Global Health Cast 39

May 31st, 2023

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Every Week

12.00 noon - CET

What we talk about today

- RSV-trials – overview
- Pre-infection COVID vaccination linked to lower Long COVID odds
- COVID-19 vaccines in Europe
- Next generation pneumococcal conjugate vaccine
- “Most Infectious Diseases” – Middle East Respiratory Syndrome

RSV Vaccines and Trial Names

Late-stage RSV pipeline			
Project	**Company**	**Description**	**Details**
Nirsevimab (SP0232)	Sanofi/ Astrazeneca	Fusion antibody	Filed; accepted under accelerated assessment in EU, Harmonie in hospitalized infants
GSK3844766A	Glaxosmithkline	Protein subunit vaccine, adjuvanted	Aresvi 004 in adults ≥60, data due H1 2022
RSVPreF3 (GSK3888550A)	Glaxosmithkline	Protein subunit vaccine, unadjuvanted	Trials on pause; Grace maternal protection trial was due to read out H2 2022
RSVpreF (PF-06928316)	Pfizer	Protein subunit vaccine	Data from Renoir (adults ≥60) and maternal protection trial due H1 2022
Ad26.RSV.preF	Johnson & Johnson	Adenovirus type 26 viral vector vaccine	Evergreen in adults ≥60, data due H2 2022, Cypress in adults ≥ 65
Clesrovimab (MK-1654)	Merck & Co	Fusion antibody	MK-1654-007 in high-risk infants; ph2/3 MK-1654-004 in healthy infants, data due 2022
Rilematovir (JNJ-53718678)	Johnson & Johnson	Oral RSV F-protein fusion inhibitor	Daisy in hospitalised children; Primrose in adult outpatients; trials started late 2021, Freesia terminated

MEDLEY, MELODY, HARMONIE

AReSVi

GRACE

RENOIR, MATISSE

EVERGREEN, CYPRESS

DAISY, PRIMROSE, FREESIA

Article

https://doi.org/10.1038/s41467-023-38388-7

Long COVID risk and pre-COVID vaccination in an EHR-based cohort study from the RECOVER program

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Published online: 22 May 2023

Check for updates

M. Daniel Brannock[1,15] ✉, Robert F. Chew[1,15], Alexander J. Preiss[1,15], Emily C. Hadley[1,15], Signe Redfield[2], Julie A. McMurry[3], Peter J. Leese[4], Andrew T. Girvin[5], Miles Crosskey[6], Andrea G. Zhou[7], Richard A. Moffitt[8,9], Michele Jonsson Funk[4], Emily R. Pfaff[4], Melissa A. Haendel[3], Christopher G. Chute[10], N3C* & RECOVER Consortia*

Long COVID, or complications arising from COVID-19 weeks after infection, has become a central concern for public health experts. The United States National Institutes of Health founded the RECOVER initiative to better understand long COVID. We used electronic health records available through the National COVID Cohort Collaborative to characterize the association between SARS-CoV-2 vaccination and long COVID diagnosis. Among patients with a COVID-19 infection between August 1, 2021 and January 31, 2022, we defined two cohorts using distinct definitions of long COVID—a clinical diagnosis ($n = 47{,}404$) or a previously described computational phenotype ($n = 198{,}514$)—to compare unvaccinated individuals to those with a complete vaccine series prior to infection. Evidence of long COVID was monitored through June or July of 2022, depending on patients' data availability. We found that vaccination was consistently associated with lower odds and rates of long COVID clinical diagnosis and high-confidence computationally derived diagnosis after adjusting for sex, demographics, and medical history.

Pre-infection COVID-19 vaccination tied to a lower likelihood of persistent symptoms 45 days after infection.

Researchers analyzed the electronic health records of patients at 11 sites who tested positive for COVID-19, covering about 1 year starting on August 1, 2021. Minimum follow-up was 164 days.

