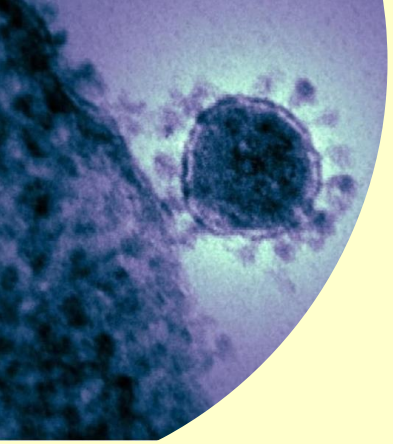


Lunchsymposium
mit freundlicher Unterstützung von GSK
Pädiatrischer Frühling
19. Mai 2022

Update Kinderimpfungen

Hans Jürgen Dornbusch

IMPFKOMMISSION ÖGKJ
ÖSTERREICHISCHE GESELLSCHAFT FÜR KINDER- UND JUGENDHEILKUNDE

EAP Vaccination

4cMenB - Impfprogramm UK

Start: Sept 2015

3-Jahres-Daten

- Seit Einführung der 4cMenB-Impfung in England (2 + 1 off label Schema)

  75% Reduktion aller invasiven MenB-Fälle in der geimpften Kohorte

  unabhängig vom Impfstatus der Kinder

  ➢ geschätzt **277 Fälle durch Impfung verhindert !**

- Signifikanter **Impfschutz** für mindestens **2 Jahre** nach 12-Monats-Booster
- Indirekte Effekte (“Herdenschutz”) bisher nicht nachweisbar
- Bisher **keine Sicherheitsbedenken** (inkl. Frühgeborenen)

  nach > 3 Millionen verimpften Dosen

Ladhani et al. Vaccination of Infants with Meningococcal Group B Vaccine (4CMenB) in England. N Engl J Med 2020; 382(4):309-17

2 Jahre Sicherheitsdaten

1,3 Mio Säuglinge

Sept 2015 – Mai 2017

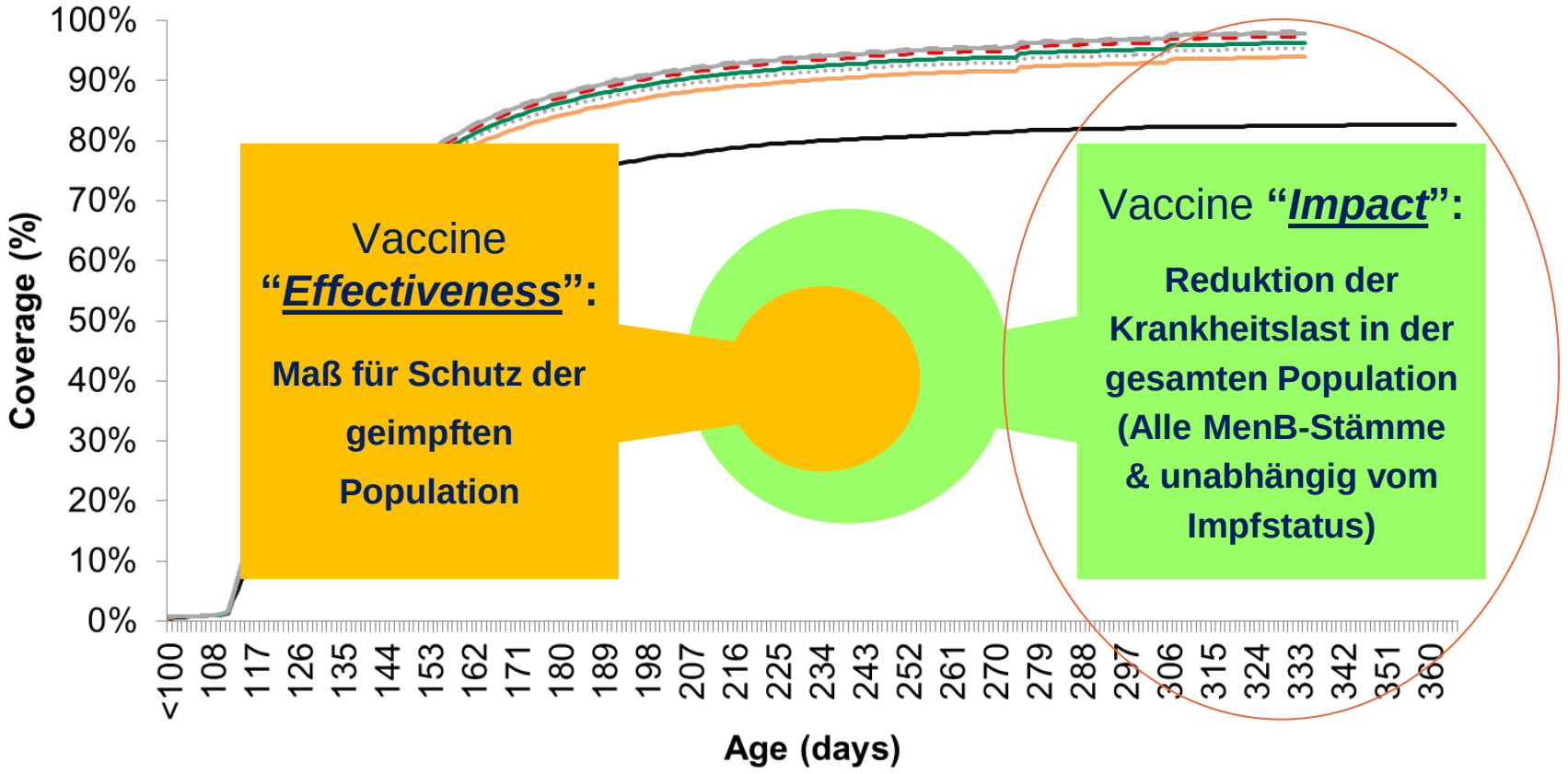
- 902 Sicherheitsmeldungen (vs. Hintergrundinzidenz):
  - 366 Lokalreaktionen
  - 364 Fieber
  - 55 Krampfanfälle **(78-199 erwartete Episoden)**
  - 3 Kawasaki Syndrom **(2-3 erwartete Fälle)**
  - 3 SIDS innerhalb von 3 Tagen nach Impfung **(9 erwartete Fälle)**
- Keine schweren unerwarteten UAW
- Compliance anderer Routineimpfungen im Säuglingsalter nicht beeinträchtigt

Fazit: Erfolgreiches MenB-Impfprogramm im UK mit
- signifikanter Reduktion der MenB-Erkrankungen bei den Säuglingen[1]
- Bestätigung des guten Sicherheitsprofils von 4CMenB[2]

1. Ladhani et al. Vaccination of Infants with Meningococcal Group B Vaccine (4CMenB) in England. N Engl J Med 2020; 382(4):309-17
2. Bryan P;Lancet Child Adolesc Health;2018;1-9

Public Health England

Durchimpfungsraten (Dosis 2)



Parikh, Ladhani et al. Public Health England: MenB disease and vaccination in England– Lancet ID March 2017

Reduktion der Erkrankungszahlen mit der MenB-Impfung: „Vaccine Impact“ in der gesamten impfberechtigten Population

Italien[1]
regional
Toskana & Venetien
2014 - 2018

Säuglinge
ab 2 Monate
(3+1) bzw. ab
7 Monate (2+1)
>80%
Durchimpfungsra
ten

68% **31%**

Australien[2]
regional
Südaustralien
2017 - 2019[5]

Jugendliche
15 – 18 Jahre
34.489 Kohorte
82% Durchimpfung
mit 2 Dosen

71%

UK[3]
nationales
Impfprogramm
2015 - 2018

Säuglinge
2 Monate,
~650.000 jährl.
Geburtskohorte
88% Impfquote

75%
(64% - 81%)
Reduktion der Fallzahlen
nach den ersten
3 Jahren

Kanada[4]
regionale
Impfkampagne[2]
2014 - 2018

Altersgruppen
2 Monate
bis 20 Jahre
59.500 Population
83% Impfquote

96%
(p < 0,0001)
Reduktion der Inzidenz
nach 4 Jahren

1. Azzari. C;Vaccines;2020; 8, 469. 2. McMillan M et al.*Clinical Infectious Diseases* 2021, ciaa1636. 3. Ladhani SN *et al. N Engl J Med* 2020; 382:309-317; 4. Deceuninck G;Vaccine;2019;37;4243-4245;

Erfahrungen mit der MenB-Impfung (*real world data*) Wirksamkeit (Vaccine Effectiveness)

Italien

Toskana & Venetien[3]
2014 - 2018

Säuglinge
ab 2 Monate (3+1)
bzw. ab
7 Monate (2+1)
>80% Impfquoten

> 90%*
Effektivität in beiden Regionen

Portugal

Fallkontroll-Studie[4]
2014 - 2019

Altersgruppen
2 Monate
bis 18 Jahre
82 MenB-Fälle
47% Impfquote

79%
(45% - 92%)
Effektivität

Hinweis auf mildere Verläufe

Australien

Region Südaustralien
2017 - 2019[5]

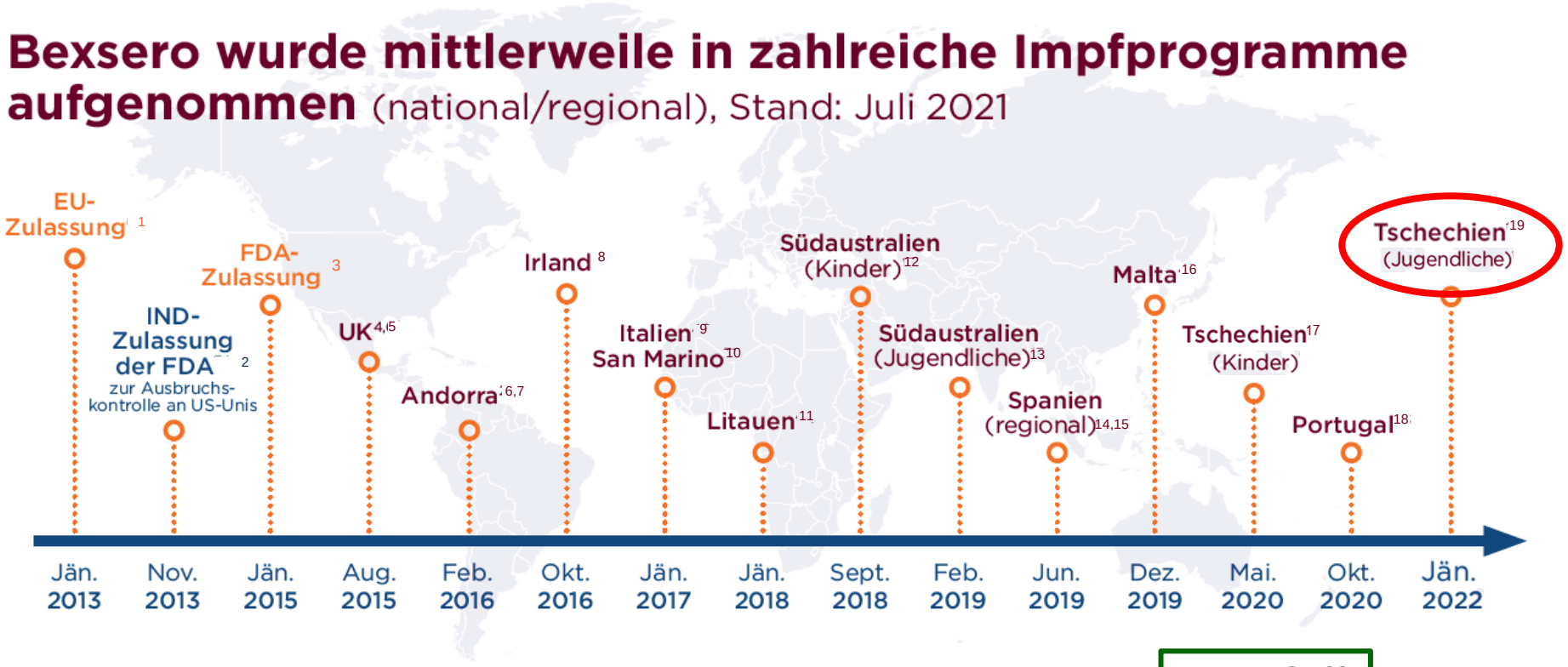
Jugendliche
15 – 18 Jahre
34.489 Kohorte
82% Impfquote
mit 2 Dosen

Keine Fälle
bei Geimpften

***Toskana 93,6%** (55,4% - 99,1%) und **Venetien 91,0%** (59,9% - 97,9 %)

1. Ladhani SN *et al. N Engl J Med* 2020; 382:309-317; 2. Deceuninck G;Vaccine;2019;37;4243-4245; 3. Azzari. C;Vaccines;2020; 8, 469. 4. Rodrigues F;*JAMA;*2020;324(21):2187-2194.; 5. McMillan M et al. *Clinical Infectious Diseases* 2021, ciaa1636.

Nationale und regionale Impfprogramme

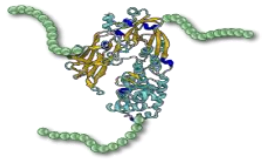


+ Men ACWY kostenfrei mit 1 Jahr

Men5 (ABCWY) - Impfstoffe ?

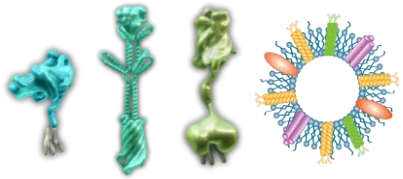
Conjugates[1,2]

- MenA[1,2]
- MenC[1,2]
- MenC-Hib[1,2]
- MenCY-Hib[1]
- MenACWY[1,2]



Protein-based[1]

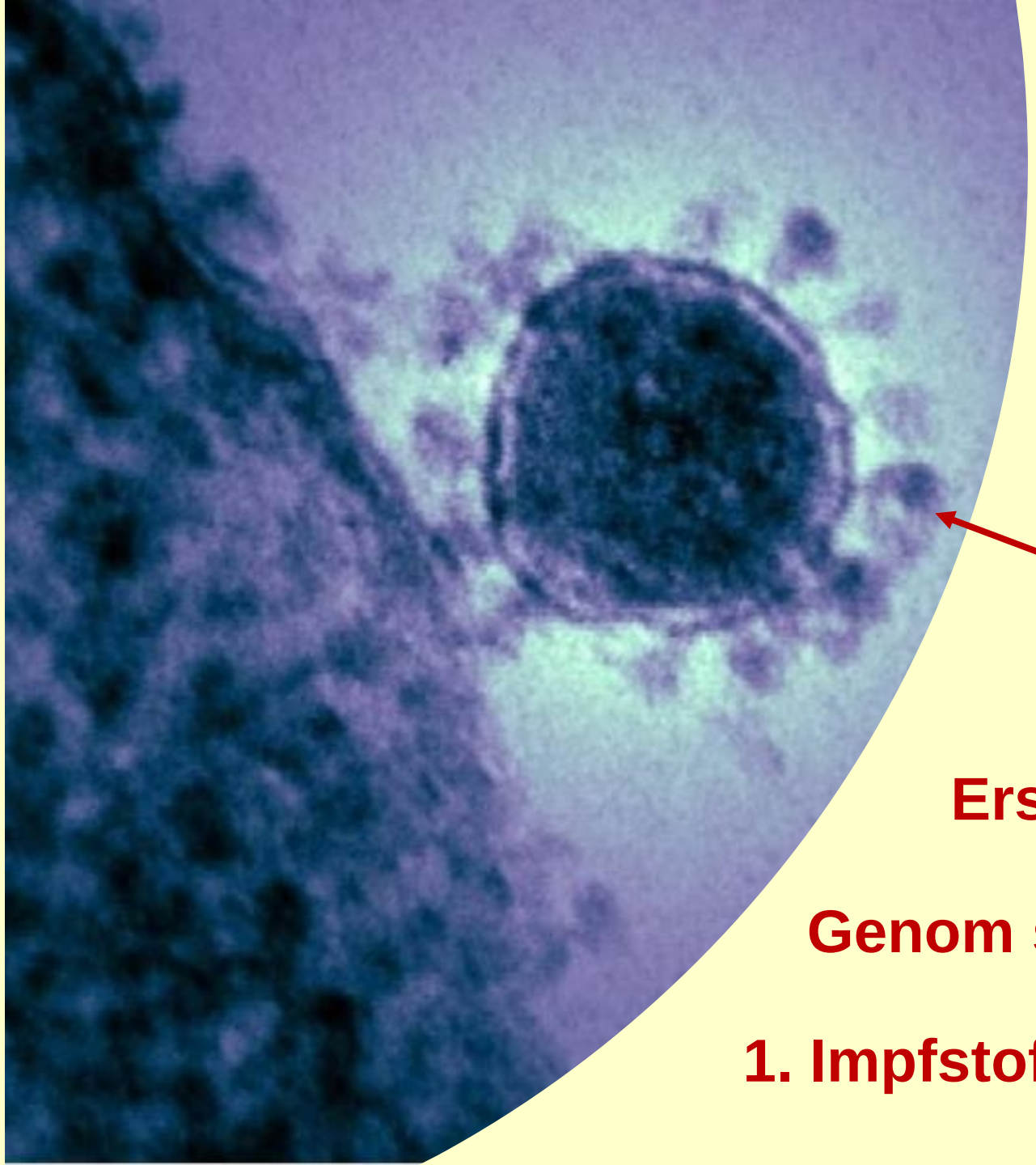
- 4CMenB
- MenB-fHbp



The next innovation?

