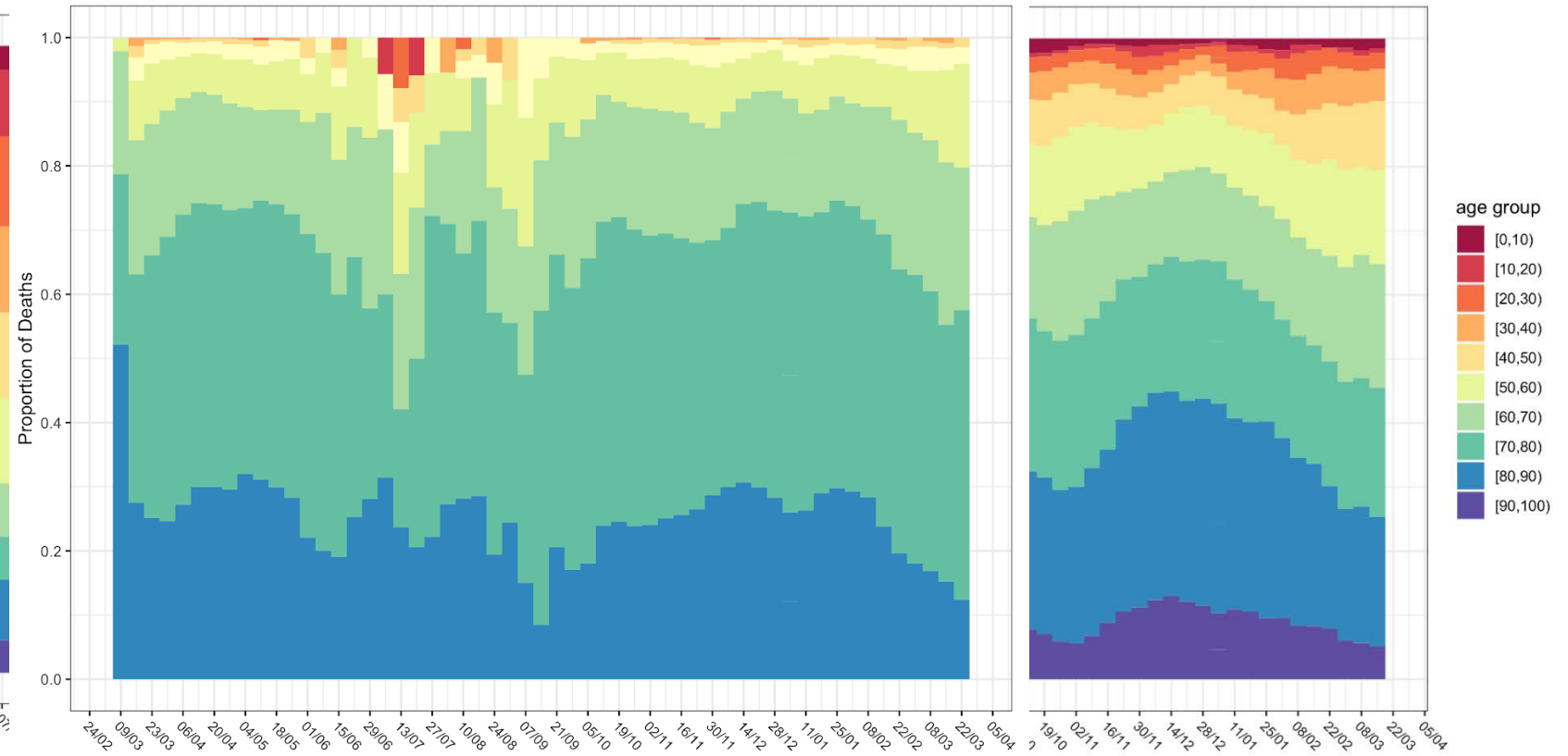
More than 75% of patients hospitalized with COVID-19 require supplemental oxygen