The researchers found protective associations of vaccination with long-COVID in both clinic-based and model-based outcomes.

EMA-authorized COVID19 Vaccines (May 18th, 2023)

Currently under rolling review

- **Sputnik V, Gam-COVID-Vac** (Gamaleya Institute)
- **COVID-19 Vaccine (Vero Cell) Inactivated** (Sinovac)

Marketing authorisation application submitted

- **Skycovion** (SK Chemicals GmbH)

Authorised for use in the EU

- **Comirnaty** (BioNTech and Pfizer)
- **COVID-19 Vaccine Valneva**
- **Nuvaxovid** (Novavax)
- **Spikevax** (Moderna)
- **Vaxzevria** (AstraZeneca)
- **Jcovden** (Janssen)
- **VidPrevtyn Beta** (Sanofi Pasteur)
- **Bimervax (previously COVID-19 Vaccine HIPRA)** (HIPRA Human Health S.L.U.)

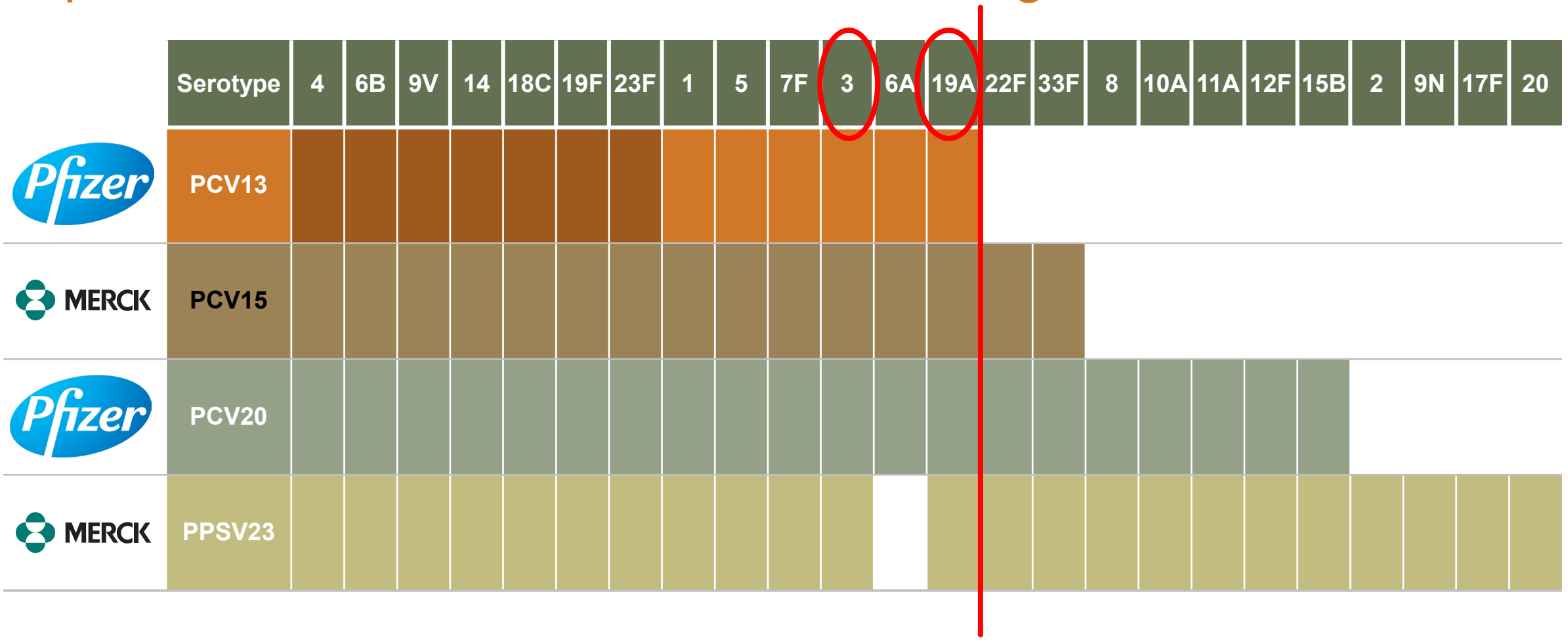
Adapted vaccines authorised for use

- **Comirnaty Original/Omicron BA.1** (BioNTech and Pfizer) ≥ 12 yrs.
- **Comirnaty Original/Omicron BA.4-5** (BioNTech and Pfizer) ≥ 5 yrs.
- **Spikevax bivalent Original/Omicron BA.1** (Moderna) ≥ 6 yrs.
- **Spikevax bivalent Original/Omicron BA.4-5** (Moderna) ≥ 12 yrs.

- **Comirnaty: (Original strain, Omicron BA.1 variants, Omicron BA.4-5 variants)**
  6 mo.- 4 yrs.: 3 µg; 5-11 yrs.: 10 µg; ≥12 yrs.: 30 µg
- **Spikevax: (Original strain, Omicron BA.1 variants, Omicron BA.4-5 variants)**
  6 mo-5 yrs: 25 µg; 6-11yrs.: 50 µg; ≥12 yrs.: 100 µg
- COVID-19 Vaccine Valneva: (Original strain)
  18-50 yrs.
- Nuvaxovid: (Original strain)
  ≥12 yrs.: 5 µg