A single formulation against serogroups A, B, C, W and Y would simplify immunisation schedules, potentially providing public health benefits of increased immunisation rates and increased breadth of coverage[3]

1. Crum-Cianflone N, Sullivan E. *Infect Dis Ther* 2016;5:89–112
2. World Health Organization (WHO) 2018. Meningococcal meningitis: Key facts https://www.who.int/en/news-room/fact-sheets/detail/meningococcal-meningitis (accessed Feb 2022)
3. Sáez-Llorens X *et al*. *Hum Vaccin Immunother* 2015;11:1507–1517
4. Rappuoli R. *F1000 Med Rep* 2011;3:16



SARS Coronavirus-2

Spike Protein

(bindet an ACE2-Rezeptor)

Erste Berichte Dez 2019

Genom sequenziert Jan 2020 !

1. Impfstoffzulassung Dez 2020 !

World Health Organization

Search by Country, Territory, or Area

Covid-19 Response Fund

Donate

WHO Coronavirus (COVID-19) Dashboard

Overview | Measures | Data Table | Explore

364.191.494 bestätigte Fälle

5.631.457 Todesfälle

Cases

Total

3.321.782
new cases in last 24hrs

364.191.494
cumulative cases

5.631.457
cumulative deaths

Globally, as of 4:00pm CET, 28 January 2022, there have been 364.191.494 confirmed cases of COVID-19, including 5.631.457 deaths, reported to WHO. As of 28 January 2022, a total of 9.854.237.363 vaccine doses have been administered.

https://covid19.who.int/

World Health Organization

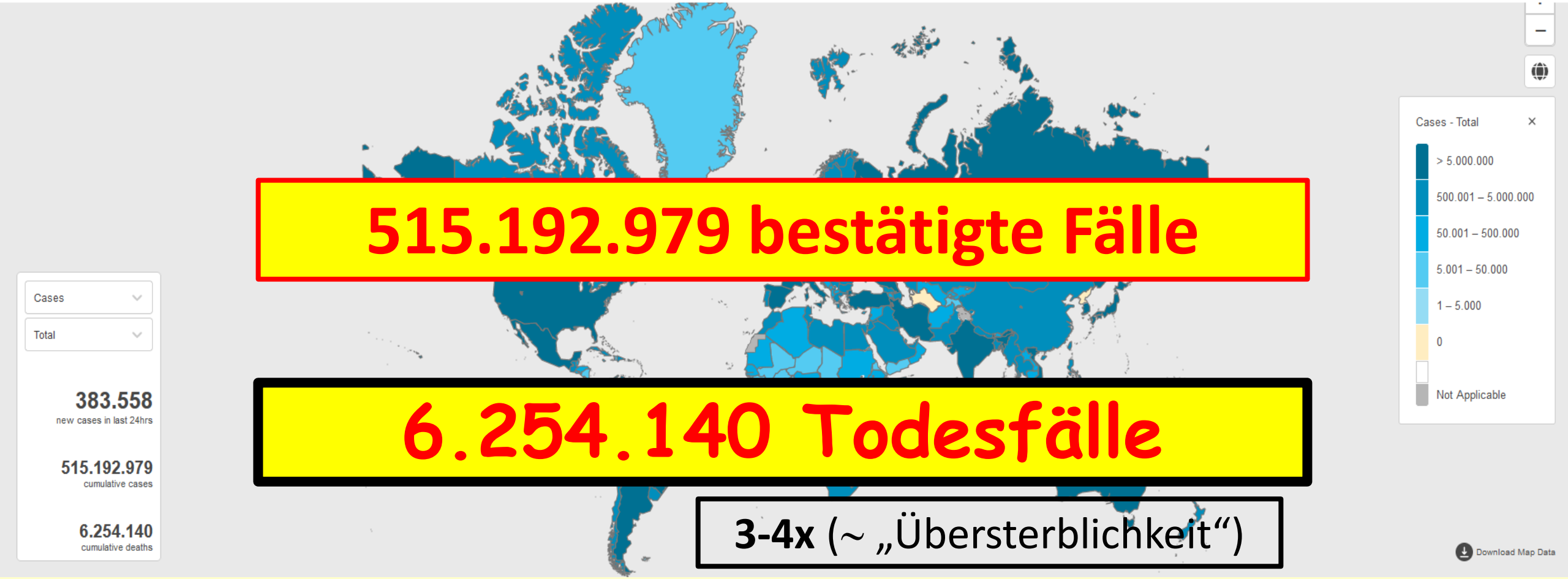
Search by Country, Territory, or Area

Covid-19 Response Fund

Donate

WHO Coronavirus (COVID-19) Dashboard

Overview | Measures | Table View | Data | More Resources



515.192.979 bestätigte Fälle

6.254.140 Todesfälle

3-4x (~ „Übersterblichkeit“)

Cases

Total

383.558
new cases in last 24hrs

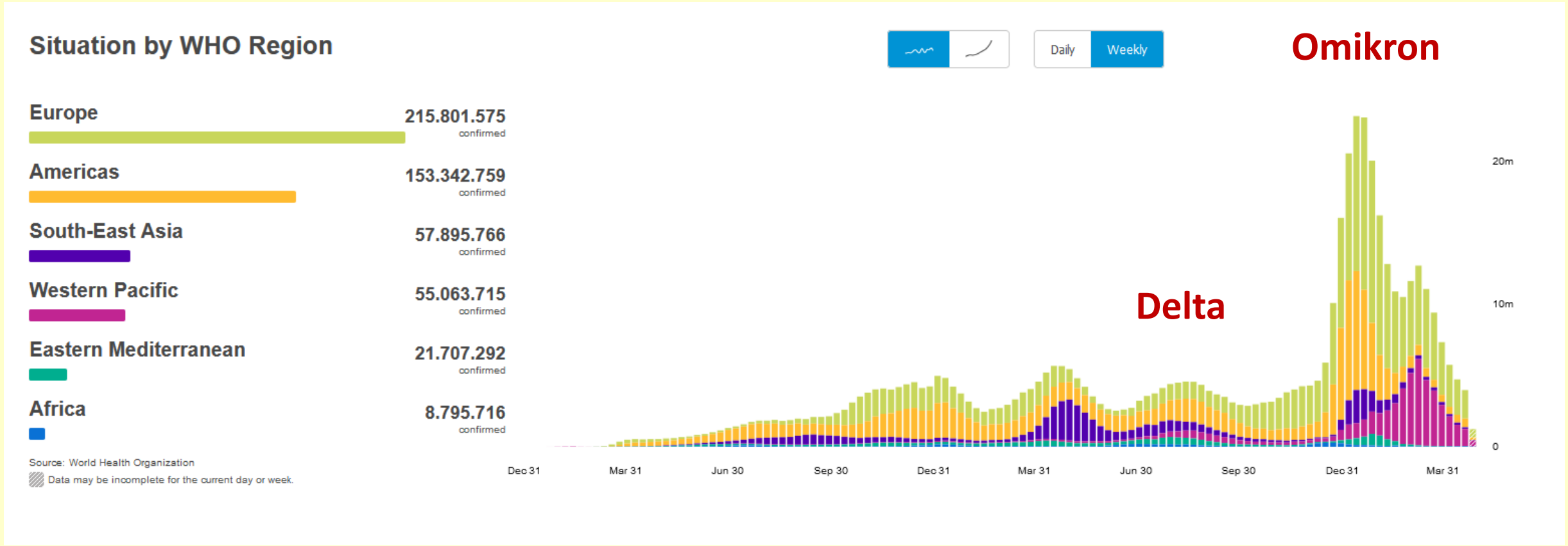
515.192.979
cumulative cases

6.254.140
cumulative deaths

Globally, as of 5:13pm CEST, 9 May 2022, there have been 515.192.979 confirmed cases of COVID-19, including 6.254.140 deaths, reported to WHO. As of 8 May 2022, a total of 11.579.263.039 vaccine doses have been administered.

https://covid19.who.int/

Laborbestätigte COVID-19 Fälle global



Immune Evasion - Accumulation of spike protein mutations protects SARS-CoV2 from neutralising antibodies

Due to numerous S-protein mutations **Omikron** „hides“ from antibody induced immunity of individuals **vaccinated or recovered** from Delta variant

Immune evasion is primarily responsible for **higher transmissibility** = **growth advantage** of Omikron (vs. Delta) in vaccinated individuals (no relevant increase of *intrinsic* transmissibility)

T-cell immunity (protecting from **severe** COVID-19) is **not/less affected by immune evasion**

Florian Krammer, *Nature* 31 Dec 2021 *https://doi.org/10.1038/d41586-021-03846-z*

Transmissibility (WT vs. Alpha vs. Delta vs. Omicron vs. >>>)

Table 2: Summary of phenotypic impacts* of Variants of Concern

WHO label	Alpha	Beta	Gamma	Delta
Transmissibility	Increased transmissibility[8]	Increased transmissibility[9,10]	Increased transmissibility[10,11]	Increased transmissibility [6,10,12,13]

Transmissibility of

Alpha vs Wild Type: **50%** (40%-80%) higher

Delta vs Alpha: **60%** higher

Omikron vs Delta: **20%-70%** higher

WHO COVID-19 Weekly Epidemiological Update, Edition 66, 16 Nov 2021

DL Richter et al. Austrian Institute for Infection Epidemiology & Surveillance

Disease Severity – Omikron vs Delta (Kaiser Permanente, CA)

Clinical outcomes among patients infected with Omicron (B.1.1.529) vs. Delta SARS-CoV-2 variant (n = 60.000)

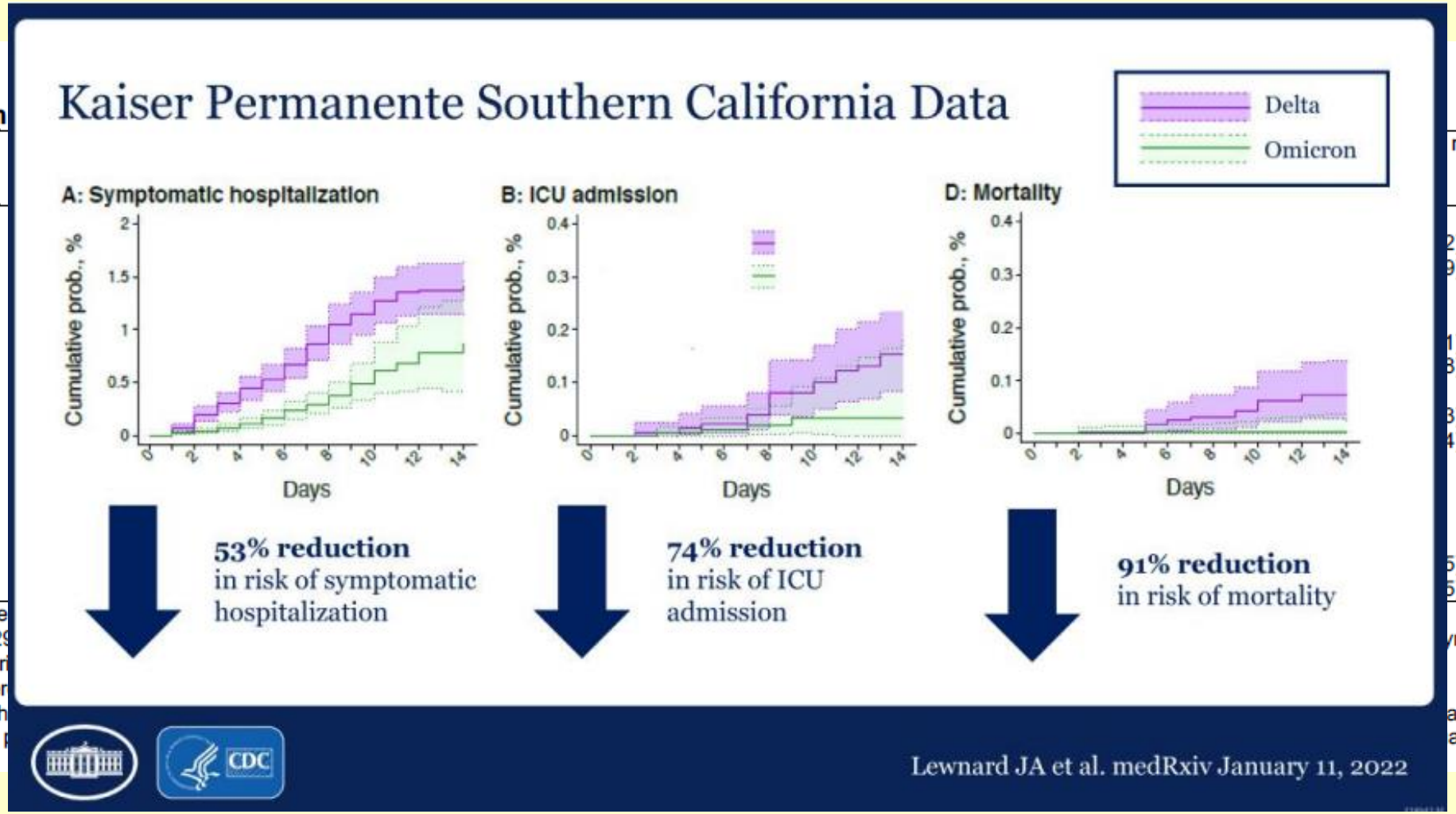
Table 1: Association

Outcome	ratio (95% CI) Adjusted
Any hospital admission	2) 0.48 (0.36, 0.64)
Symptomatic hospital admission	9) 0.72 (0.58, 0.88)
ICU admission[2]	1) 0.47 (0.35, 0.62)
Mechanical ventilation[3]	8) 0.62 (0.49, 0.77)
Death[2]	3) – –
	4) – –
	– –
	– –
	5) – –
	5) – –

SGTF: S gene target failure
[1]Sample sizes include 52,29 admissions as those occurri
[2]Adjusted hazard ratios wer
[3]Unadjusted and adjusted h patients and among SGTF p 6.8×10^{-6}, respectively.

ymptomatic hospital

atients among all SGTF al to 6.7×10^{-6} and



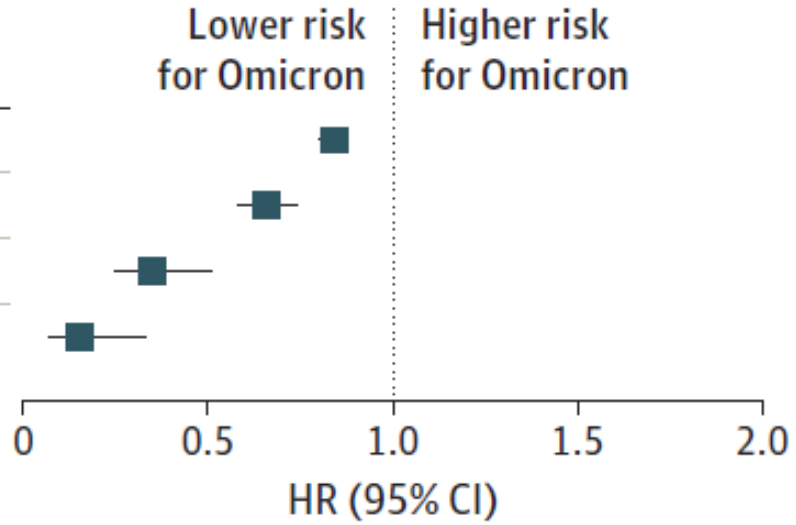
medRxiv preprint doi: https://doi.org/10.1101/2022.01.11.22269045

Disease Severity under 5 years – Omicron vs. Delta

66 US HCOs
n = 22.769 x 2

Clinical outcomes of SARS-CoV-2 infection in children younger than 5 years of age Omicron vs. Delta cohorts

Outcome	Matched Omicron cohort, No. (%)	Matched Delta cohort, No. (%)	HR (95% CI)
ED visits	4637 (20.36)	5602 (24.60)	0.84 (0.80-0.87)
Hospitalizations	401 (1.76)	741 (3.25)	0.66 (0.58-0.74)
ICU admissions	38 (0.17)	115 (0.51)	0.35 (0.25-0.51)
Mechanical ventilation	10 (0.04)	51 (0.22)	0.15 (0.07-0.33)



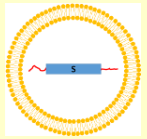
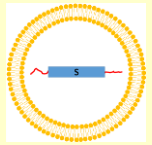
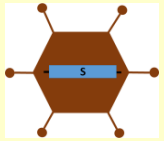
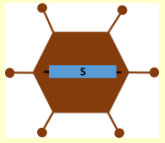
Incidence = 6-8 x higher

Wang et al. JAMA Pediatrics April 2022

Zugelassene COVID-19 Impfstoffe

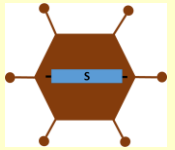
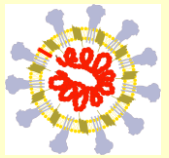
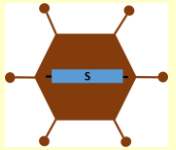
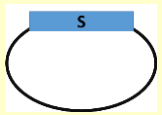
(% Schutz vor Erkrankung / Phase III)

- **Pfizer (95%)**
  Comirnaty®
- **Moderna (94%)**
  Spikevax®
- **AstraZeneca (60-90%)**
  Vaxzevria®
- **J&J (72%)**
  Jcovden®
- **Novavax (89-96%)**
  Nuvaxovid®


Non-EU Zulassungen

- **Gamaleya (91.6%)**
- **Sinovac/Sinopharm/Bharat etc. (50-90%)**
- **Cansino (66%)**
- **ZyCov-D (66%)**
- **Soberana-2 (62%)**


F. Krammer (adaptiert)

Wirksamkeit der Impfung gegen SARS-CoV-2 Varianten ?