Cases

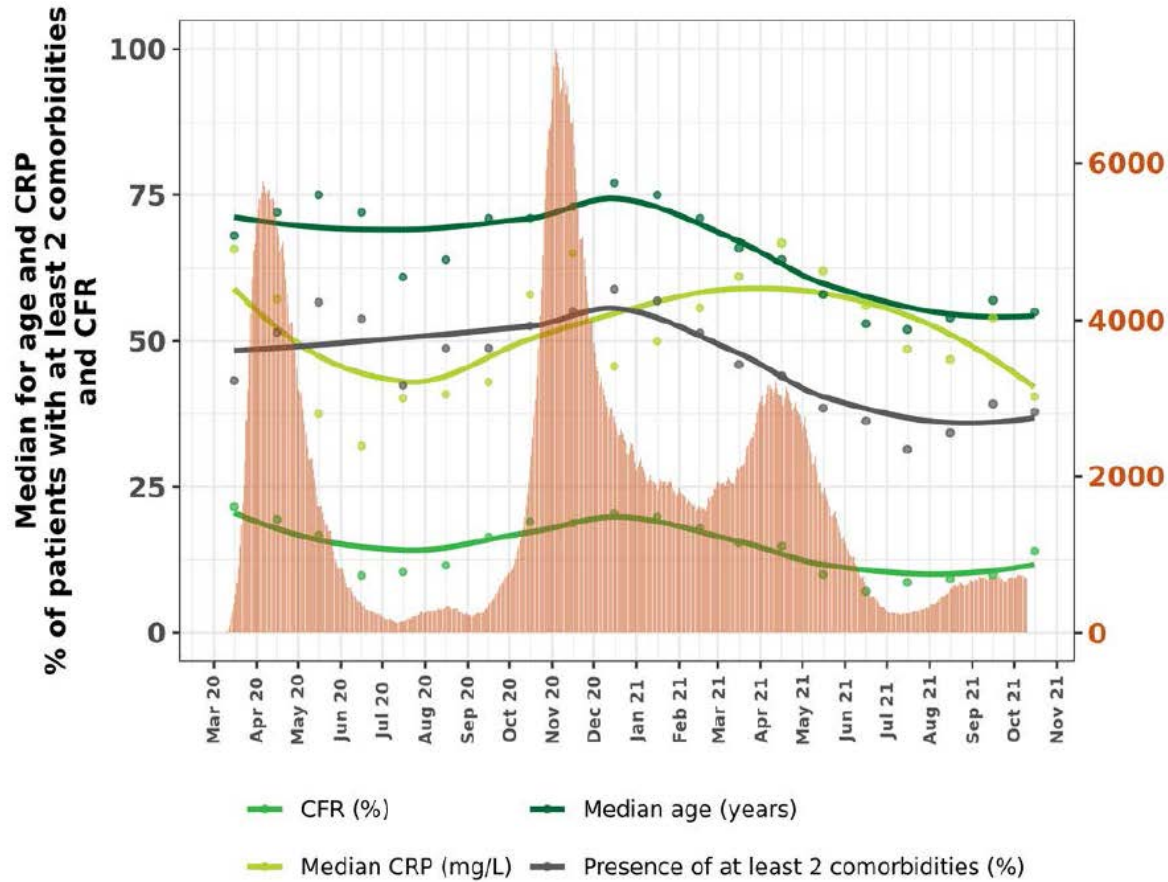


Hospitalisations

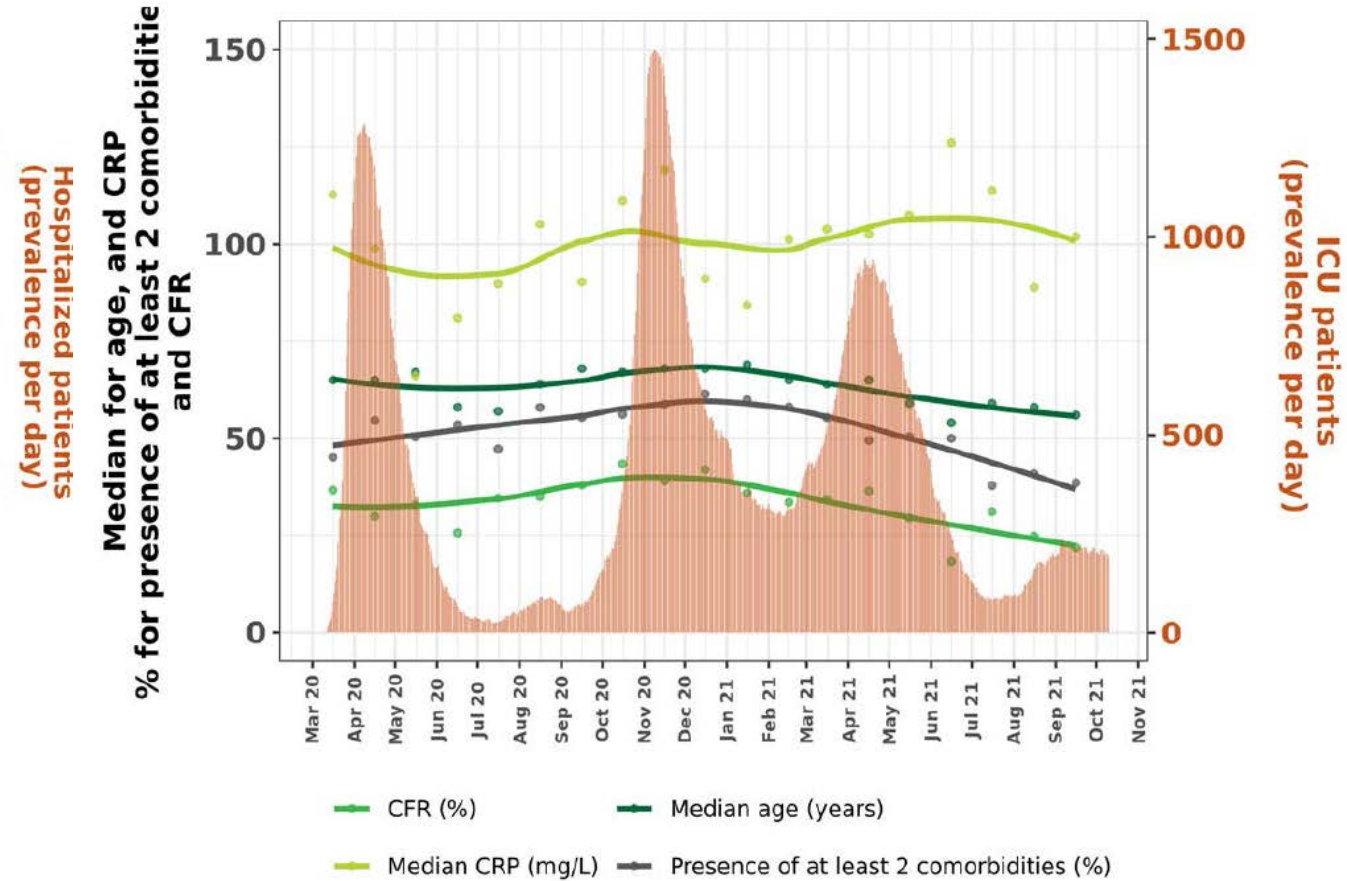


Hospital

ICU



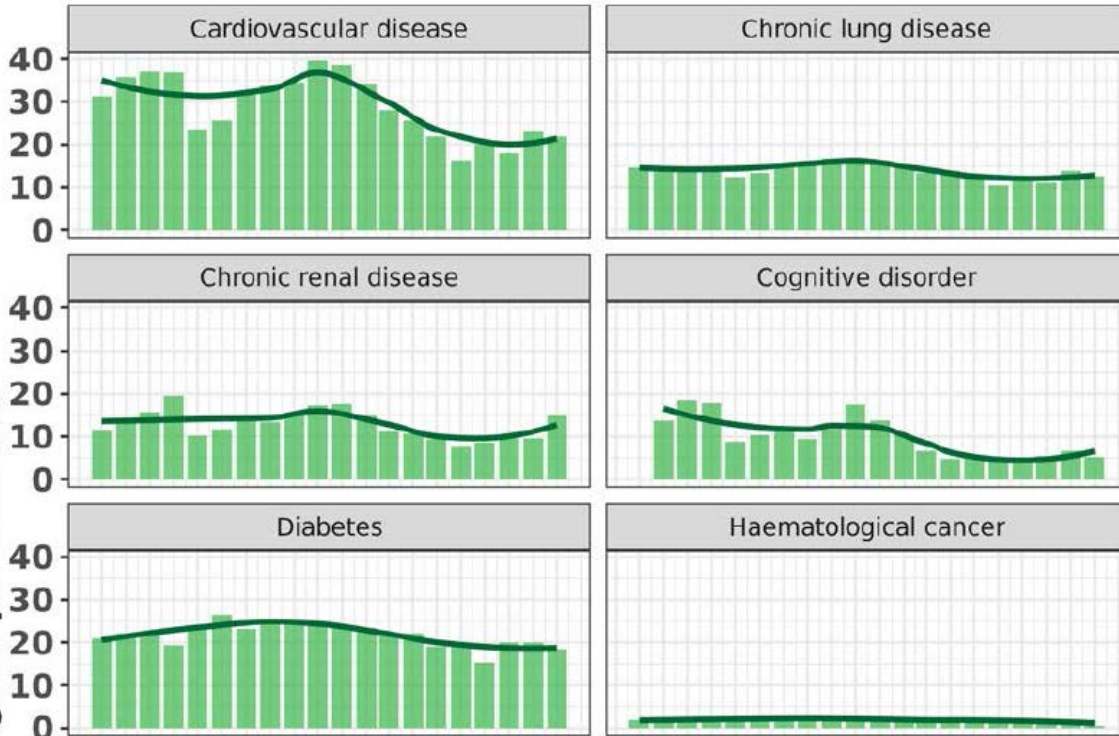
Actual CFR ~10%



Actual CFR ~24%

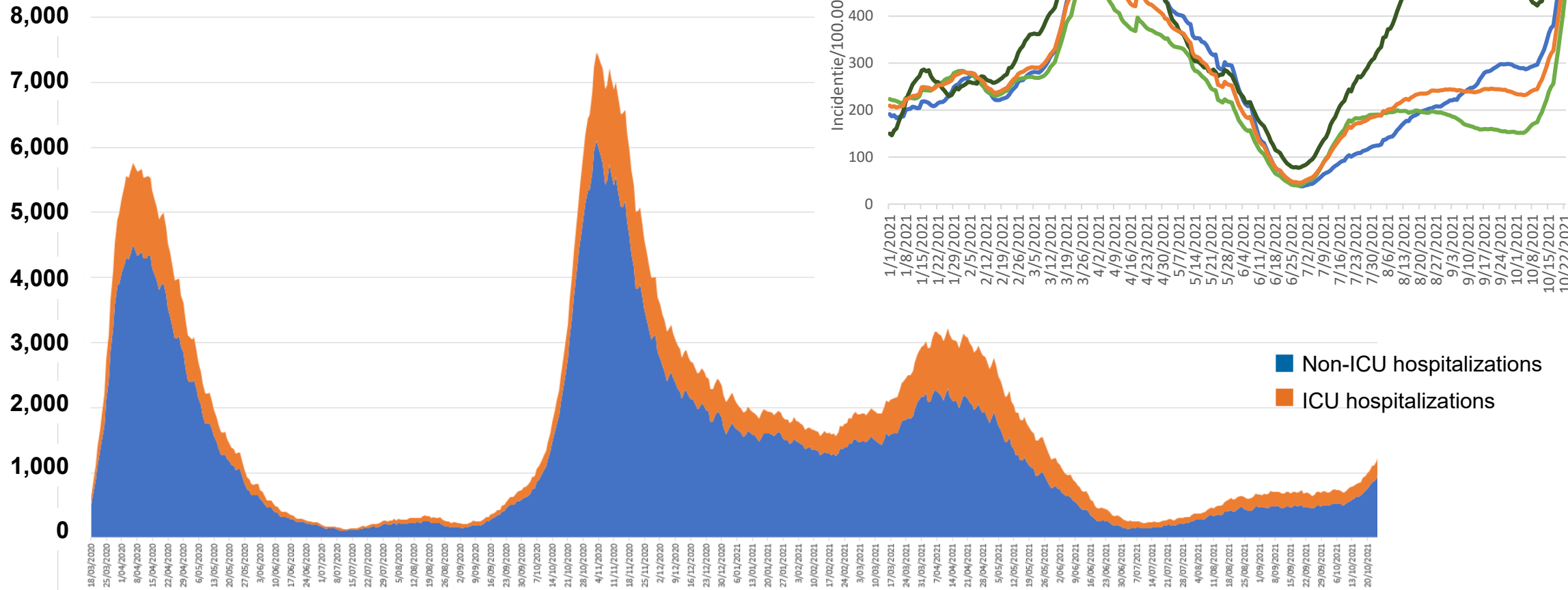


Co-morbidities (hospital)