- Vaxzevria: (Original strain)
  ≥18 yrs.
- Jcovden: (Original strain)
  ≥18 yrs.
- VidPrevtyn Beta: (Beta variant)
  ≥18 yrs.: 5 µg
- Bimervax: (Alfa + Beta variant)
  ≥16 yrs.: 40 µg

COVID-19 vaccines | European Medicines Agency (europa.eu)

Pipelines of Vaccine Producers for Next-generation PCVs



See respective EPARs

EMA-authorized Pneumococcal Vaccines (May18th, 2023)

Vaccine	Age group	Number of Doses	Dose	Indication
PPV23 *Pneumovax23®*	≥ 50 yrs. ≥ 2 yrs. (with certain medical condition at increased risk for infection)	One dose	**25µg**/polysaccharide	IPD, Pneumonia
PCV10 *Synflorix®*	6 weeks-5 yrs.	• 6 weeks-6 mo.: 3 doses • 7mo.-11 mo.: 2 doses • 12 mo.-5 yrs.: 2 doses	**1µg**/polysaccharide (Except serotype 4, 18C1,3 & 19F1,4: 3 µg)	IPD, Pneumonia, AOM
PCV13 *Prevenar13®*	≥ 6 weeks	• 6 weeks-6 mo.: 4 doses • 7 mo.-11 mo.: 3 doses • 12 mo.-23 mo.: 2 doses • ≥ 2 yrs.: one dose	**2.2µg**/polysaccharide (Except serotype 6B:**4.4** µg) individually conjugated to CRM_{197}	• 6 weeks-17 yrs.: IPD, Pneumonia, AOM • Adults and elderly: IPD, Pneumonia
PCV15 *Vaxneuvance®*	≥ 6 weeks	• 6 weeks-18yrs.: • ≥ 18 yrs.: one dose	**2.0 µg**/polysaccharide (Except serotype 6B: **4.0 µg**) individually conjugated to CRM_{197}	• 6 weeks-18 yrs.: IPD, Pneumonia, AOM • ≥ 18 yrs.: IPD, Pneumonia
PCV20 *Appexnar®*	≥ 18 yrs.	One dose	**2.2µg**/polysaccharide (Except serotype 6B: **4.4 µg)** individually conjugated to CRM_{197}	IPD, Pneumonia