Summary of
Vaccine Effectiveness (VE) against Delta / B.617.2 VoC
(full vaccination)

F Krammer > ECDC 2021

Study (location)	Measurement	Endpoint	Percent efficacy/effectiveness	Link
Fowlkes *et al.* (CDC/US)	Effectiveness	Any infection including asymptomatic infection in HCW	66% combined for BNT162b2, mRNA-1273 and J&J	https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm
Lopez Bernal *et al.* (England)	Effectiveness	Symptomatic infections, general population	88% for BNT162b2 67% for AZ	https://www.nejm.org/doi/full/10.1056/nejmoa2108891
Sheik *et al.* (Scotland)	Effectiveness	Any infection including asymptomatic infection , general population	79% for BNT162b2 60% for AZ	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01358-1/fulltext
Nasreen *et al.* (Canada)	Effectiveness	Symptomatic infections, general population	85% for BNT162b2	https://www.medrxiv.org/content/10.1101/2021.06.28.21259420v2
Tang *et al.* (Qatar)	Effectiveness	Any infection including asymptomatic infection , general population	53.5% for BNT162b2 84.8 for mRNA-1273	https://www.medrxiv.org/content/10.1101/2021.08.11.21261885v1.full.pdf
Puranik *et al.* (US)	Effectiveness	Any infection including asymptomatic infection , general population	42% for BNT162b2 76% for mRNA-1273	https://www.medrxiv.org/content/10.1101/2021.08.06.21261707v3.full.pdf
Pouwels *et al.* (UK)	Effectiveness	Any infection including asymptomatic infection , general populations	82% for BNT162b2 67% for AZ 73% for previous infection	https://www.medrxiv.org/content/10.1101/2021.08.18.21262237v1.full.pdf
Rosenberg *et al.* (US, NY)	Effectiveness	Any infection including asymptomatic infection,	79.8% combined for BNT162b2, mRNA-1273 and	https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1
Robert Koch Institut (Germany)	Effectiveness	Symptomatic infection , general population	83-84% combined for AC, J&J, BNT162b2 and mRNA-1273	https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Situationsberichte/Wochenbericht/Wochenbericht_2021-09-02.pdf?__blob=publicationFile
Robert Koch Institut (Germany)	Effectiveness	Hospitalization	84-95% combined for AC, J&J, BNT162b2 and mRNA-1273	https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Situationsberichte/Wochenbericht/Wochenbericht_2021-09-02.pdf?__blob=publicationFile
Statens Serum Institut (Denmark)	Effectiveness	Any infection including asymptomatic infection, general population	84.6% for BNT162b2 88.9% for mRNA-1273	https://files.ssi.dk/covid19/gennembrudsinfektion/rapport/gennembrudsinfektion-covid19-uge35-2021-83op
Statens Serum Institut (Denmark)	Effectiveness	Hospitalization, general population	94.4% for BNT162b2 100% for mRNA-1273	https://files.ssi.dk/covid19/gennembrudsinfektion/rapport/gennembrudsinfektion-covid19-uge35-2021-83op
Veneti *et al.* (Norway)	Effectiveness	Hospitalization, general population	0.97 RR of Delta over Alpha for (mostly) BNT162b2 and mRNA-1273	https://www.medrxiv.org/content/10.1101/2021.09.02.21263014v1.full.pdf

42 - 93 % „any disease“

83 - 95 % „hospitalisation“

Vaccine effectiveness vs SARS-CoV-2 *infection* with the Omikron vs. Delta variant following a 2-dose or booster BNT162b2 or mRNA-1273 vaccination series

Danish nationwide database

- **2 dose VE vs. Omikron significantly lower than VE vs. Delta infection and**
- **2 dose VE decreases after 2 months (60d) to 15-30%**

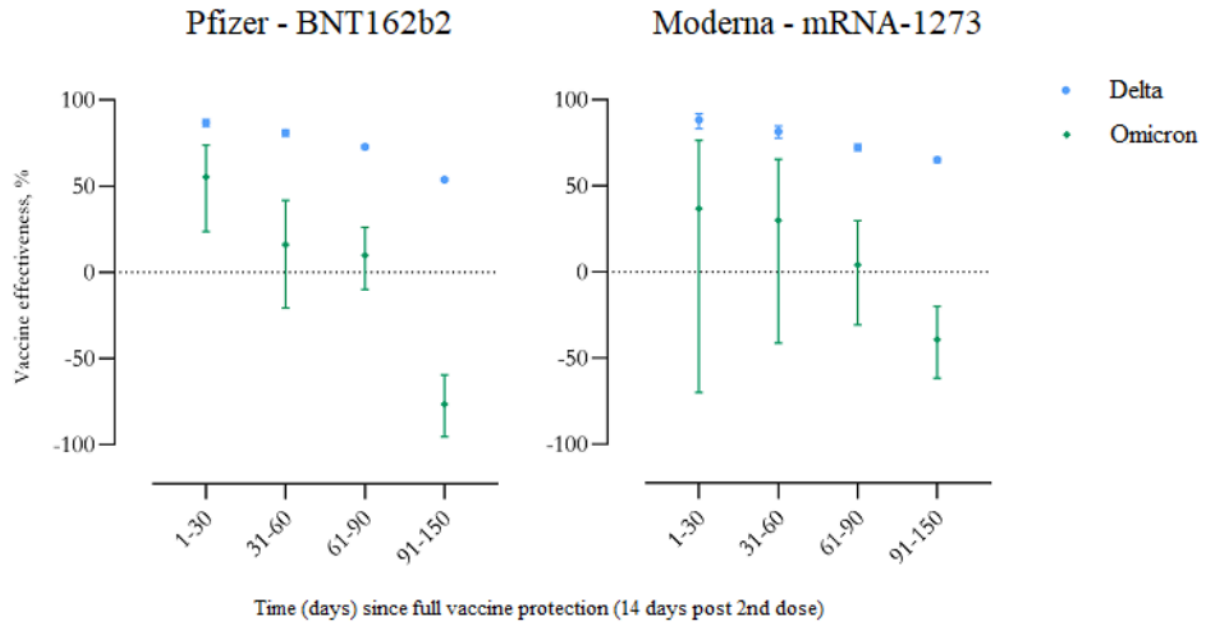


Figure Vaccine effectiveness against SARS-CoV-2 infection with the Delta and Omicron variants, shown separately for the BNT162b2 and mRNA-1273 vaccines. Vertical bars indicate 95% confidence intervals.

VE re-established with BNT162b2 booster

54.6%

(95% CI: 30.4-70.4%)

Danish cohort study. https://www.medrxiv.org/content/10.1101/2021.12.20.21267966v2

VE vs. severe COVID-19 due to Omikron (UK)

2+1 dose vaccination protects up to 88% from Hospitalisation

Individuals with reported symptoms (community tested 27 Nov - 24 Dec 2021) were included in the analysis

Table 6: Vaccine effectiveness against hospitalisation for Omicron (all vaccine brands combined). OR = odds ratio, HR = hazard ratio, VE = vaccine effectiveness (CI=Confidence interval)

Dose	Interval after dose	OR against symptomatic disease (95% CI)	HR against hospitalisation (95% CI)	VE against hospitalisation (95% CI)
1	4+ weeks	0.74 (0.70-0.77)	0.65 (0.30-1.42)	52% (-5-78)
2	2-24 weeks	0.82 (0.80-0.84)	0.33 (0.21-0.55)	72% (55-83)
2	25+ weeks	0.98 (0.95-1.00)	0.49 (0.30-0.81)	52% (21-71)
3	2+ weeks	0.37 (0.36-0.38)	0.32 (0.18-0.58)	88% (78-93)

UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing: Update on hospitalisation and vaccine effectiveness for Omicron VOC-21NOV-01 (B.1.1.529). Dec 31, 2021

Omikron & Immune Evasion & Booster Dose
Current Scientific Consensus

- **3rd dose* re-establishes immune protection vs. Omikron infection**, however, **on lower level compared with Delta infection**

- **3rd dose* re-establishes immune protection vs. severe Omikron-infection, on relatively high level !**

- **Cellular immunity (conferred by vaccination or infection) remains effective vs. severe disease !**

* Jan 2022 ➨ FDA approved BNT162b2 **booster** dose for age group **12-17 years**

+ 3rd dose (3 + 1) for **immunocompromised** individuals

* April 2022 ➨ **Zulassung (Österreich) BNT162b2 Booster-Dosis für Altersgruppe 5-11 Jahre**

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-data-demonstrating-high-immune

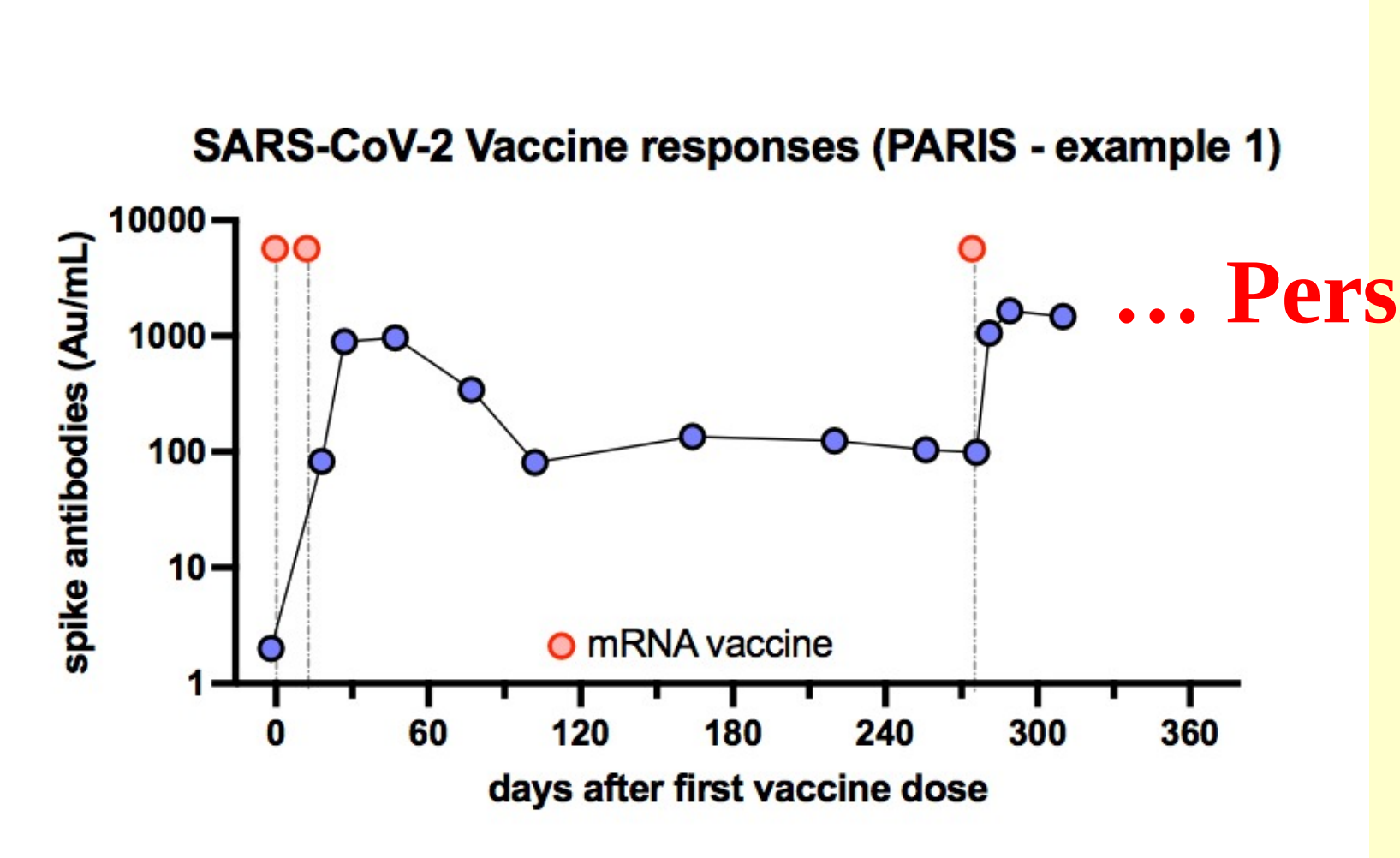
Pfizer Press Release, 14 April 2022

In the Phase 2/3 clinical trial, data were analyzed from **140 children** **5 through 11 years of age** received a **booster** dose approximately **6 months after the second dose** of the Pfizer-BioNTech COVID-19 vaccine 10-µg primary series. Data from a subanalysis of 30 sera from this study indicate that serum antibodies induced by a third dose neutralize the SARS-CoV-2 **Omicron** variant in this age group, as demonstrated by a **36-fold increase** **in neutralizing antibody titers** compared to levels seen after two doses of the Pfizer-BioNTech COVID-19 vaccine. A robust response was observed **regardless of prior SARS-CoV-2 infection**.

…….

To date, **more than 10,000 children under the age of 12** have participated in clinical trials investigating the Pfizer-BioNTech COVID-19 vaccine, and in this most recent booster data readout (n=401) the vaccine was **well tolerated** with **no new safety signals** observed.

Booster-Impfung



… Persistenz ?

F Krammer et al. PARIS Study

Ist die 4. Dosis nötig ?