COVID-19 in Belgium

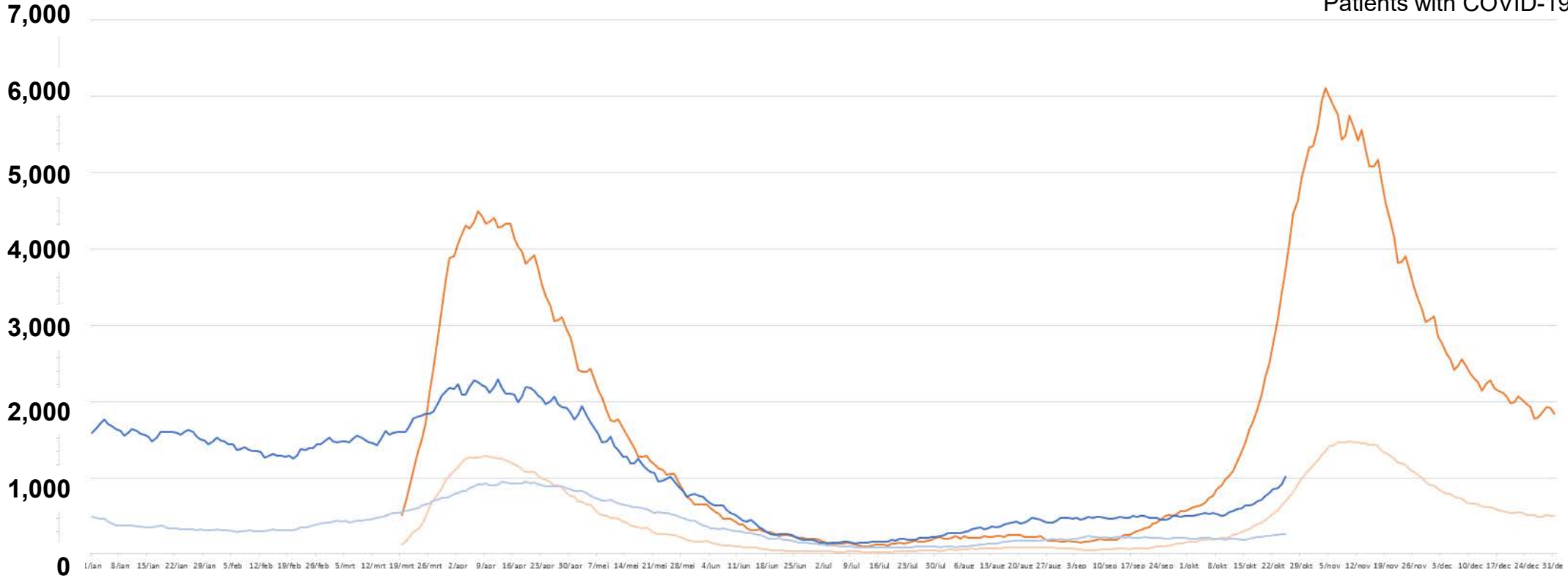
COVID-19 Hospital admissions



Fourth wave in Belgium

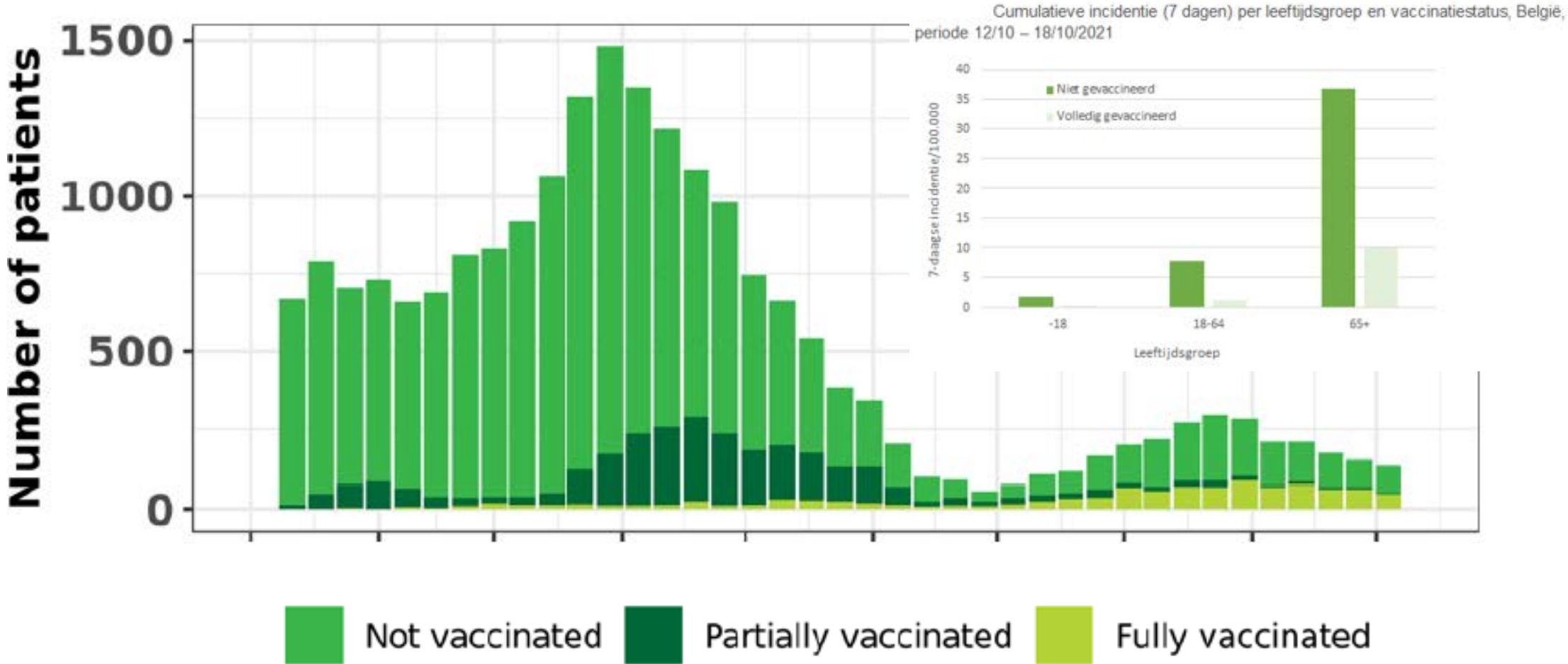
Waves comparison 2020-2021 Brussels

- Patients with COVID-19 non-ICU 2020
- Patients with COVID-19 in ICU 2020
- Patients with COVID-19 non-ICU 2021
- Patients with COVID-19 in ICU 2021

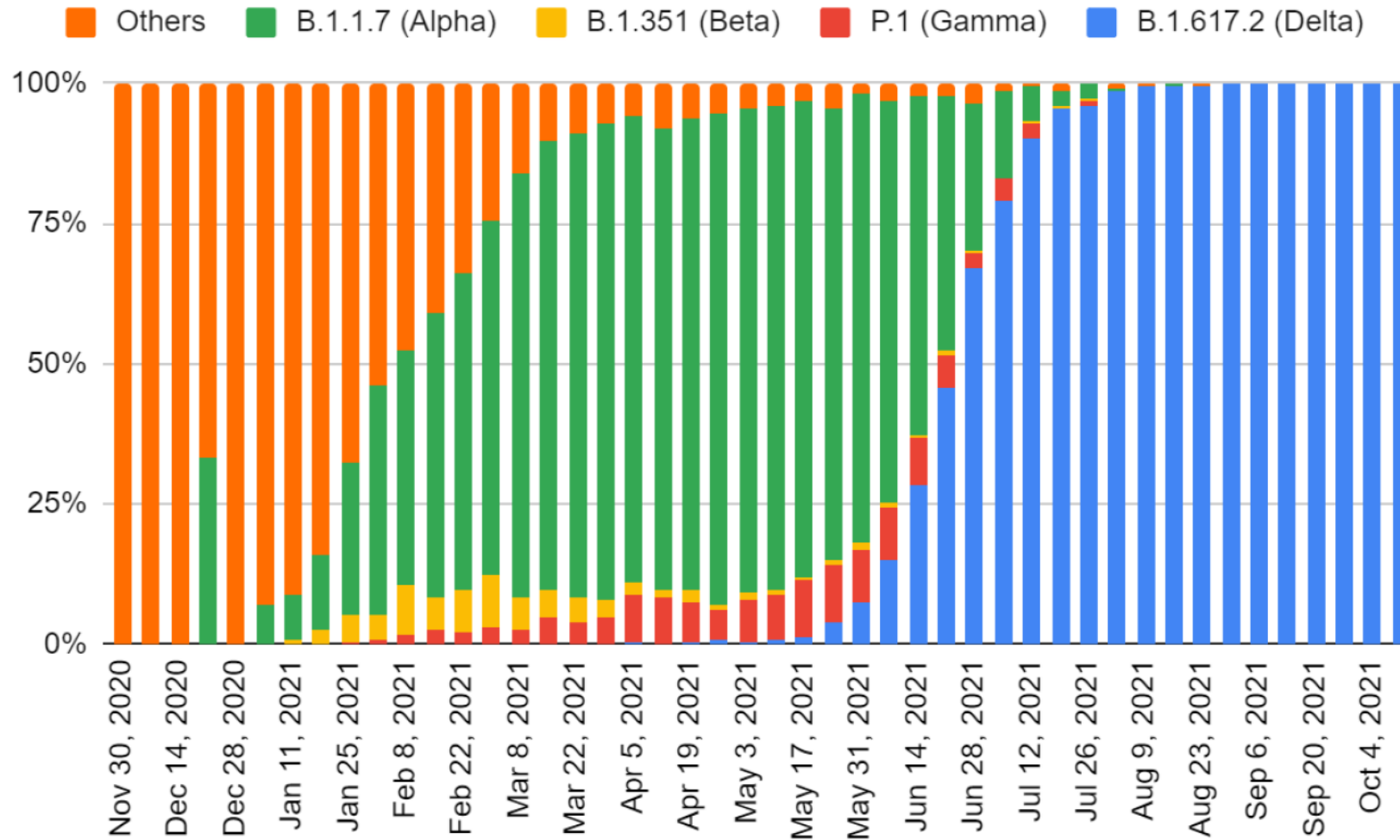


Who needs hospitalisation October 2021?