Für Gesunde eher nicht

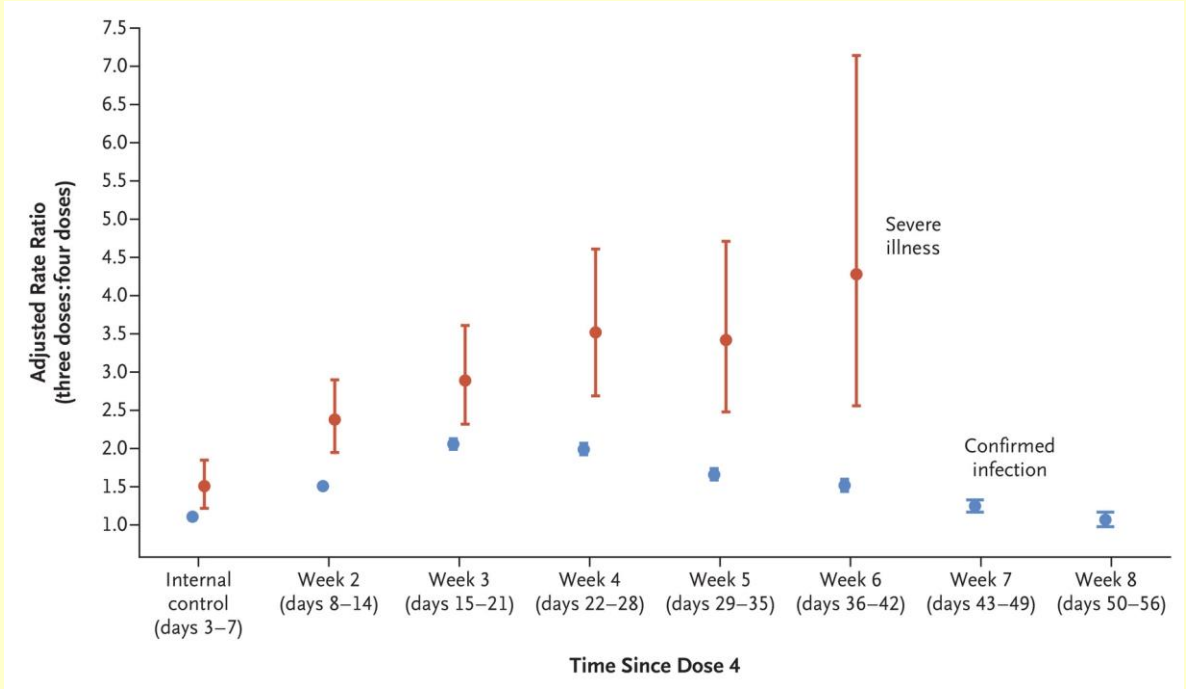
Empfehlung
- bei Immunsuppression und
- für Senioren

The NEW ENGLAND JOURNAL of MEDICINE

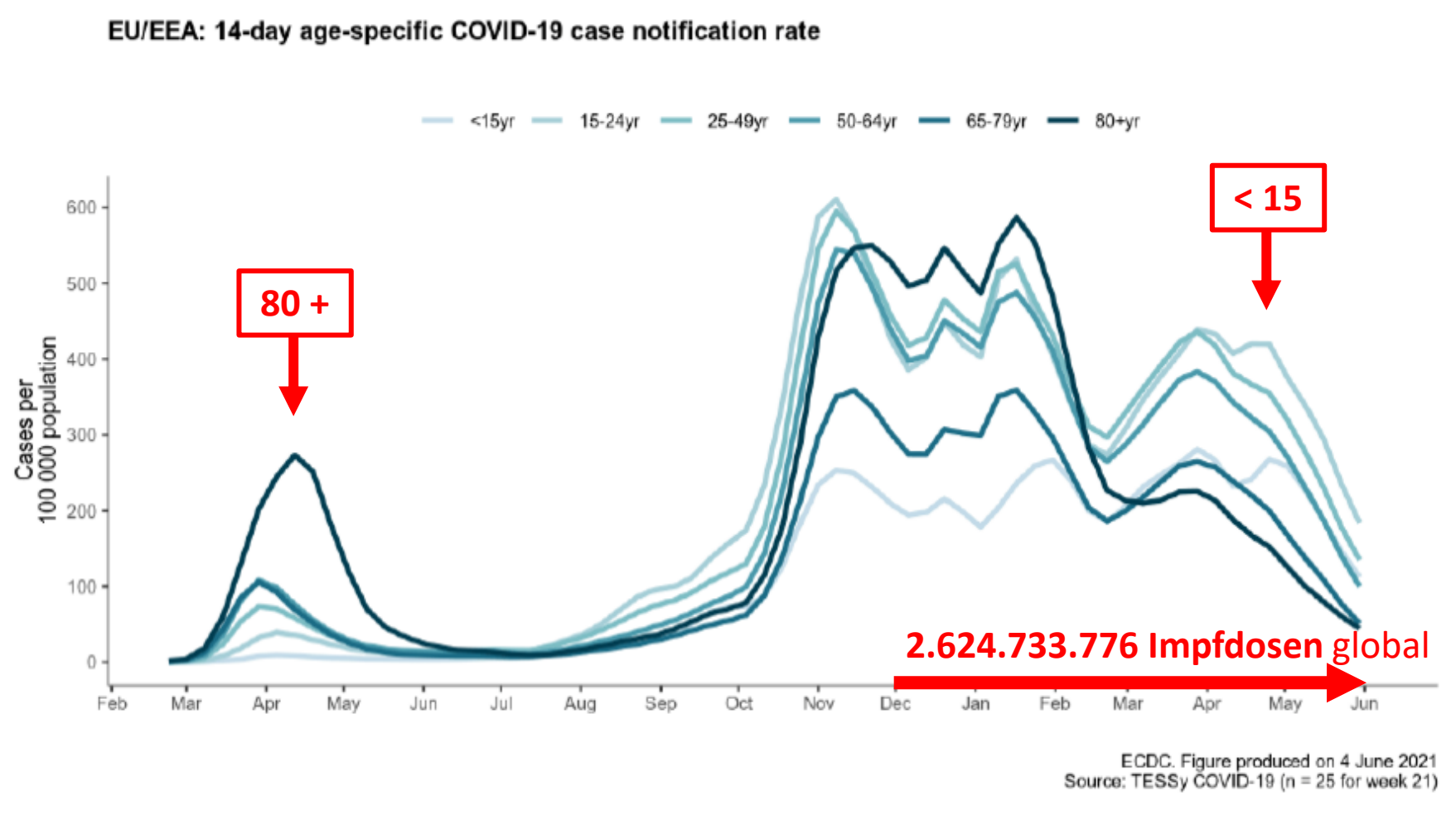
ORIGINAL ARTICLE

Protection by a Fourth Dose of BNT162b2 against Omicron in Israel

Yinon M. Bar-On, M.Sc., Yair Goldberg, Ph.D., Micha Mandel, Ph.D., Omri Bodenheimer, M.Sc., Ofra Amir, Ph.D., Laurence Freedman, Ph.D., Sharon Alroy-Preis, M.D., Nachman Ash, M.D., Amit Huppert, Ph.D., and Ron Milo, Ph.D.



Altersspezifische COVID-19 Fallmeldungen
EU/EEA, März 2020 bis Mai 2021



WHO 24. Juni 2021

ECDC Juni 2021

„Pädiatrische“ COVID-19 Impfung

Zugelassene COVID-19 Impfstoffe < 18 Jahren (EU)

Comirnaty® - BioNTech/Pfizer

21. Dez 2021
≥ 16 Jahre

28. Mai 2021
12 - 15 Jahre

25. Nov 2021
5 - 11 Jahre

< 5 Jahre?

Spikevax® - Moderna

6. Jan 2021
≥ 18 Jahre

23. Juli 2021
12-17 Jahre

24. Feb 2022
6 - 11 Jahre

< 6 Jahre ?

Paediatric BNT162b2 Trial Phase 1/2/3

BIONTECH

Pfizer

Assessment of Safety & Immunogenicity

- **2 groups:** 6 -24 months, 2 - 4 years
- 2 doses (3 µg) with 21 days interval

Interim analysis Dec 2021

- No safety signals of concern
- Age group 6-24 months met non-inferiority vs. 16-25 year-olds
- **No sufficiently robust immune response in age group 2-5 years**

Paediatric BNT162b2 Trial Phase 2/3

BIONTECH

Pfizer

Consequence (6 months – 4 years):

- **+ 3rd dose with 3 µg after 2 months** ← **submitted to FDA (… EMA ?)**

- 2nd study with 5 µg / 2 dose schedule (0, 21 days) **?**

Moderna mRNA-1273

Phase II/III study under 6 years of age

n ~ 4200 (6 months – < 2 years)
N ~ 2500 (2 - 5 years)

← Submitted to EMA & FDA

2 doses (**25 µg**) 28 days apart

- **Robust immune response** – neutralising antibody titers ≥ young adults
  GMR (6 mts – <2 yrs): 1.3 (95% CI: 1.1, 1.5)
  GMR (2 - 5 yrs): 1.0 (95% CI: 0.9, 1.2)
- **44%** (< 2 yrs) / **36%** (2-5 yrs) **effective**
- **Good safety / reactogenicity profile:** fever 15-17% (vs. 24% in 6-12 y/o)
- **No deaths, peri/myocarditis, MIS-C**

https://investors.modernatx.com/news/news-details/2022/Moderna-Announces-its-COVID-19-Vaccine-Phase-23-Study-in-Children-6-Months-to-Under-6-Years-Has-Successfully-Met-Its-Primary-Endpoint/default.aspx

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

COVID Data Tracker

COVID-19 Vaccinations < 18 years (USA)

12-17 years

17,539.535
1x vaccinated

14,967.666
2x vaccinated

5-11 years

10,193.645
(1x vaccinated)

8,266.088
2x vaccinated

10 May 2022

https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic

Reported AEFIs after 2nd dose BNT 162b2

Event	% of v-safe enrollees reporting reaction or health impact*	
	Dose 1 (N = 42,504)	Dose 2 (n = 29,899)
Any injection site reaction	54.8	57.5
Itching	3.8	3.7
Pain	52.7	55.8
Redness	3.7	4.4
Swelling	3.9	4.9
Any systemic reaction	34.7	40.9
Abdominal pain	5.1	6.4
Myalgia	7.1	10.2
Chills	3.9	6.8
Diarrhea	2.6	2.2
Fatigue	20.1	25.9
Fever	7.9	13.4
Headache	13.9	19.8
Joint pain	2.1	2.9
Nausea	5.0	6.9
Rash	1.2	1.0
Vomiting	2.3	2.7

Symptoms in children 5-11 years, who had at least one „v-safe“ health check within 7 d following Comirnaty® vaccination
(n = 42.504)

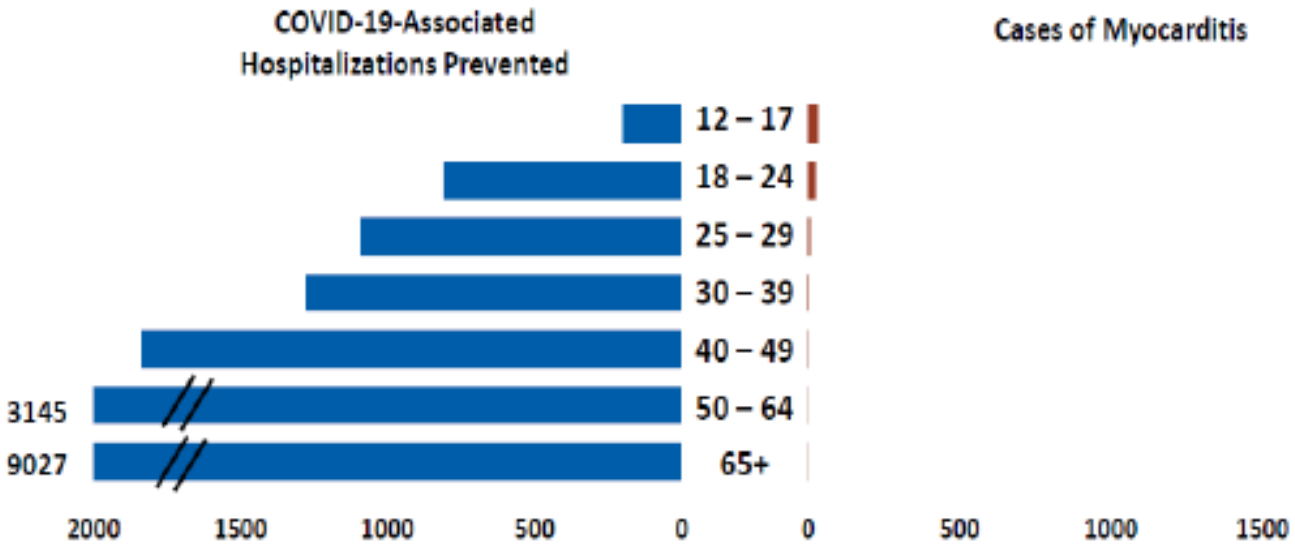
Hause AM et al. COVID-19 Vaccine Safety in Children Aged 5–11 Years — United States, November 3–December 19, 2021- MMWR 31.12.2021,

Myocarditis and paediatric benefit-risk of mRNA COVID vaccines

- Occurs after mRNA COVID-19 vaccination (Pfizer-BioNTech or Moderna), especially in male adolescents and young adults
- More often after the second dose
- Usually within several days after vaccination (4-5 days)
- US rate 12.6 cases per million 2nd doses
- Most cases mild in severity
- Sequelae?

Benefits and risks after dose 2, by age group

For every **million** doses of mRNA vaccine given with current US exposure risk[1]



Myocarditis following SARS-CoV-2 Vaccination in Children 5-11 Years of Age (VAERS)

Reports / VAERS (as of 10 Dec 2021)
Doses administered: 7,141.428 (9 Dec 2021)

- 3.233 reports to VAERS regarding 5- to 11-year-old children
- 14 cases of myocarditis
- 8 cases met CDC definition
  - 4 boys, 4 girls
- 2 cases after 1st dose, 6 cases after 2nd dose
- Only mild clinical courses

- **Incidence approx. 1:500.000** (in accordance with **background morbidity** in this age)

Su JR. Adverse events among children ages 5–11 years after COVID-19 vaccination: updates from v-safe and the Vaccine Adverse Event Reporting System (VAERS). Atlanta, GA: US Department of Health and Human Services, CDC; 2021. https://www.cdc.gov/vaccines/acip/ meetings/downloads/slides-2021-12-16/05-COVID-Su-508.pdf

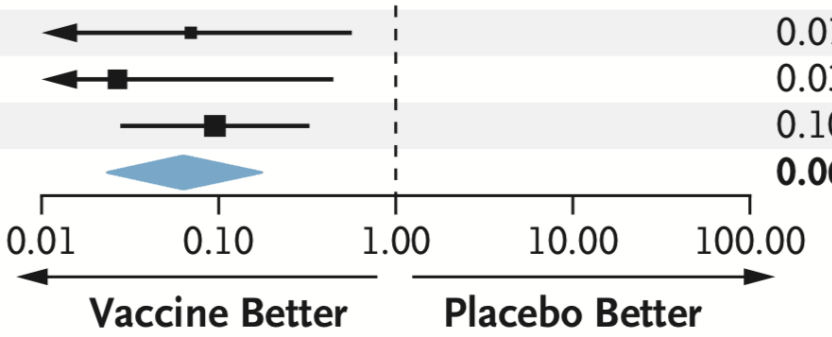
Confirmed COVID-19 after 2nd Dose BNT 162b2 (5-11 years)

Confirmed Covid-19 after the Second Injection, Regardless of Previous SARS-CoV-2 Infection

Trial	Vaccine	Placebo	Weight	Risk Ratio (95% CI)
	no. of events/total no. of participants		%	
Ali et al.	1/2139	7/1042	19.1	0.07 (0.01–0.56)
Frenck et al.	0/1119	18/1110	37.7	0.03 (0.00–0.44)
Walter et al.	3/1450	16/736	43.1	0.10 (0.03–0.33)
Total (95% CI)	**4/4708**	**41/2888**	**100.0**	**0.06 (0.02–0.18)**

Heter (P=0.68); I^2=0%

=5.23 (P<0.001)



Delta Period

- **No severe COVID-19**
- **No MIS-C**
- **No fatality**

Fang S et al. BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age. NEJM 2022; DOI: 10.1056/NEJMc2118775

BNT162b2 Protection against Delta vs. Omikron Variant (Hospitalization) in Children and Adolescents

Subgroup	Vaccinated Case Patients	Vaccinated Control Patients	Vaccine Effectiveness (95% CI)
	no. of patients/total no. (%)		%
Adolescents 12–18 yr of age			
Age group			
12–15 yr	63/543 (12)	313/828 (38)	83 (77 to 88)
16–18 yr	59/375 (16)	229/529 (43)	82 (74 to 88)
Delta-predominant period	33/684 (5)	442/1161 (38)	92 (89 to 95)
2–22 wk since vaccination	25/676 (4)	372/1091 (34)	93 (89 to 95)
23–44 wk since vaccination	6/657 (1)	60/779 (8)	92 (80 to 97)
Omicron-predominant period	89/234 (38)	100/196 (51)	40 (9 to 60)
2–22 wk since vaccination	35/180 (19)	39/135 (29)	43 (–1 to 68)
23–44 wk since vaccination	52/197 (26)	59/155 (38)	38 (–3 to 62)
Children 5–11 yr of age			
Omicron-predominant period	20/267 (7)	50/270 (19)	68 (42 to 82)

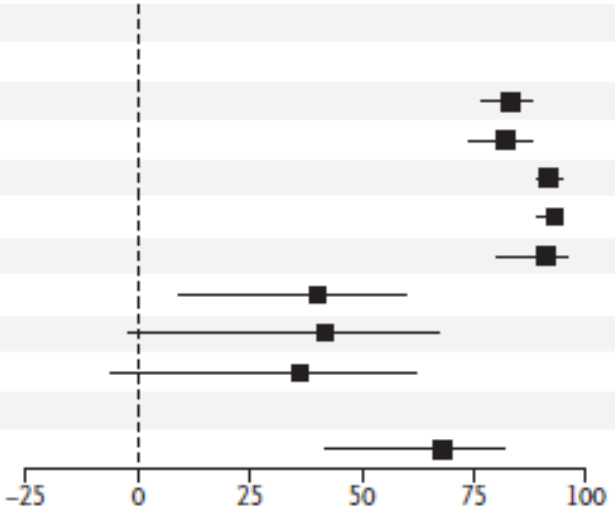


Figure 2. Effectiveness of the BNT162b2 Vaccine against Hospitalization for Covid-19, Stratified According to Age and Variant.

The delta-predominant period was defined as July 1, 2021, through December 18, 2021. The omicron-predominant period was defined as December 19, 2021, to February 17, 2022. For children 5 to 11 years of age, evaluation was limited to the omicron period because of the recent introduction of vaccination in this group (on October 29, 2021). For the subgroup analysis of time since vaccination, 4 case patients were not included because of missing dates of vaccination. Vaccine effectiveness was calculated as (1 – adjusted odds ratio) × 100, where the odds ratio is the odds of vaccination in case patients as compared with controls.

AM Price et al. NEJM March 2022

BNT162b2 Protection against Delta vs. Omikron Variant (critical vs. noncritical COVID-19) in Adolescents

Subgroup	Vaccinated Case Patients	Vaccinated Control Patients	Vaccine Effectiveness (95% CI)
	no. of patients/total no. (%)		%
Adolescents 12–18 yr of age			
Delta-predominant period	33/684 (5)	442/1161 (38)	92 (89 to 95)
Critical Covid-19	6/198 (3)	442/1161 (38)	96 (90 to 98)
Noncritical Covid-19	27/486 (6)	442/1161 (38)	91 (86 to 94)
Omicron-predominant period	89/234 (38)	100/196 (51)	40 (9 to 60)
Critical Covid-19	11/51 (22)	100/196 (51)	79 (51 to 91)
Noncritical Covid-19	77/175 (44)	100/196 (51)	20 (–25 to 49)

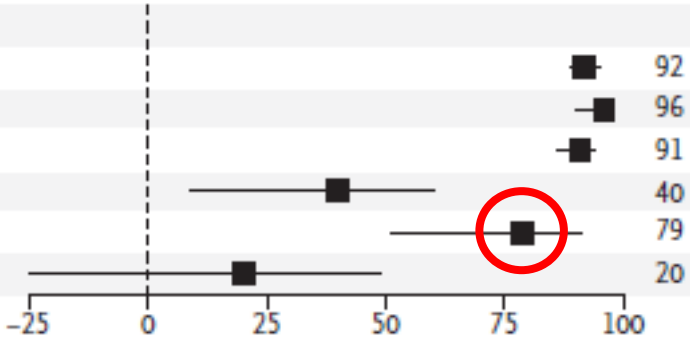


Figure 3. Effectiveness of the BNT162b2 Vaccine against Hospitalization for Critical as Compared with Noncritical Covid-19 in Adolescents 12 to 18 Years of Age, Stratified According to Variant.

Numbers were insufficient to stratify the analysis according to disease severity among children 5 to 11 years of age. In this analysis, only subgroups of case patients were based on disease severity; the entire control group (regardless of disease severity) served as the basis for comparison. Critical Covid-19 was defined as Covid-19 leading to life support (i.e., noninvasive mechanical ventilation [bilevel positive airway pressure or continuous positive airway pressure] or invasive mechanical ventilation, vasoactive infusions, or extracorporeal membrane oxygenation) or death. Information on this outcome was missing for 8 case patients admitted during the omicron period. Vaccine effectiveness was calculated as (1 – adjusted odds ratio) × 100, where the odds ratio is the odds of vaccination in case patients as compared with controls.

AM Price et al. NEJM March 2022

Weitere COVID-19 Impfstoffe für Kinder/Jugendliche

- **Studien (12-17 Jahre)**
- Derzeit keine Studien < 12 Jahre

Johnson & Johnson

- COV006 dzt. **keine Rekrutierung** (?)
  (kein Eintrag in clinicaltrials.gov)

AstraZeneca

- **Phase III Studien** in Altersgruppe **12-17 Jahre**

novavax

⇤ bei EMA eingereicht

COVID-19 Impfstoffe für Kinder (non-EU)

- **Soberana 2** (RBD-conj - Finlay Institute) ≥ 2 y (Cuba)
- **Abdala** (Subunit - CIBG) ≥ 2 y (Cuba)
- **Coronavac** (VP - Sinovac) 3-17 y (China)
- **BBIBP-CorV** (VP - Sinopharm) 3-17 y (China)
- **Covaxin** (VP - Bharat) 12-17 y (India)
- **Zycov D** (Plasmid-DNA - Zydus Cadila) 12-17 y (India)

Pipeline

Icahn School of Medicine at Mount Sinai

An Egg Based Covid-19 Study

The Icahn School of Medicine at Mount Sinai is looking for Healthy, Adult Volunteers who are **both:**

- ✔ **Vaccinated** (last dose > 6months ago) and
- ✔ Have **Never** been infected with COVID-19

to help investigate a NEW COVID-19 vaccine.

This NEW COVID-19 vaccine has *No Adjuvants* and *No Preservatives*. It is developed and produced by Researchers at Mount Sinai.

Volunteers will be financially compensated.

The vaccine utilized in this study was developed by faculty members at the Icahn School of Medicine at Mount Sinai. Mount Sinai is actively seeking to advance this vaccine to be available for commercial use.

Participants must be healthy adults between the ages of 18 and 59. Participants cannot be healthcare workers with direct patient care or laboratory workers who handle SARS-CoV-2.

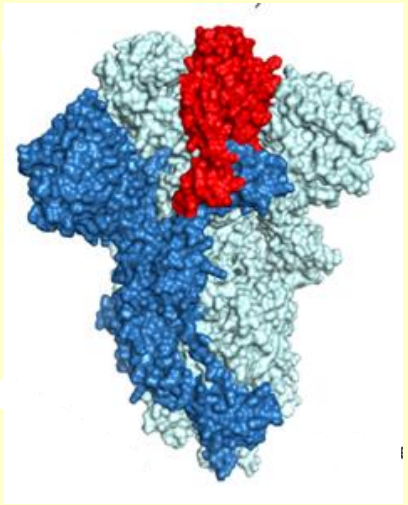
To see if you qualify,
Call **212-824-7714** or Email **COVIDTRIALSINFO@MOUNTSINAI.ORG**

Wann sind an neue SARS-CoV-2 Varianten adaptierte Impfstoffe zu erwarten ?

- **Moderna**
  - **Omikron-spezifischer (mRNA-1273.529) und bivalenter Booster-Impfstoff (mRNA-1273.214) in klinischen Studien – Daten ante portas**
- **Pfizer**
  - **BNT162b2 Omikron-Daten möglicherweise im Spätsommer**

- **<u>Problem:</u> Zulassungsmodus noch unklar** (dzt. zeitraubende Studien erforderlich).
  Methodik zur rascheren Entscheidungsfindung ? (“bridging” Studien ?)
  WHO und Zulassungsbehörden zuständig

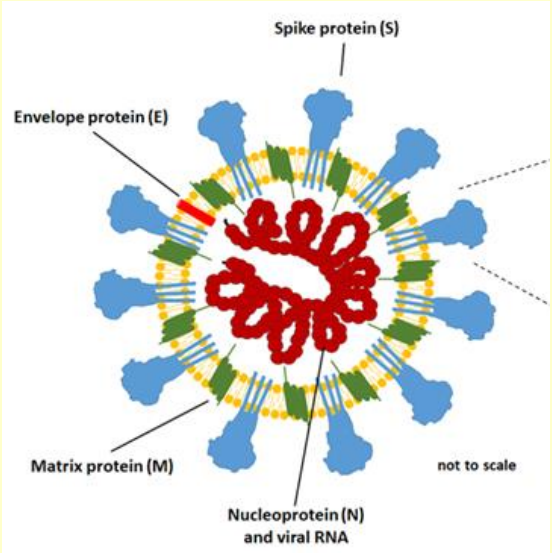
Vakzin-induzierte Immunität



Ein “Consensus” Spike Protein

- **Systemische Immunität**

Infektions-induzierte “natürliche” Immunität

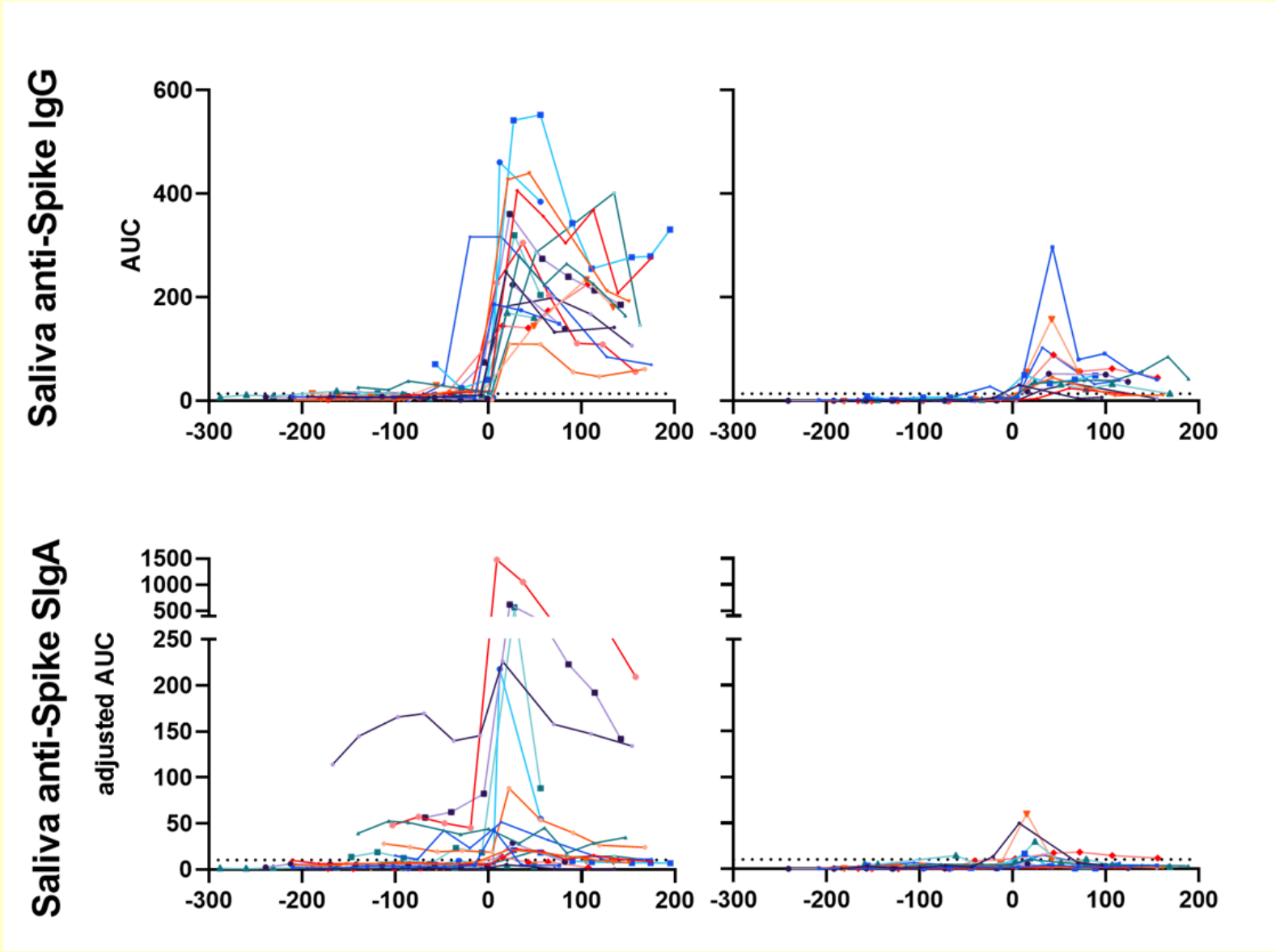


+ alle anderen “non-structure” Proteine
Gewisse intra-host Sequenz-Diversität wahrscheinlich
Potentiell längere Antigen-Präsenz

- **Systemische Immunität**
- **Mukosale Immunität**

Impfung induziert mukosale Antikörperantwort spezifisch in Individuen mit vorangegangener SARS-CoV-2-Infektion

(Speichelproben)



https://www.medrxiv.org/content/10.1101/2021.12.06.21267352v1

SARS-CoV-2 Antikörper …

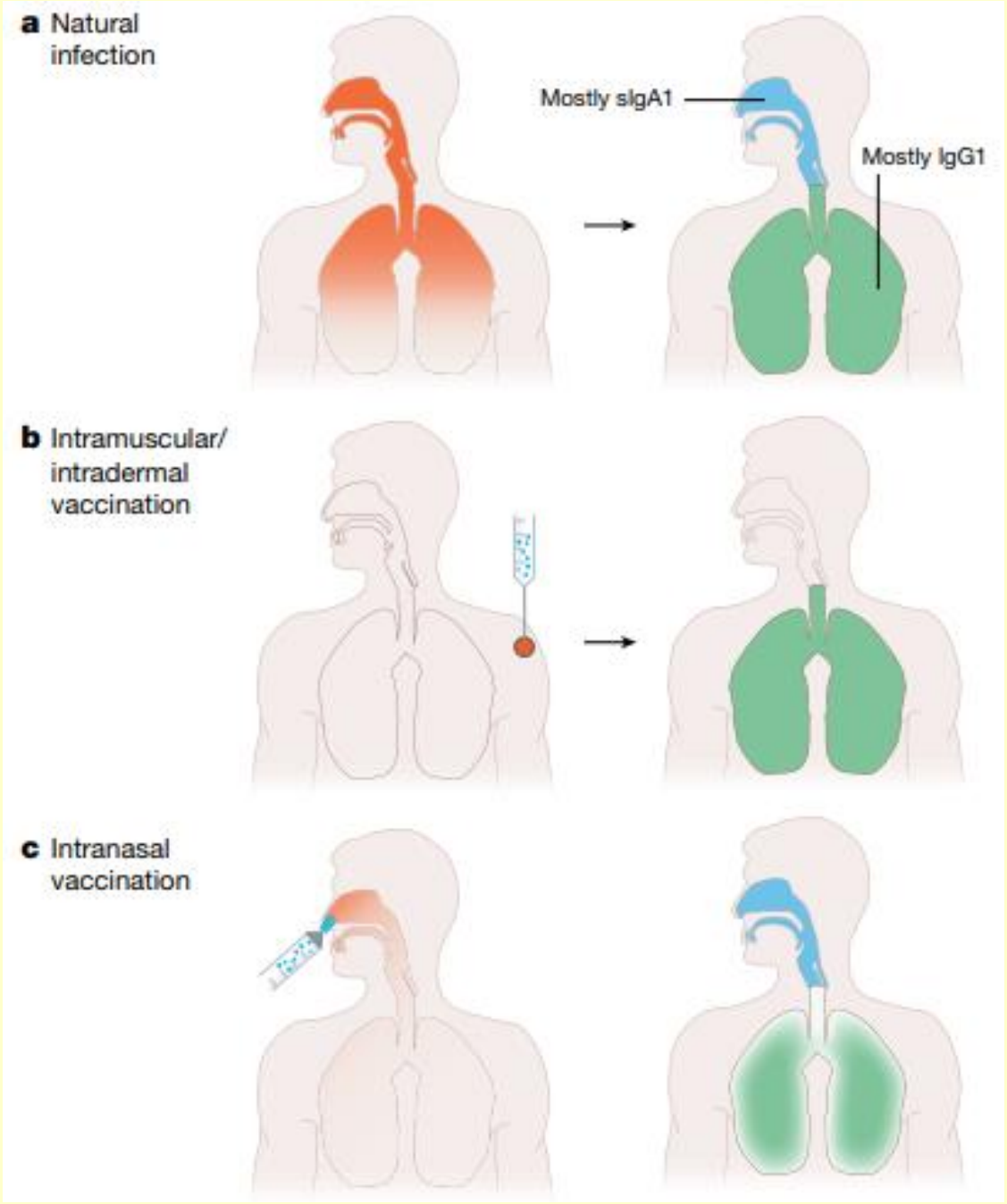
- **Titer vs. Spike-Protein korrelieren +/- mit Schutz vor Infektion, aber Varianten erschweren Interpretation**
- **Wahl des Antigens entscheidend**
- **(Schutz vor schweren Verläufen beruht auf anderen Mechanismen)**
- **Antikörpertests sind hilfreich für**
  - **Impfstoffentwicklung und -zulassung durch Immunobridging-Studien**
  - **Erkennung früherer Infektionen**
  - **Management von immungeschwächten Patienten**

Florian Krammer – „personal communication“

Intranasale Impfstoffe ?