Hospitalisatie en incidentie (niet-) gevaccineerden



Weekly evolution of the frequency of variants of concern reported by the baseline surveillance network using a WGS approach



The power of delta

Infection (start with 4 infected people)	R0	After 10 generations	H.I.T. (perfect vaccine)
Seasonal influenza	1.5	684	33.3%
SARS-CoV-2 (first wave)	3.0	354.292	66.7%
SARS-CoV-2 (Alpha)	5.0	48,828,124 (~50 million)	80.0%
SARS-CoV-2 (Delta)	8.0	4,908,534,052 (~5 billion)	87.5%



Relation Cases – Hospitalizations for Belgium

Belgium: Effect on hospitalizations when confirmed cases double

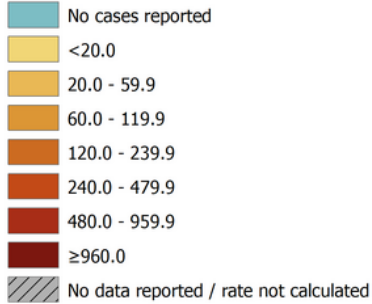
Wave	Time frame	Flanders	Wallonia	Brussels
Wave 2 (wildtype / Spanish)	31 August – 2 November 2020	54% [52%;56%]	51% [49%;54%]	51% [48%;54%]
Wave 3 (Alpha)	1 February – 12 April 2021	56% [55%;58%]	52% [50%;54%]	49% [47%;51%]
Wave 4 (Delta)	21 June – current	35% [34%;37%]	35% [33%;37%]	37% [35%;38%]



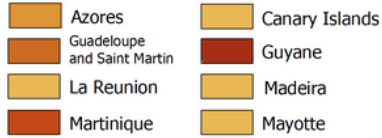
COVID-19 in Europe



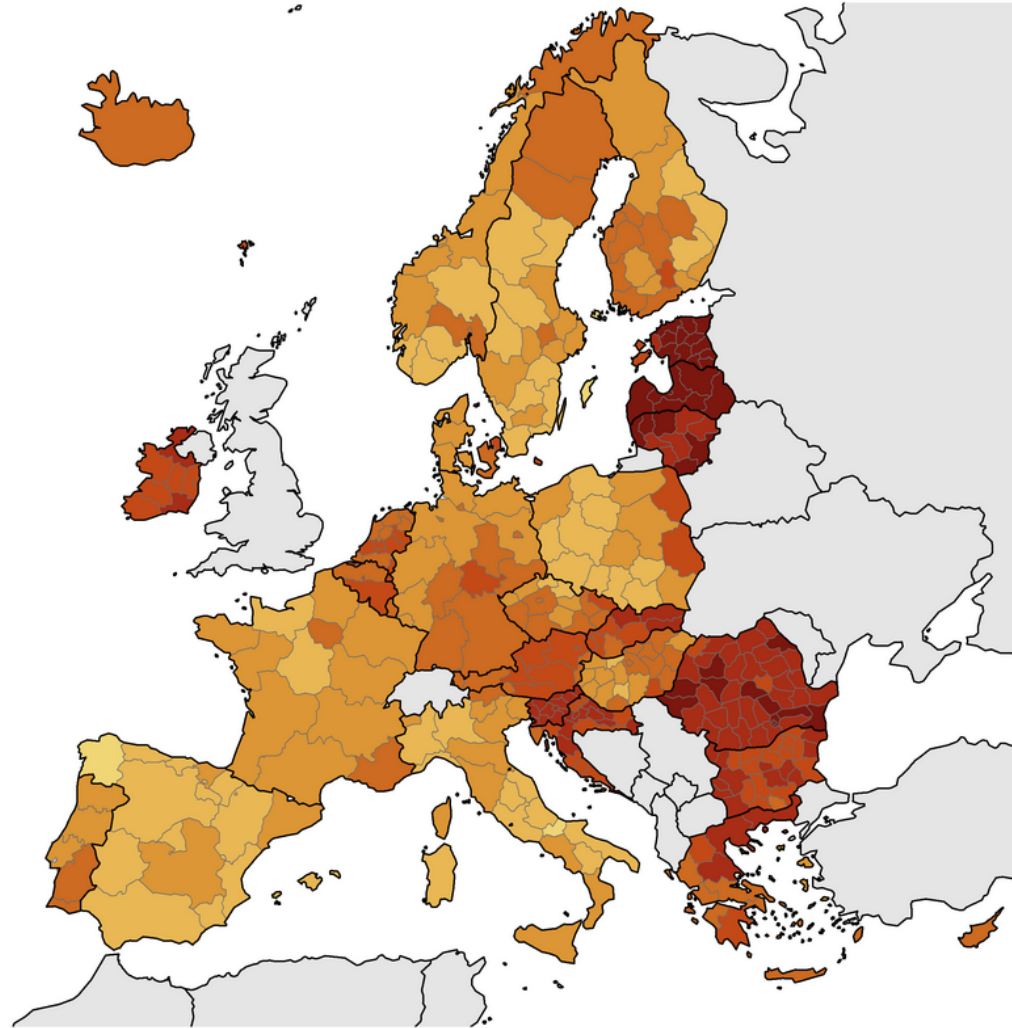
14-day COVID-19 case notification rate per 100 000 population 2021-w40 to 2021-w41



Regions not visible in the main map extent



Countries not visible in the main map extent



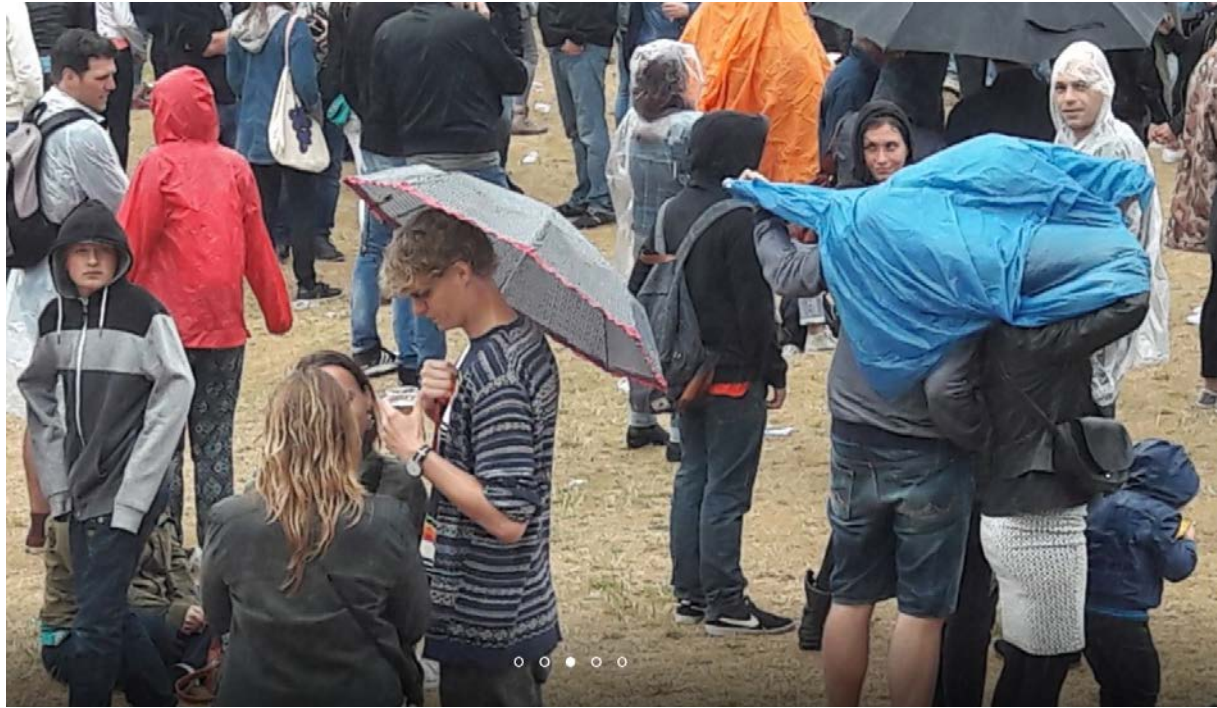
Administrative boundaries: © EuroGeographics © UN-FAO © Turkstat. ©Kartverket ©Instituto Nacional de Estatística - Statistics Portugal. The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on: 20 Oct 2021



What are the remaining risks?