Alle derzeit verwendeten Impfstoffe werden injiziert – ohne wesentliche mukosale Immunantwort

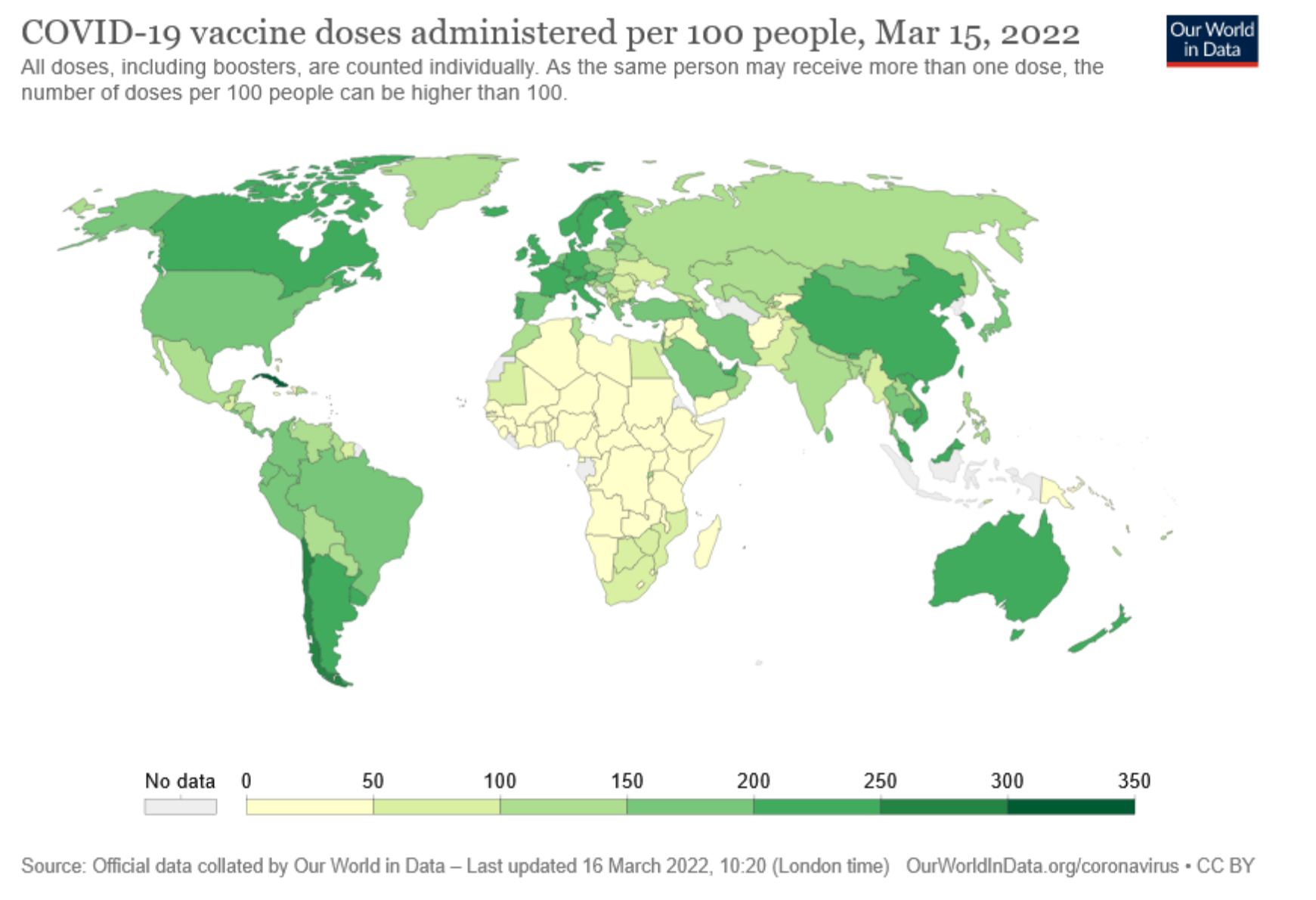
Intranasale Impfstoffe in klinischer Entwicklung (verfügbar 2023/2024 ?)



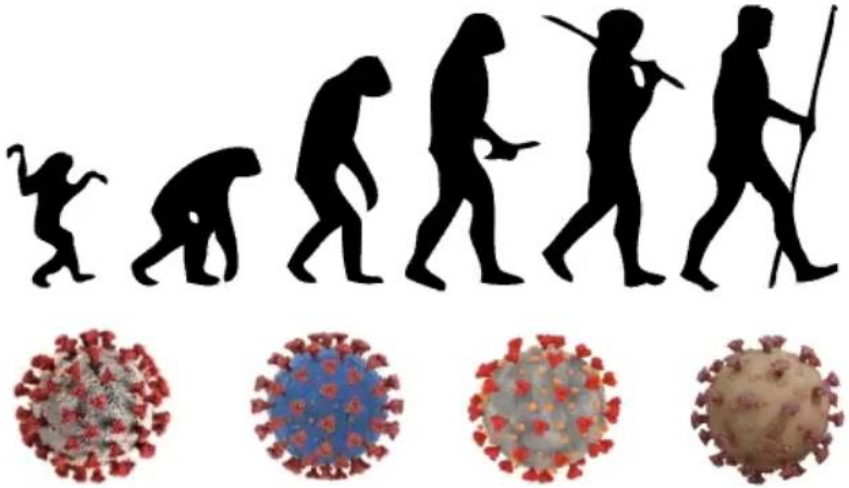
Krammer, Nature, 2020

Ist das Ende der Pandemie in Sicht ?

SARS-CoV-2 Durchimpfungsraten (global)



SARS-CoV-2 Varianten – „Evolution im Zeitraffer“



BA.2.12.1

BA.4

BA.5

WT > > > > Delta > Omikron > > > ?

↑ Transmissibilität !

↓ Schweregrad (?)

Laborbestätigte COVID-19 Fälle (& verabreichte Impfstoffe) global

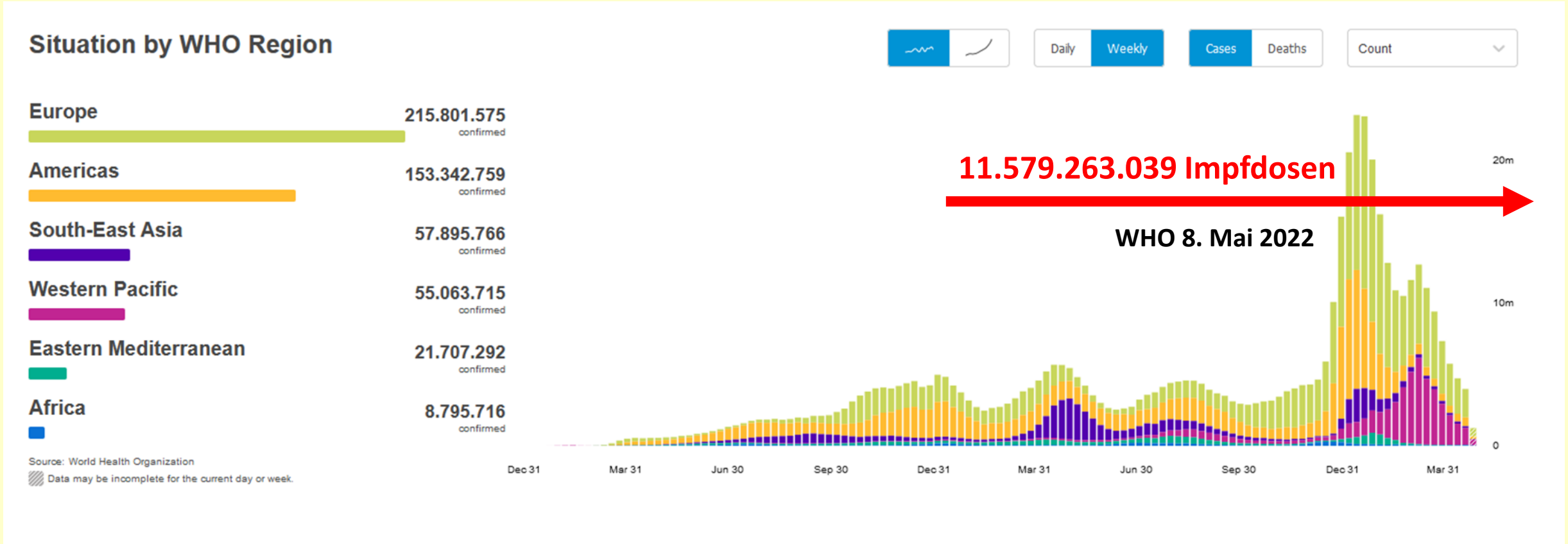
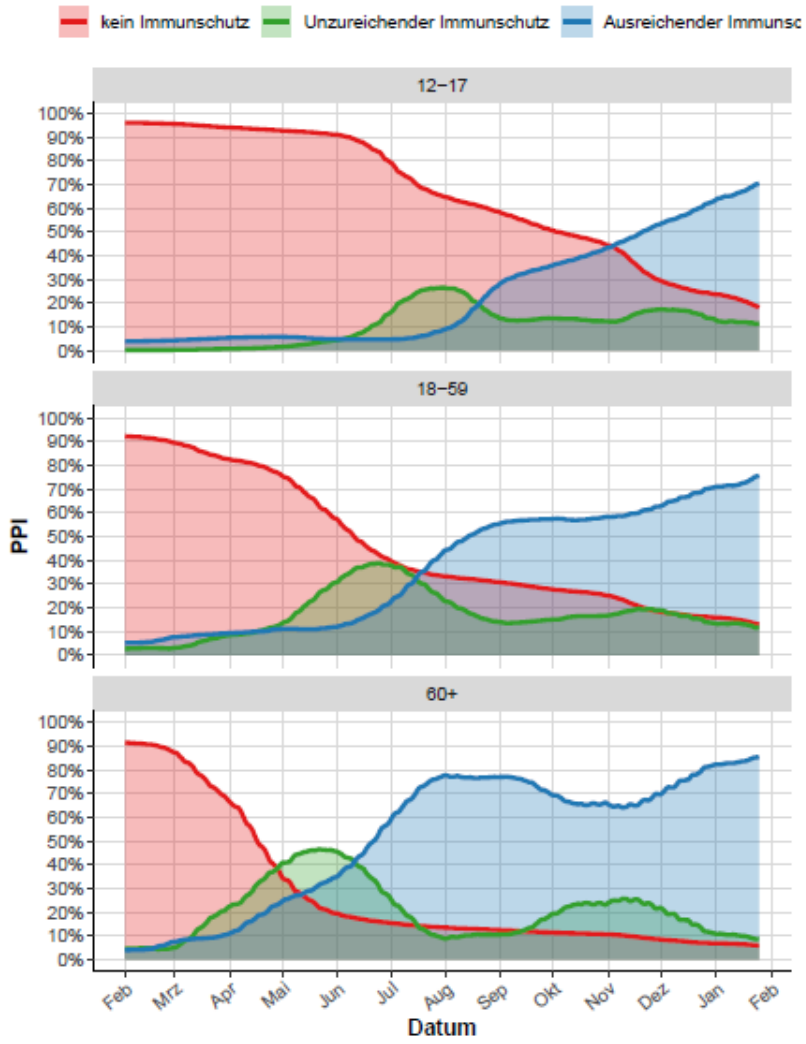


Abbildung 5: Prozentualer Anteil der Individuen der Population Österreich nach Kategorie des Immunschutzes (kein, unzureichend, ausreichend) und Altesrgruppe, vermutet auf Basis des Impf- und Genesen-Status, PPI (i.e. proportion population immunised) pro Tag, von 01.02.2021 bis 25.01.2022.



PPI =
"Population Proportion Immunized"

Immunprotektion der Bevölkerung basierend auf **Impfung *und*** **Genesenenstatus** (01 Feb 2021 - 26 Jan 2022)

Geschätzte PPI / Österreich Jan 2022

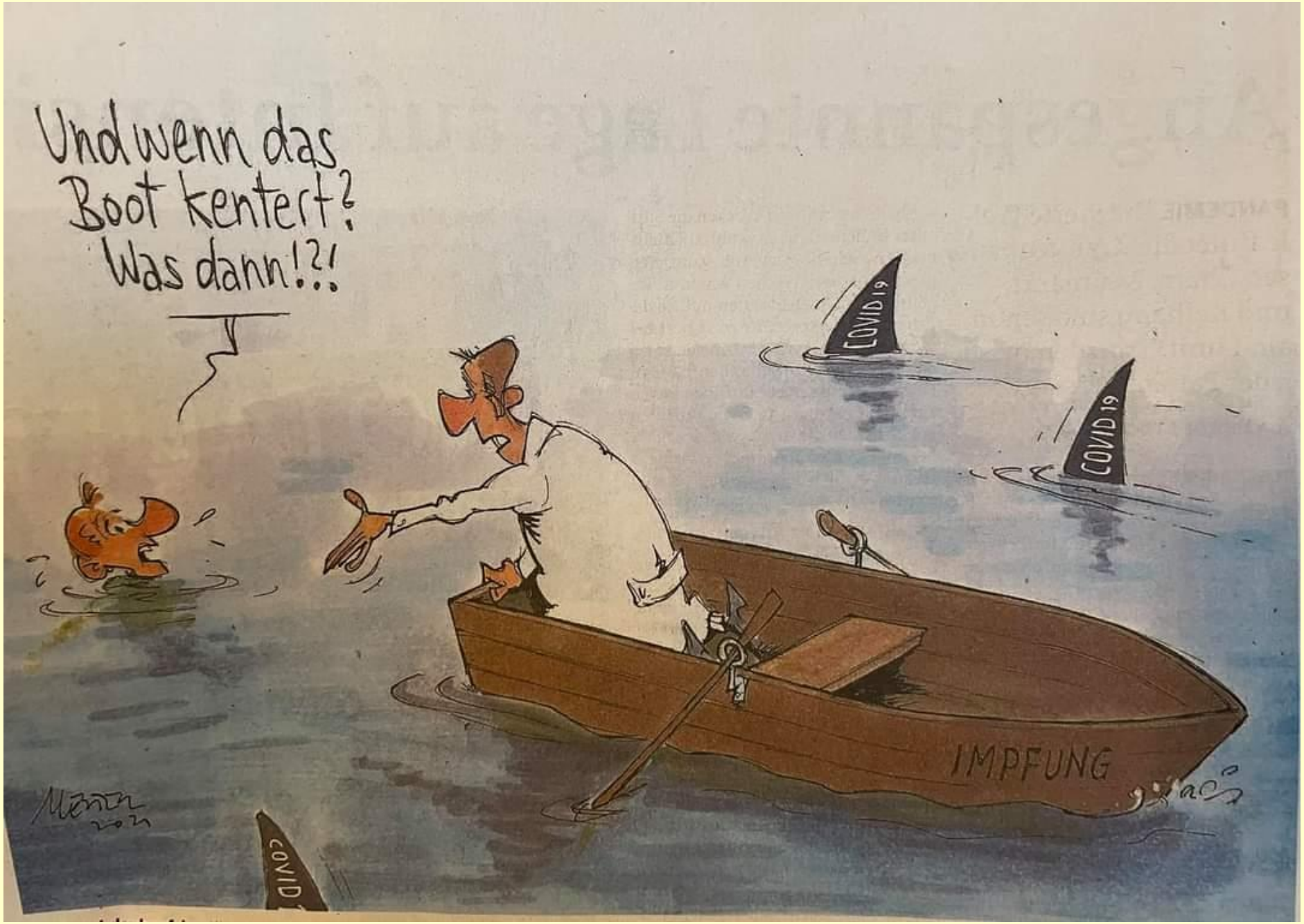
- > 20 % nur geimpft
- > 30% geimpft + genesen
- > 15% genesen/ Omikron