- ▶ Season, behaviour, indoor, ill ventilation → more at risk contacts → more cases
- ▶ Increased n of cases
 - Absenteism (school, job)
 - Outbreaks in schools, workplace, nursing homes, health care centres
 - Hospitalisation of non-vaccinated and frail vaccinated
 - Long covid
 - International image (travel, tourism, business, image,...)
- ▶ Increased n of hospitalisations
 - Occupation of beds, ICU
 - Postponing non-COVID-care
 - Nosocomial COVID-infections
 - Increased mortality (already x 2 since september = 13+ per day = 4745 additional deaths/y)





Combination 'worst case' case influenza + covid

► COVID: + 20% contacts

- max n hosp. 100-200/day
- max ICU: 350-400 beds

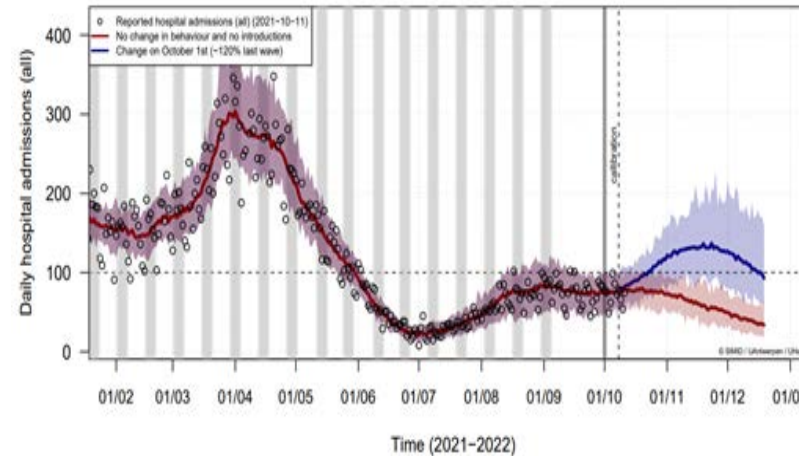
► Influenza

- max 1575 hosp./week = 225 extra hosp./day
- max 80 ICU/week

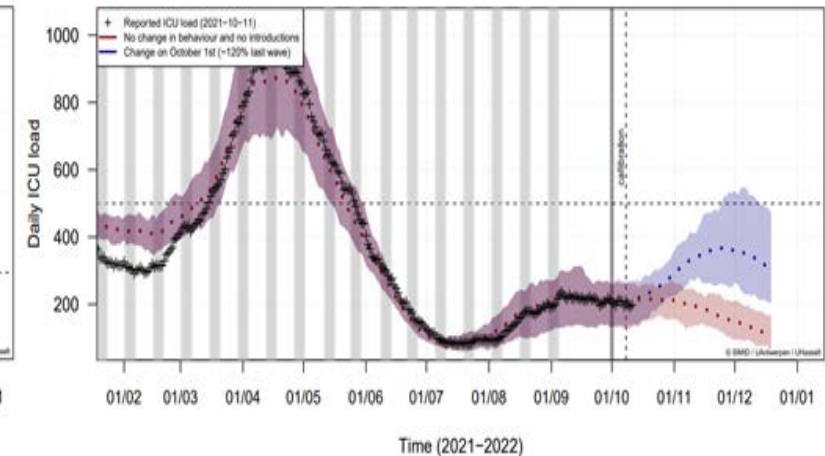
► Combined:

- Tot > 400 extra hosp./day
- Tot ICU 550-600 beds

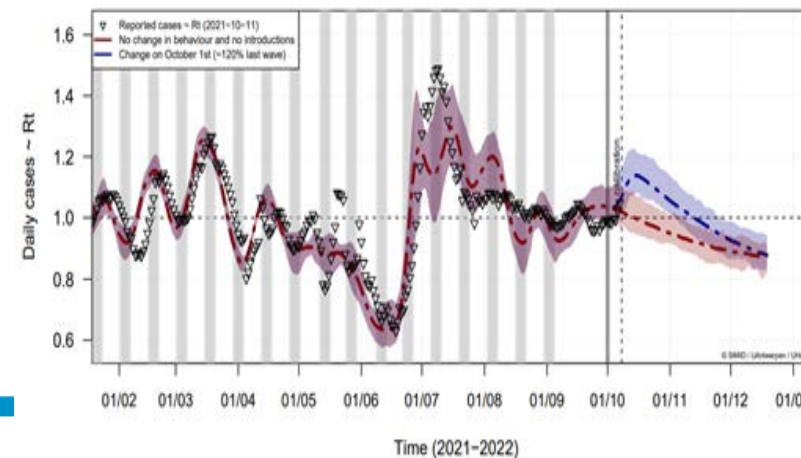
Daily hospital admissions



ICU occupancy

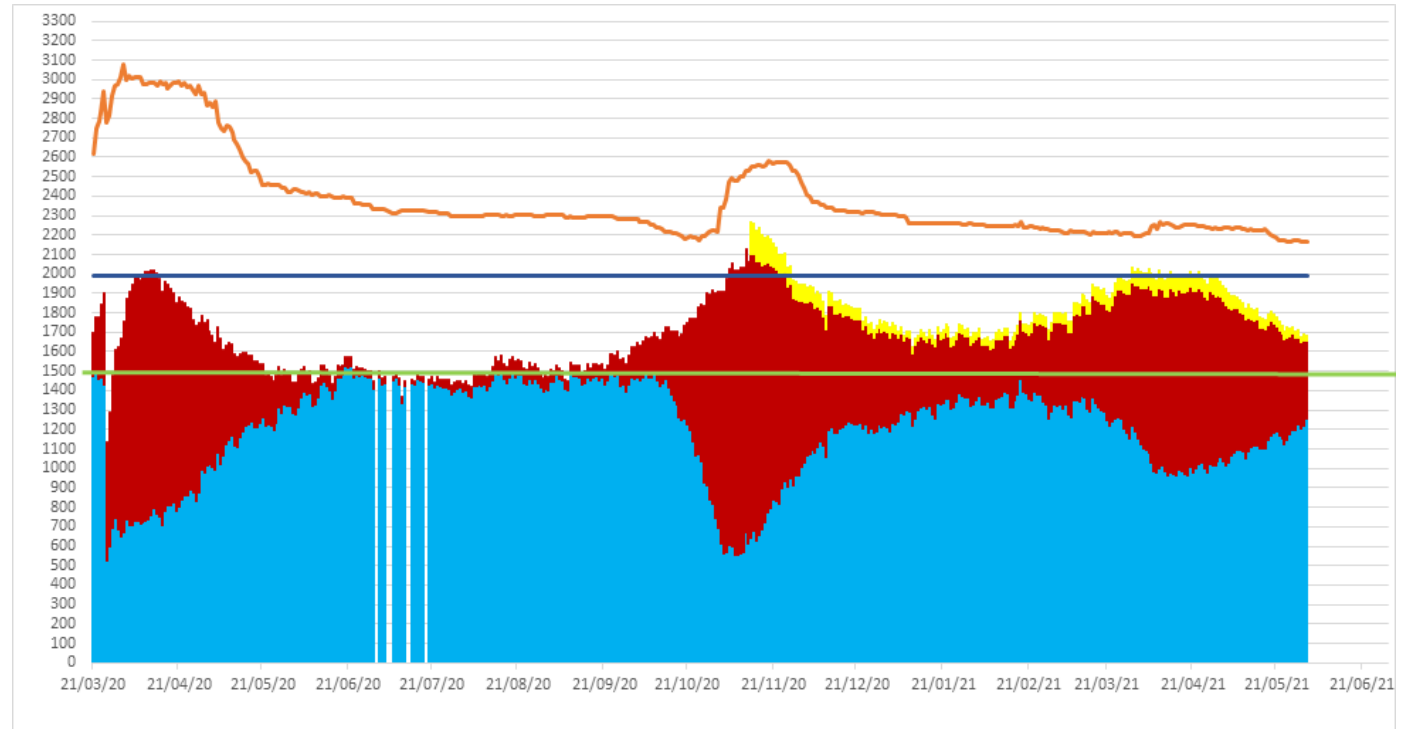
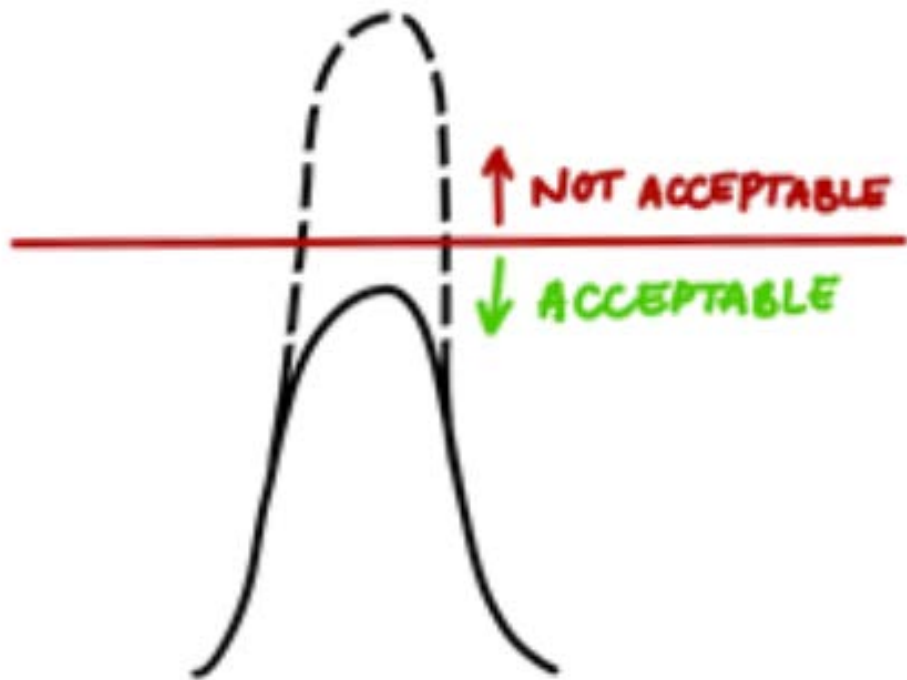