> 75 %

Daniela Schmid - Austrian Institute for Infection Epidemiology & Surveillance
N Popper - Centre for Computational Complex Systems, Vienna, Austria

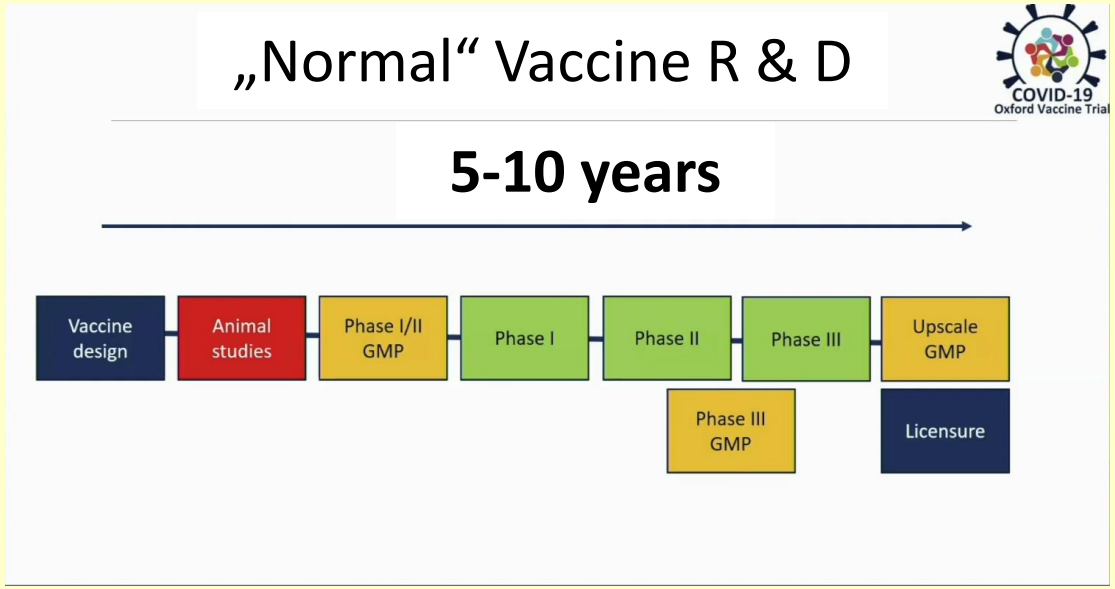
Künftige Ziele für SARS-CoV-2 Impfung

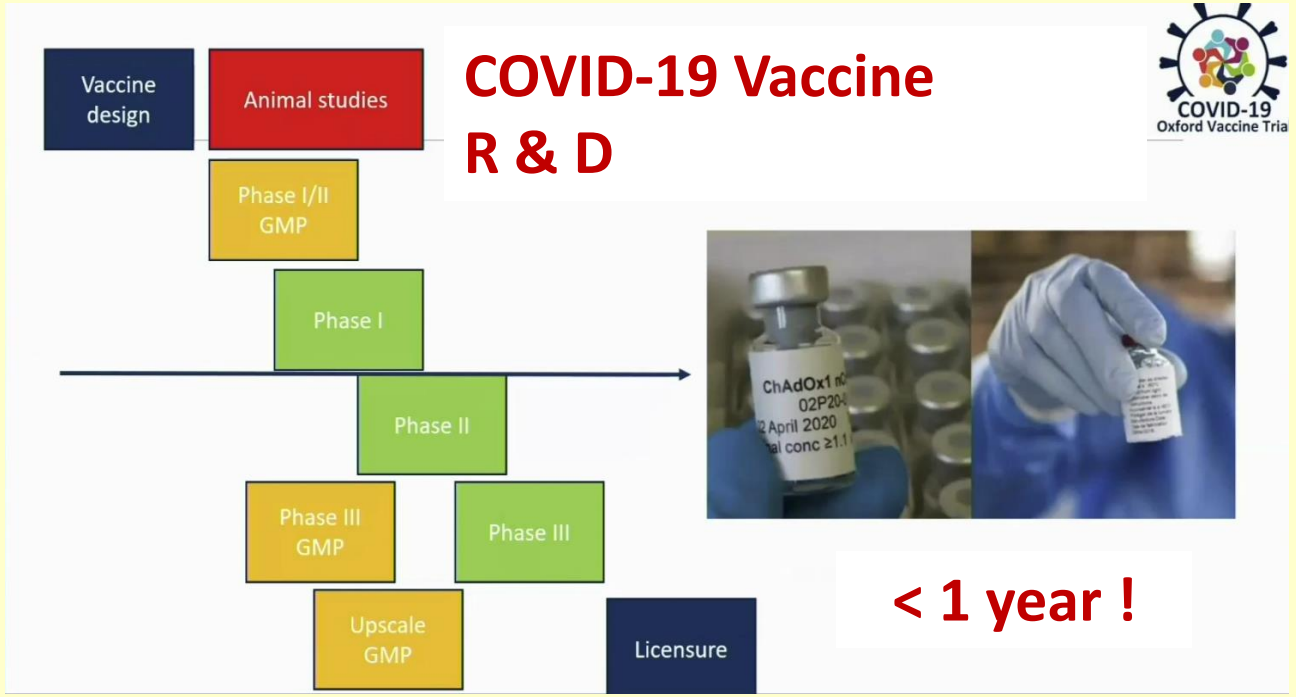
- **An SARS-CoV-2 Varianten adaptierte Impfstoffe**
  - **Prozess für "fast track" Zulassung zu entwickeln, idealerweise durch Zulassungsbehörden**
- **Verbesserte COVID-19 Impfstoffe**
  - **Mukosale Immunität = Schutz gegen Infektion und Transmission**
  - **Impfstoffe (z. B. multivalent) mit breiter Immunantwort einschließlich gegen künftige VoCs**
- **Fortgesetzte Bemühungen um Schließen der Impflücken**
  Abwägung der Evidenzlage zur Impfung von Vorschulkindern
- **Fortgesetzte Überwachung**
- **Verbesserte Methoden zur Überwindung der Impfverunsicherung !**


Und wenn das Boot kentert? Was dann!?!
COVID 19
COVID 19
IMPFUNG
COVID

Corona - Kollateraleffekte

Entwicklung von Impfstoffen





Andrew Pollard, Oxford Vaccine Group

3.–5. LEBENSMONAT

Körpergewicht 5445 g Körperlänge 64 cm Kopfumfang 42 cm

	ja	nein		
Stillen:	☒	☐	voll ☐	teilweise ☒
Ernährung altersgemäß	☒	☐	Pre-Nahrung ☐	
Rachitisprophylaxe: Vitamin D täglich	☒	☐	1er-Nahrung ☐	

+ Beikost

Ernährungsschwierigkeiten	☐	☒
Zwischenzeitliche Erkrankung	☒	☐
Greifbewegungen	☒	☐
Reaktion auf Licht/Bewegung	☒	☐
Strabismus	☐	☒
Reaktion auf Geräusche	☒	☐
Hebt Kopf in Bauchlage bis 90°	☒	☐
Oberkörper in Bauchlage auf		
Arme gestützt	☒	☐
Dreht sich um	☒	☐
Spreizhemmung	☐	☒

Untersuchungsbefund:	auffällig	unauffällig
Allgemeinzustand	☐	☒
Ernährungszustand	☐	☒
Entwicklungsstand	☐	☒
Augen: brechende Medien	☐	☒
sonstige Organbefunde	☒	☐

(detaillierte ärztliche Vermerke siehe nächste Seite)

LEBENSMONAT

Weitere Untersuchungsbefunde, Laborbefunde, fachärzlich-orthopädische Kontrolle, Erkrankungen, Therapie etc. falls erforderlich hier eintragen.

Information zu empfohlenen Impfung laut Impfplan durchgeführt ☒

RSV-Bronchiolitis (Aug 2021)

Diagnose: Bg Skoliose nach RSV-Infekt
HN II° Bds
Naevi flammei, Naevi coerulei

Kontrollen dringend empfohlen ☐

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Stempel, ärztliche Unterschrift

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NEJM 18 April 2022

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Prefusion F Protein–Based Respiratory Syncytial Virus Immunization in Pregnancy

Simões EAF et al. DOI: 10.1056/NEJMoa2106062

CLINICAL PROBLEM

An effective vaccine is needed to prevent respiratory syncytial virus (RSV) infection, which is associated with the deaths of approximately 118,200 children worldwide annually, half of whom are infants younger than 6 months of age.

CLINICAL TRIAL

Design: A phase 2b randomized, placebo-controlled trial examined the safety and immunogenicity of an investigational vaccine against RSV F protein, the target of neutralizing antibodies, in pregnant women.

Interventions: 406 pregnant women were randomly assigned to one of five groups and received an injection of either 120 μg or 240 μg of the RSV prefusion F protein–based (RSVpreF) vaccine, with or without aluminum hydroxide, or placebo at 24 through 36 weeks' gestation. The primary end points of the interim analysis were safety, in the recipients and their infants during follow-up, and immunogenicity, indicated by 50% titers of neutralizing antibodies in recipients' serum and in umbilical-cord blood at delivery.

RESULTS

Safety: The most common local side effect was mild-to-moderate pain at the injection site. In the 5.5 months from trial entry to the interim analysis, no adverse events were attributed to the vaccine.

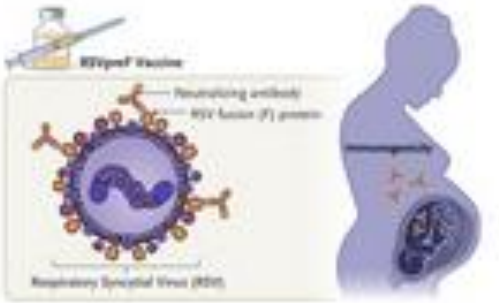
Immunogenicity: Neutralizing immunogenic responses occurred in the vaccine recipients and their infants but not in the placebo recipients and their infants.

LIMITATIONS AND REMAINING QUESTIONS

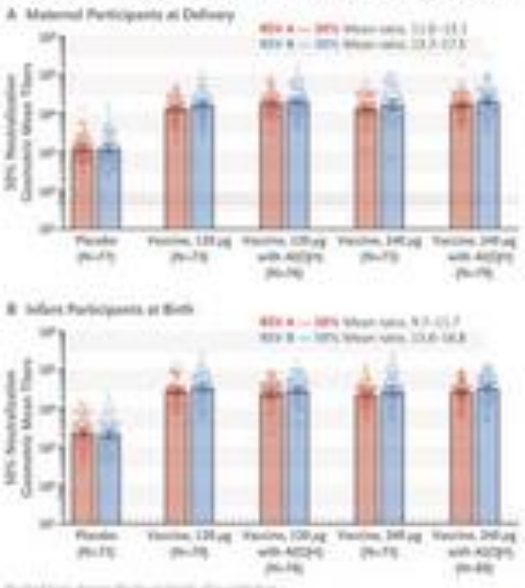
Further study is required to understand the following:

- Vaccine efficacy, which the trial was not designed to test.
- Potential findings in non-White, non-U.S. pregnant women and their infants, given that this interim analysis included only U.S. participants and most were White.
- Vaccine effects with receipt at 24 to 27 weeks' gestation, a period that was underrepresented in this interim analysis.

Links: Full Article | NEJM Quick Take



Geometric Mean 50% Neutralizing Titers in RSV A and RSV B Assays



CONCLUSIONS

In this interim analysis, RSVpreF vaccine induced neutralizing antibody responses and transplacental transfer of RSV neutralizing antibodies without eliciting any safety concerns in pregnant women or their infants.

Weitere Impfungen in der Schwangerschaft

Konzept I

Direkter Schutz der Schwangeren

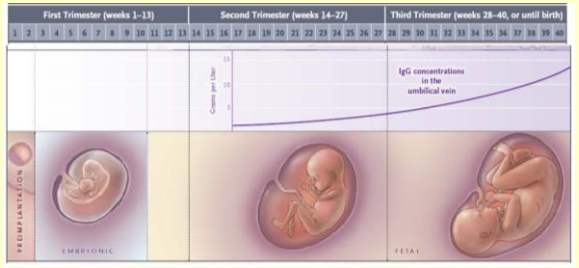
Direkter Schutz des Fötus

Empfehlung

- **Influenza** (seit 2005)
- **Pertussis** (seit 2013)
- (… GBS ?)

Konzept II

Indirekter Schutz des Neugeborenen durch transplazentaren IgG-AK-Transfer

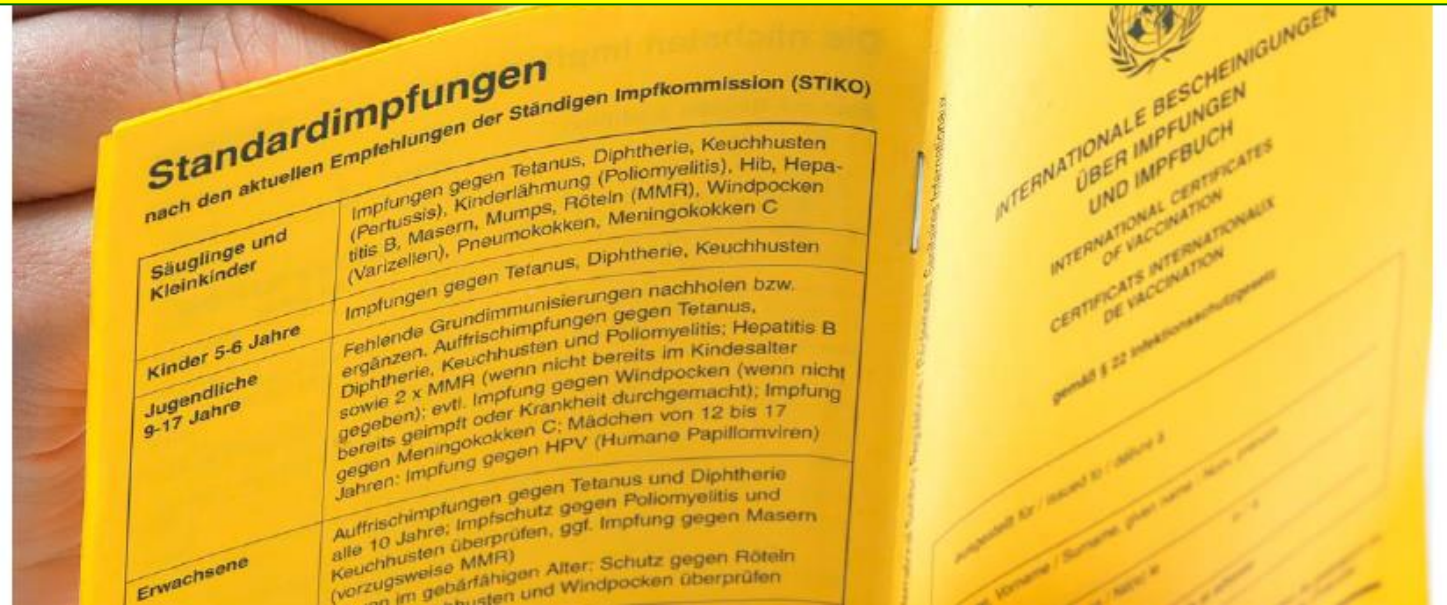


Bundesministerium
Soziales, Gesundheit, Pflege
und Konsumentenschutz

IMPFKOMMISSION ÖGKJ
ÖSTERREICHISCHE GESELLSCHAFT FÜR KINDER- UND JUGENDHEILKUNDE

Seit Herbst 2020

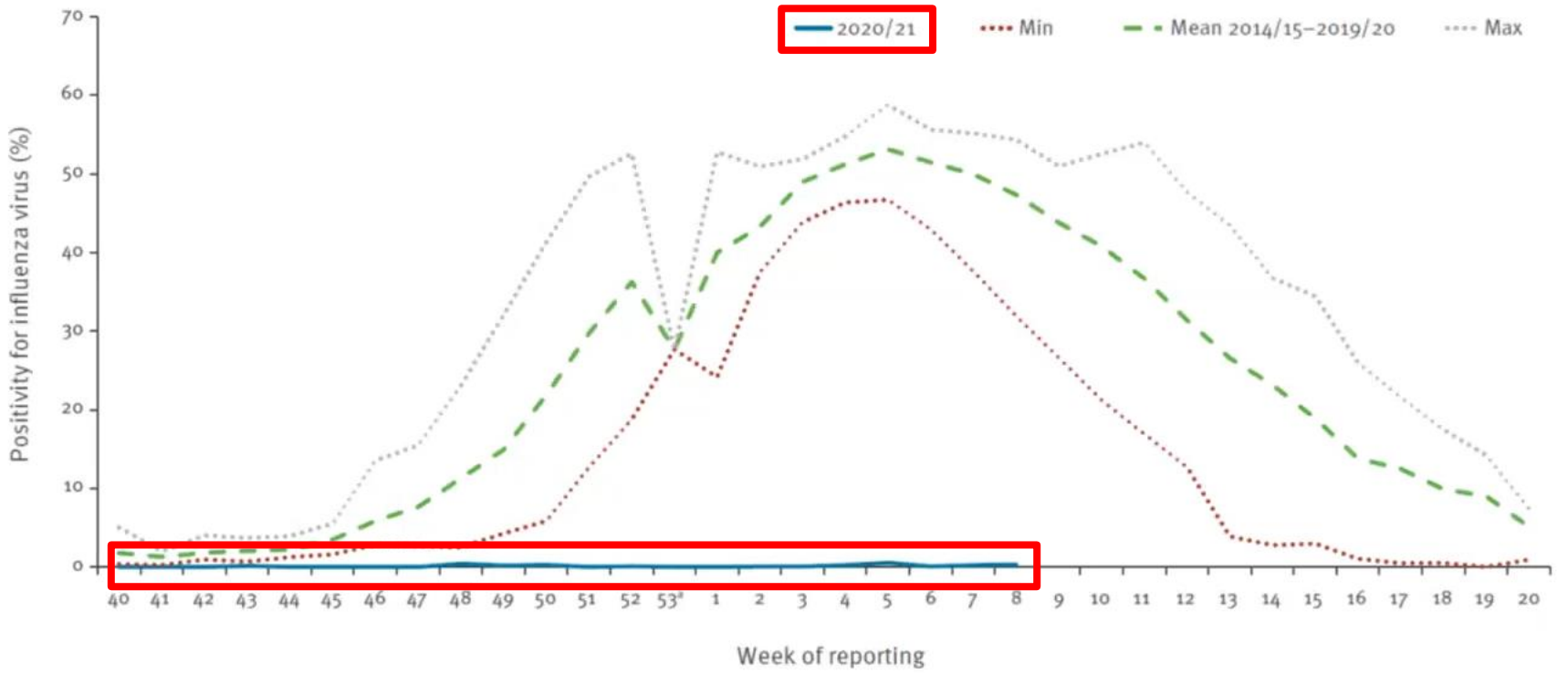
kostenfreie Influenzaimpfung für Kinder, Jugendliche bis 14 Jahre und Senioren



Influenza-"Ebbe" (2020 – 2021)
Während der COVID-19 Pandemie in Europa

FIGURE 3

Proportion of specimens testing positive (positivity) for influenza virus in sentinel surveillance in weeks 40 2020–8 2021 compared with minimum, mean and maximum of previous seasons in 2014/15–2019/20, WHO European Region

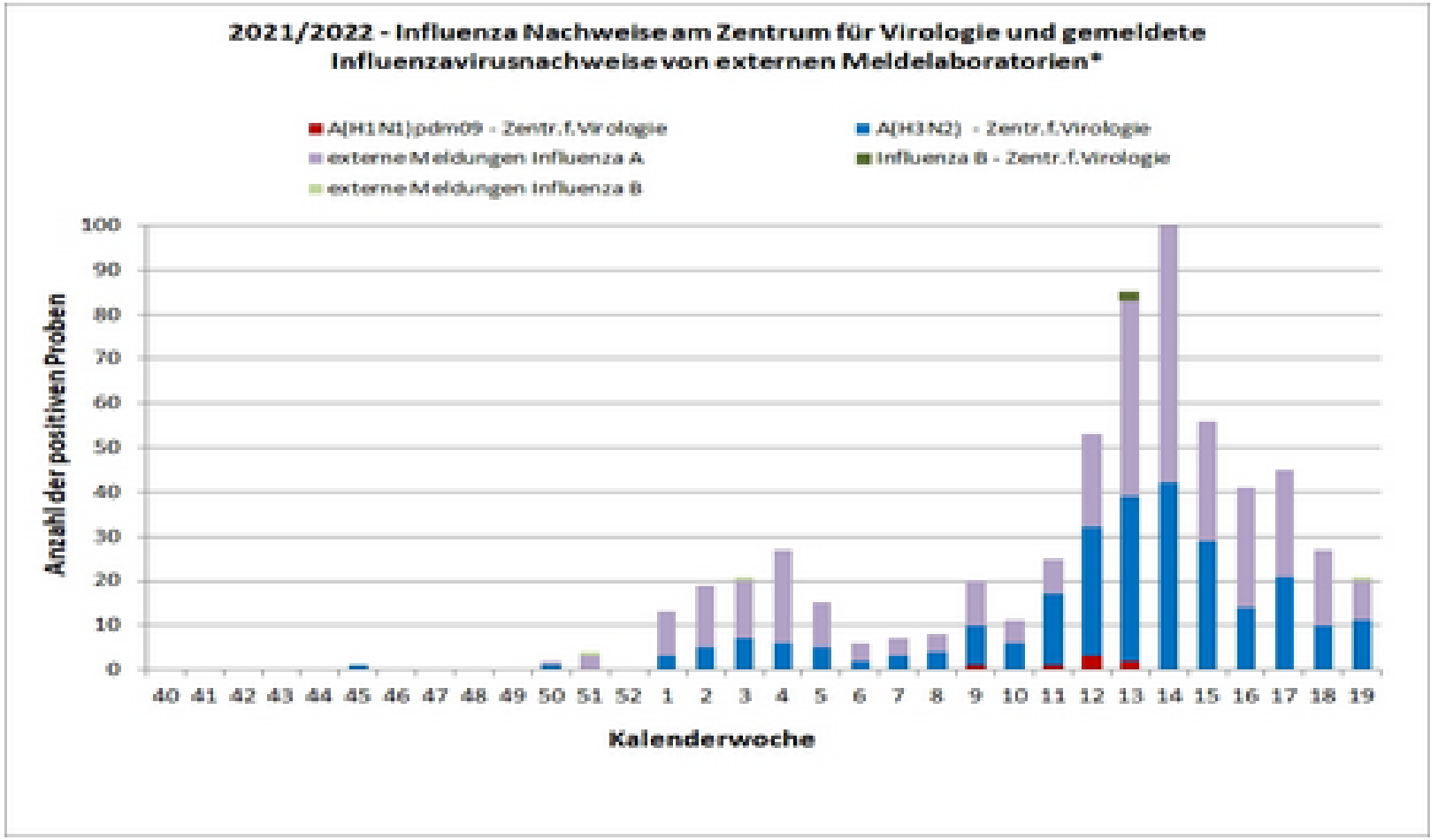


Max: maximum; min: minimum; WHO: World Health Organization.

[a] Only seasons 2015/16 and 2020/21 had week 53.

Adlhoch et al, Eurosurveillance 2021

"Grippewelle" (2021 – 2022)
Während der COVID-19 Pandemie in Europa



www.influenza.at

Cell Research

www.nature.com/cr
www.cell-research.com

ARTICLE

Coinfection with influenza A virus enhances SARS-CoV-2 infectivity

Lei Bai[1], Yongliang Zhao[1], Jiazhen Dong[1], Simeng Liang[1], Ming Guo[1], Xinjin Liu[1], Xin Wang[1], Zhixiang Huang[1], Xiaoyi Sun[1], Zhen Zhang[1], Lianghui Dong[1], Qianyun Liu[1], Yucheng Zheng[1], Danping Niu[1], Min Xiang[1], Kun Song[1], Jiajie Ye[1], Wenchao Zheng[1], Zhidong Tang[1], Mingliang Tang[1], Yu Zhou[1], Chao Shen[1], Ming Dai[2], Li Zhou[1,2], Yu Chen[1], Huan Yan[1], Ke Lan[1,2,3] and Ke Xu[1]

The upcoming flu season in the Northern Hemisphere merging with the current COVID-19 pandemic raises a potentially severe threat to public health. Through experimental coinfection with influenza A virus (IAV) and either pseudotyped or live SARS-CoV-2 virus, we found that IAV preinfection significantly promoted the infectivity of SARS-CoV-2 in a broad range of cell types. Remarkably, in vivo, increased SARS-CoV-2 viral load and more severe lung damage were observed in mice coinfected with IAV. Moreover, such enhancement of SARS-CoV-2 infectivity was not observed with several other respiratory viruses, likely due to a unique feature of IAV to elevate ACE2 expression. This study illustrates that IAV has a unique ability to aggravate SARS-CoV-2 infection, and thus, prevention of IAV infection is of great significance during the COVID-19 pandemic.

Cell Research (2021) 31:395–403; https://doi.org/10.1038/s41422-021-00473-1

INTRODUCTION

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at the end of 2019 has led to a worldwide pandemic. Until 13 January 2021, there have been more than 90 million

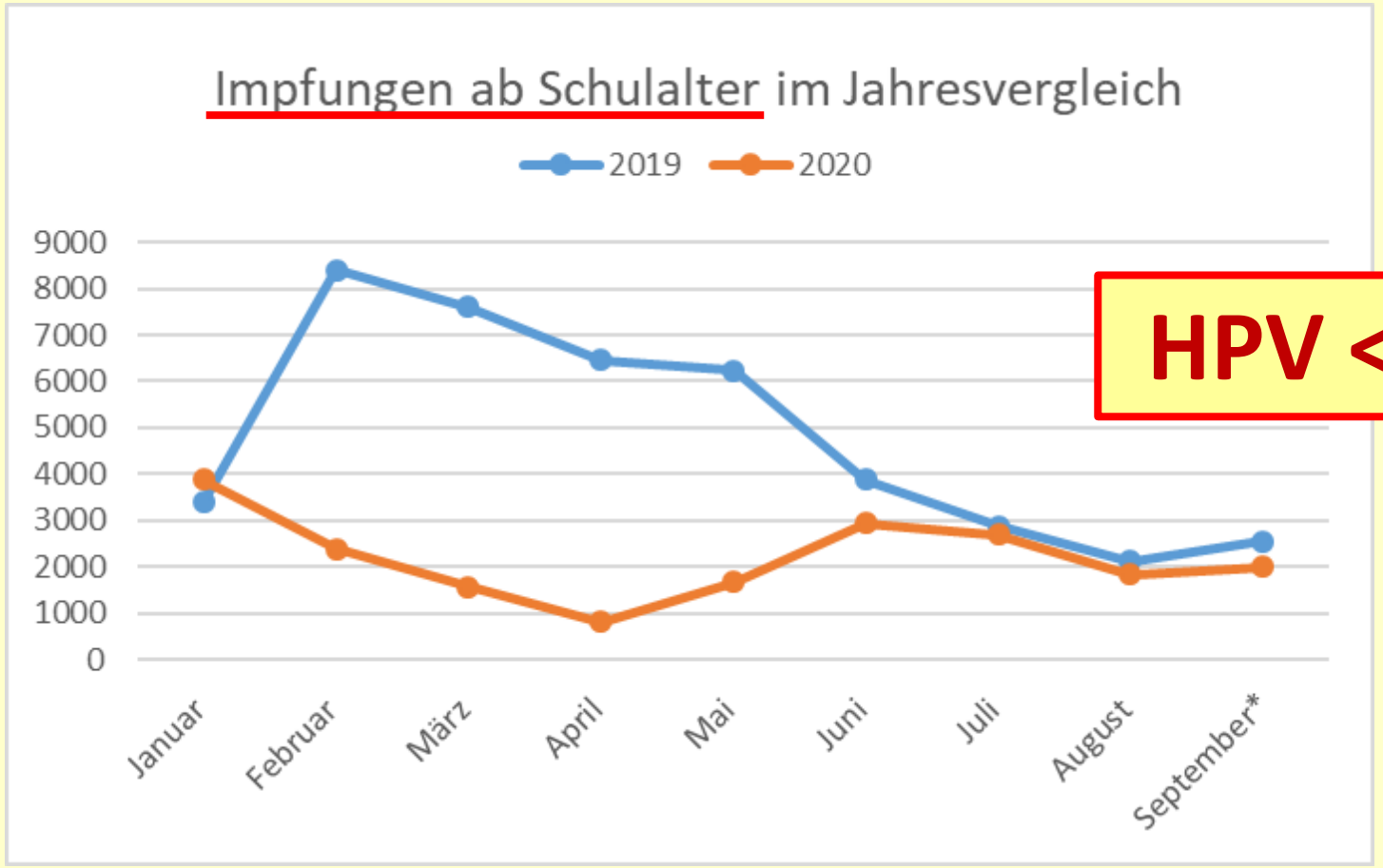
contrast, another study only reported mild symptoms in limited coinfection outpatients.[10] A retrospective study found that the coinfection rate of SARS-CoV-2 and influenza virus was as high as

Single dose HPV Vaccination ?

WHO-Empfehlung (für Entwicklungsländer)

Stellungnahme NIG/BMG
www.sozialministerium.at

Durchimpfungsraten 2019 vs 2020



HPV < 40% !

Quelle: Steirische Impfdatenbank, Wissenschaftliche Gesellschaft für Vorsorgemedizin

THE OFFICIAL NEWSMAGAZINE OF THE AMERICAN ACADEMY OF PEDIATRICS

AAP News

DEDICATED TO THE HEALTH OF ALL CHILDREN

Ensure adolescents who missed vaccines during pandemic catch up

by Meryam Jan M.D.; Margaret A. Stager M.D., FAAP

Though routinely recommended vaccines have improved the health and well-being of adolesc
19 pandemic has led to new challenges and decreased immunization rates.

A recent report from the Centers for Disease Control and Prevention (CDC) found a substa
to 71% in routine vaccine doses administered to adolescents during the COVID-19 pand
2018 and 2019 (Murthy BP, et al. *MMWR Morb Mortal Wkly Rep.* 2021;70:840-84).

The easing of nationwide restrictions and opening of schools introduce a new risk for dis
adolescents who may have missed routine immunizations due to the pandemic. Ther
pediatricians to ensure adolescents are up to date on their vaccines.

Pressekonferenz Impfen - Graz Landhaushof, 12. Juli 2021

LR J Bogner-Strauß, LR D Kampus, ÄK-Präs H Lindner, WAVM-Obmann M Adomeit,

HJ Dornbusch

Die Zahlen sprechen für sich: Die niedergelassenen steirischen Fachärztinnen und Fachärzte für Kinder- und Jugendheilkunde haben gemeinsam mit ihren hausärztlichen Kolleginnen und Kollegen die steirischen Kinder und Jugendlichen mit Riesen-Engagement betreut. Das Ergebnis sind beeindruckend: Sie haben bei Vorschulkindern um **fast 2.000 Impfungen mehr verabreicht als im Jahr 2019**. Damit konnten sie die Rückgänge, die es im öffentlichen Bereich Corona-bedingt natürlich gab, nicht nur ausgleichen, sondern auch das Gesamtergebnis steigern.

Ca. 40 KJFÄ

fast 90% der Kinderimpfungen

Gesundheitsämtern wurde kaum genützt, auf die effektive Möglichkeit der Impfung in Kinder- und Jugendordinationen wurde leider nicht hingewiesen.
Durch (im Regierungsprogramm vorgesehene) routinemäßige „**Juniorchecks**“ zwischen 6 und 18 Jahren - analog zu MKP-Untersuchungen bei Vorschulkindern bzw. Vorsorgeuntersuchungen bei Erwachsenen – könnten die Impfraten in dieser Altersgruppe deutlich verbessert werden. Solche Juniorchecks werden seit einigen Jahren von der Sozialversicherung der Selbstständigen angeboten, von ÖGK, BVA und KFA leider nicht.

Lassen Sie mich ein bisschen die Werbetrommel für die HPV-Impfung rühren – eine Impfung, die für Kinder und Jugendliche seit 2014 im kostenfreien Kinder-Impfprogramm

„Impfmythen“

Verschwörungs-theorien

Impf-Verunsicherung

Conclusio

- **Sinkende Impfraten - eine (schleichende) schwerwiegende globale Bedrohung !**
- Mit geringerem Impfschutz und reduzierten Schutzmaßnahmen drohen schwere Epidemien (RSV, Influenza) und vermehrtes Auftreten anderer impfpräventabler Infektionen (Masern, Diphtherie, invasive bakterielle Infektionen, …).
- „Pro-aktive“ Gegenmaßnahmen sind unbedingt nötig !
- **Catch-up Impfungen bei jeder Gelegenheit !**


Danke für die Aufmerksamkeit