Reproduction number over time (Rt)



‘Zero risk does not exist...’

‘The health care system will cope...’



■ NON-COVID IN ICU ■ COVID IN ICU ■ COVID IN HFNO
— ICU BEDS ACRED — TOTAL ICU BEDS (ACRED+NEW)





Epidemics = behaviour → NPI's

- Reduction of social contacts, lockdowns
- Protocols, crowd control
- Physical distancing
- Hand & Cough hygiene
- Masks, ventilation
- Testing and I/Q
- Reduce international travel
- ...

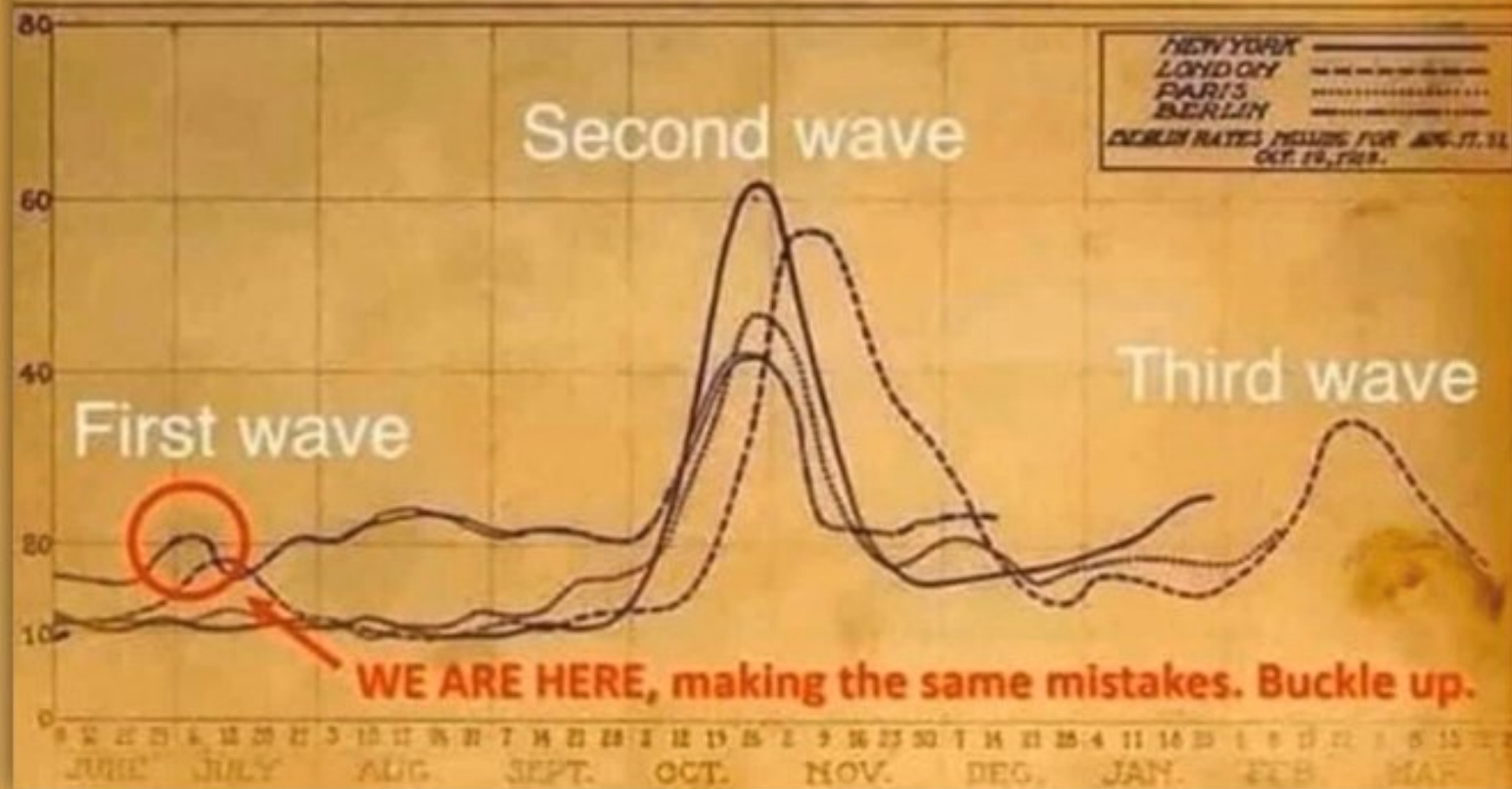




INFLUENZA PANDEMIC

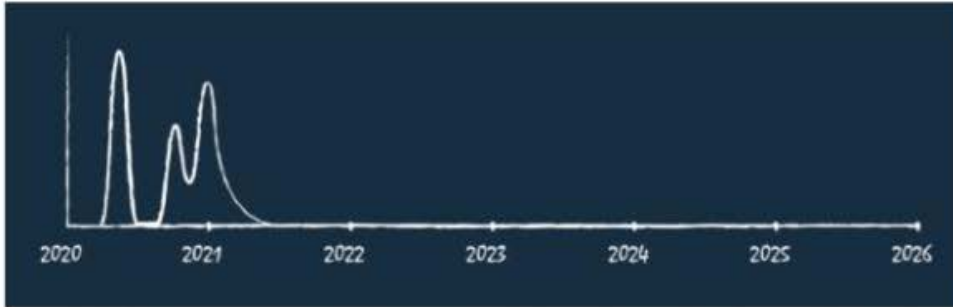
MORTALITY IN AMERICA AND EUROPE DURING 1918 AND 1919

DEATHS FROM ALL CAUSES EACH WEEK
EXPRESSED AS AN ANNUAL RATE PER 1000



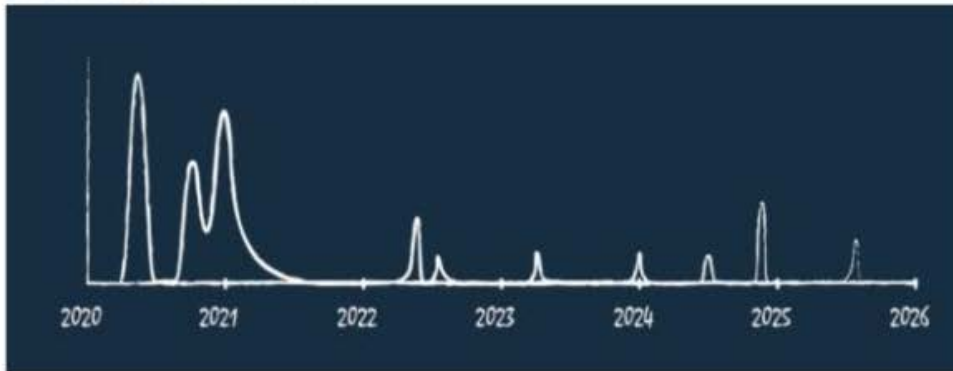
Possible scenario's for the future... (KNAW/WRR)

Back to normal



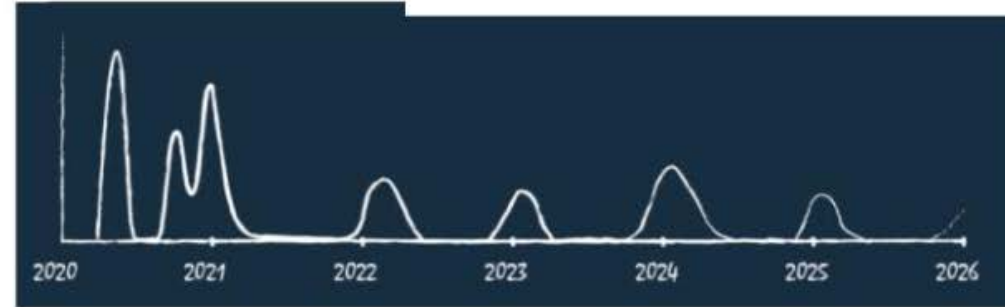
Wereldwijd zijn voldoende mensen immuun door (herhaalde) vaccinatie of doormaken van de infectie; geen immune escape. **Focus on entrenching learnings for future pandemics and targeted revax**

Externally-driven risk



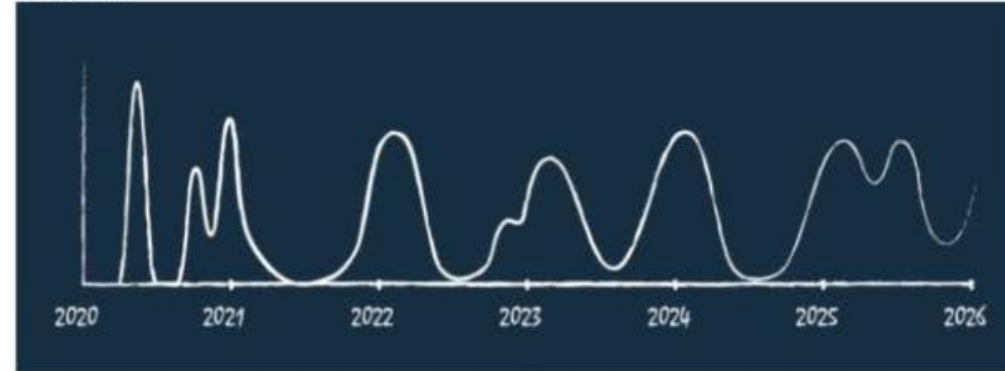
In België / EU onder controle maar in veel andere landen niet, met permanent risico op herintroductie. **Focus on strong EU approach on travel flows; good outbreak management measures to bend the curve. Ongoing high vaccination coverage.**

Influenza-type dynamics



COVID-19 wordt endemisch met jaarlijkse golven in de winter. Iedereen >18 is gevaccineerd. Het virus blijft muteren, maar niet op een manier die veel verandert aan ernst. Enkel kwetsbare groepen hebben hoger risico om ernstig ziek te worden. **Focus on effort on (re)vaccinations and protection of vulenrat**

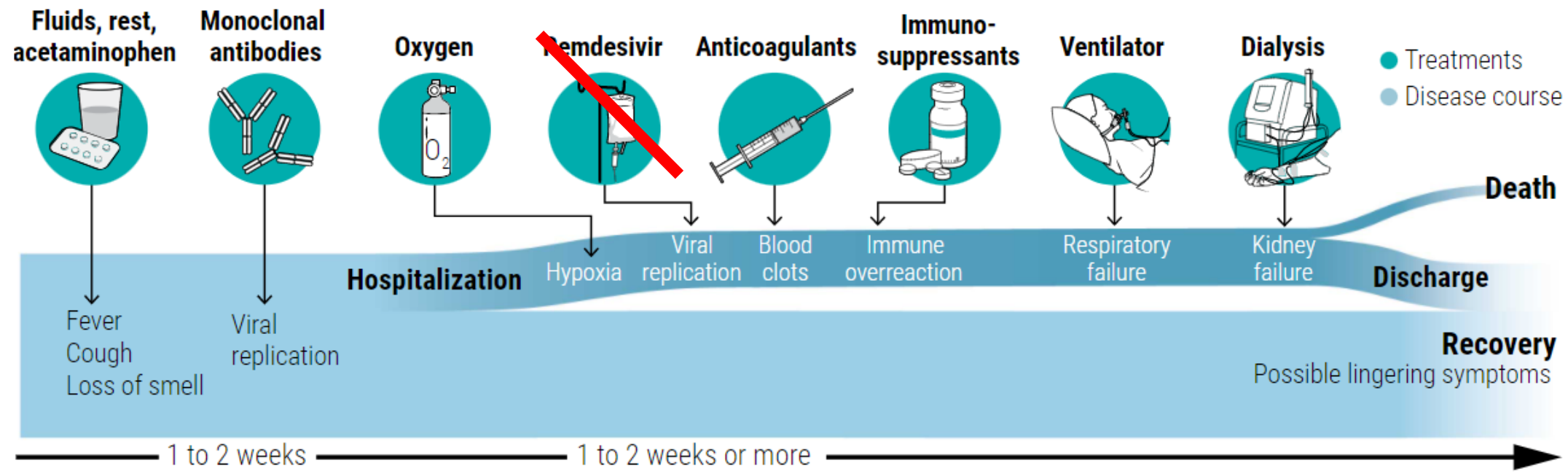
Ongoing



COVID-19 blijft een serieuze bedreiging. Vaccins werken niet voldoende (lang) en er komen steeds nieuwe varianten bij. **Focus on readiness to prepare a bold and short response, with strong signal detection and dynamic understanding of evolution towards constraints.**



Treatment options during the disease course (or not?)



Monoclonal antibodies appear to reduce risk of hospitalization in outpatients at high risk of severe disease—provided patients can access them.

Oxygen, delivered through nasal prongs, a mask, or an invasive breathing tube, is crucial to COVID-19 care. But how it's administered varies among hospitals.

The antiviral remdesivir is widely used in hospitalized patients, but evidence is mixed on its ability to shorten hospital stays; it hasn't been shown to improve survival.

Anticoagulants can prevent blood clots that are common in COVID-19 patients, but physicians must weigh the risk of bleeding when deciding the right dose.

The immunosuppressant drugs dexamethasone and tocilizumab have both reduced mortality in large clinical trials of hospitalized patients, showing that it's possible to tame the potentially deadly inflammation that characterizes severe disease.



2.1.1. Dexamethasone, systemic corticosteroids

Main message: Systemic corticosteroids (dexamethasone) are recommended for COVID-19 patients with severe disease. In case dexamethasone is not available, the WHO recommends using equivalent doses of other

2.4. Monoclonal antibodies

Main message: Treatment with monoclonal antibodies (mAbs) should be considered in patients with mild or moderate COVID-19, when they are at high risk of disease progression. MAbs should preferably be administered within 10 days of symptom onset.

They can also be considered as salvage therapy among (hospitalized) patients with persistent viral shedding due to an immunocompromised condition.



Eligibility criteria for treatment with monoclonal antibodies*

Screening for criteria 1: Laboratory-confirmed, non-severe COVID-19 infection

- SARS-CoV-2 RT-PCR or antigen positive test
- Mild or moderate COVID-19 disease severity**
- Symptom onset <10 days and SARS-CoV-2 positive test <5 days
- Age ≥12 years old
- Informed consent documented in patient's medical dossier

If no to any of the following bullet points: not eligible for mAb treatment

If yes to all bullet points, proceed to next step

*Monoclonal antibodies

- Bamlanivimab + etesivimab
- Casirivimab + imdevimab
- Regdanvimab
- Sotrovimab

Bamlanivimab monotherapy is not recommended due to documented resistance to B.1.617 and B.1.617.2 variants

Screening for criteria 2: Risk factors for severe COVID-19 disease

- Immunocompromised, defined as:
 - Hematological malignancy
 - Solid cancer undergoing treatment
 - Solid organ or hematopoietic stem cell transplantation
 - Primary immune deficiency
 - HIV with CD4 <200/mm³ and/or detectable viral load
 - Prednisolone ≥20mg ≥14 days, or other immunosuppressive drugs: see Superior Health Council list of (potentially) immunosuppressive drugs (link)
 - Sickle-cell anemia
 - Major thalassemia

OR

- At least one comorbidity, defined as:
 - Age ≥65 years old
 - Obesity with BMI ≥30 kg/m²
 - Cardiovascular disease, including uncontrolled hypertension
 - Chronic lung disease, including asthma
 - Type 1 or type 2 diabetes mellitus
 - Chronic kidney disease (eGFR <30 ml/min), including hemodialysis
 - Chronic liver disease (Child Pugh B or C)
 - Chronic neurological disease

If patient has no listed comorbidity: not eligible for mAb treatment

If patient has a risk factor (immunosuppression or ≥1 comorbidity), proceed to next step

**Disease severity

- Mild:** symptoms of COVID-19 without lower respiratory tract involvement such as dyspnea or abnormal chest imaging
- Moderate:** clinical or radiological evidence of lower respiratory tract disease and SpO₂ ≥ 94% (or no supplemental oxygen required for patients with chronic hypoxia)
- Severe:** ≥1 of the following:
- Respiratory rate ≥30/min; ≥40/min (children < 5y)
 - Blood oxygen saturation ≤93% or need supplemental oxygen
 - PaO₂/FiO₂ ratio <300
 - Lung infiltrates >50% of the lung field within 24-48 hours



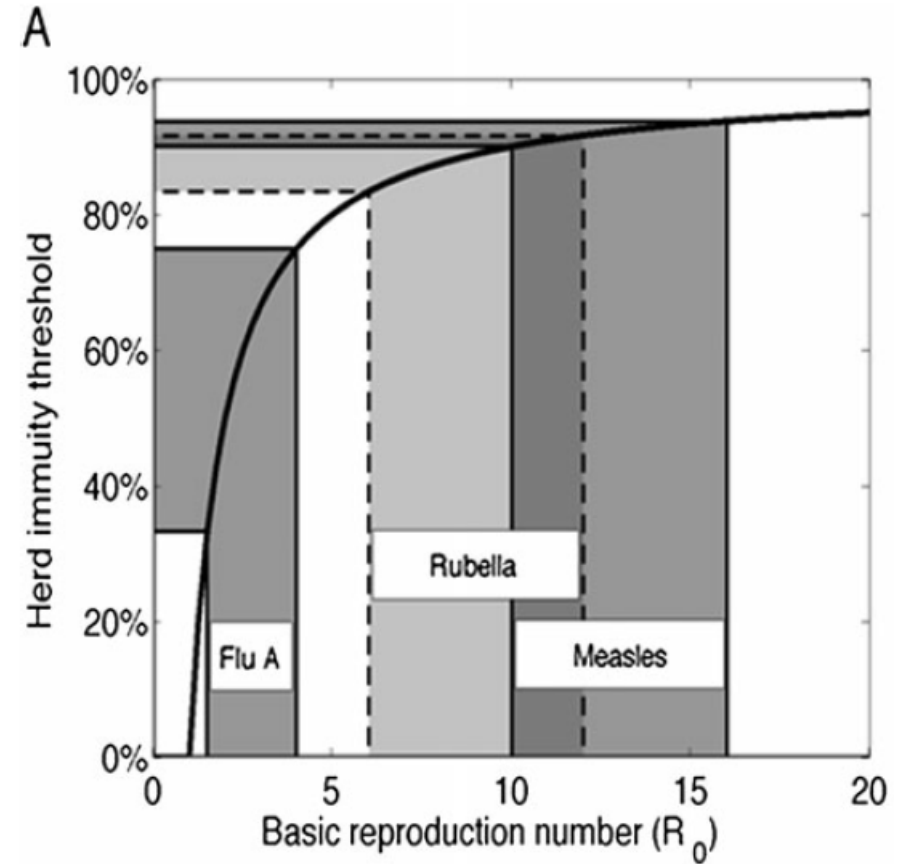
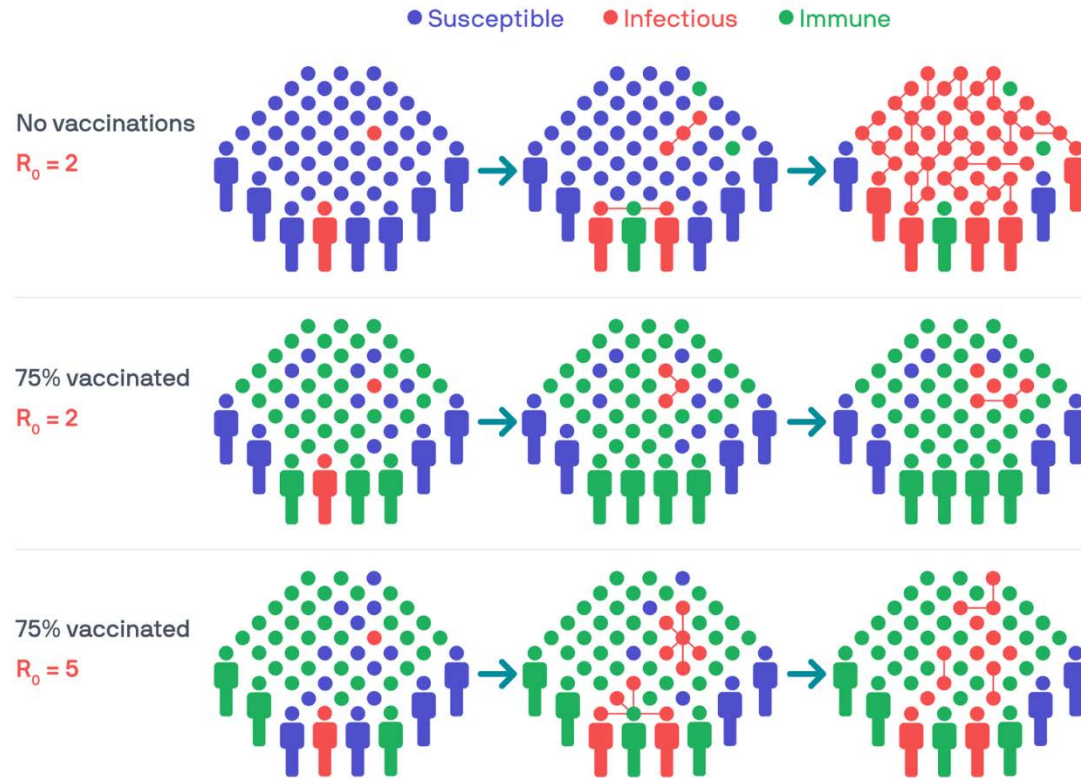
Molnupiravir

2.11. Molnupiravir

Molnupiravir is a new antiviral with demonstrated activity against SARS-CoV-2 in ferret and mouse models (as prophylaxis and treatment). After preliminary phase 1 and phase 2 data suggest the drug is safe and has antiviral activity in humans as well, a phase 3 trial has been initiated in non-hospitalized patients at risk of severe disease progression (PHASE 3 MOVE- OUT trial:NCT04575597). The trial was just stopped before finishing recruitment, based on the recommendation of the independent Data Monitoring Committee, and in consultation with the U.S. Food and Drug Administration (FDA), due to positive results observed at the interim analysis. A press release by Merck communicated that Molnupiravir reduced the risk of hospitalization or death by approximately 50%; 7.3% of patients who received molnupiravir were either hospitalized or died through Day 29 following randomization (28/385), compared with 14.1% of placebo-treated patients (53/377); $p=0.0012$. Through day 29, no deaths were reported in patients who received molnupiravir, as compared to 8 deaths in patients who received placebo ([link](#)). The published results of the trial are awaited.



When/how will we reach herd immunity (or somethings that looks like it...)?



Some considerations

- ▶ Aim to achieve with 'herd immunity'?
 - Individuals with no or low immune responses benefiting from group immunity around
 - Eradication/control/total freedom from NPI's...
- ▶ % population immunity \neq % vaccination coverage
- ▶ Actual vaccines' impact on severe disease (~90%) vs. transmission (~50%)
- ▶ Delta R0 ~7 \rightarrow immunity threshold ~85% \rightarrow population vaccination ~95%...
- ▶ Actual Belgian total population vaccination coverage = 74,1%...



		Totale bevolking ⁽¹⁾	Bevolking van 18 jaar en ouder ^(1,2)	Bevolking van 65 jaar en ouder ^(1,2)
Vaccinatiegraad minstens 1 dosis	België	75,4%	87,3%	93,2%
	Brussel ⁽³⁾	56,8%	69,6%	82,9%
	Vlaanderen ⁽³⁾	80,6%	92,2%	96,0%
	Wallonië ^(3,4)	70,4%	82,1%	89,5%
	Duitstalige Gemeenschap ⁽³⁾	65,7%	76,4%	88,1%
Vaccinatiegraad volledig gevaccineerd	België	74,1%	86,1%	92,3%
	Brussel ⁽³⁾	54,5%	67,2%	81,6%
	Vlaanderen ⁽³⁾	79,8%	91,4%	95,3%
	Wallonië ^(3,4)	68,8%	80,5%	88,3%
	Duitstalige Gemeenschap ⁽³⁾	64,1%	74,9%	86,7%



In conclusion

- ▶ COVID-19 is a new disease
- ▶ Actual 4th wave, in spite of succesful vaccination campaign
- ▶ Remaining risk for immunedpressed patient
 - Prevention (3 d shot, behaviour of pt and people around them)
 - For those who nevertheless become ill: innovations in treatment?
- ▶ Mid long term: pandemic → endemic = gradual proces
- ▶ Remaining importance of non-pharmaceutical interventions