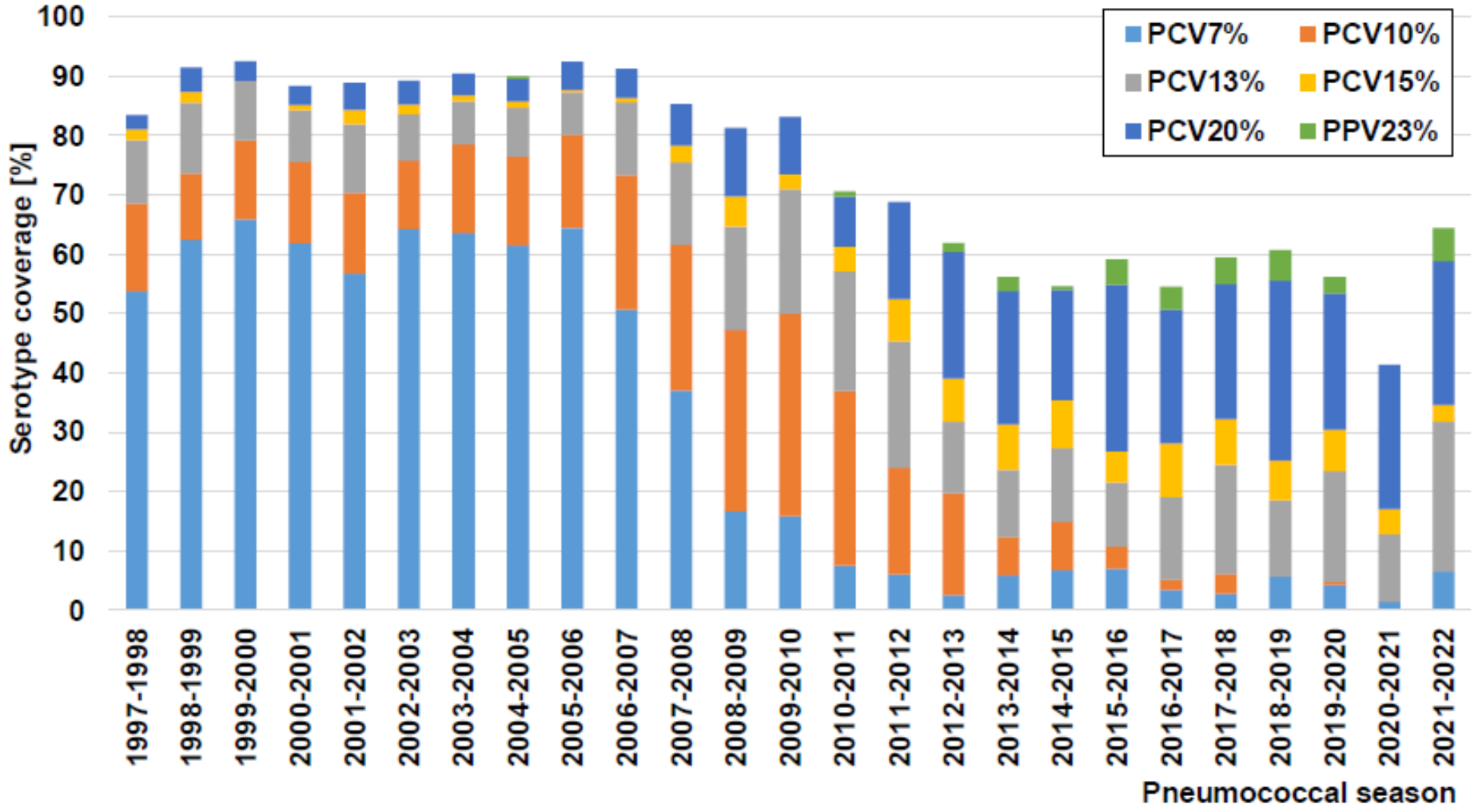
FDA-authorized Pneumococcal Vaccines

Vaccine	Age group	Number of Doses	Dose	Indication
PPV23 *Pneumovax23®*	≥ 50 yrs. ≥ 2 yrs. (with certain medical condition at increased risk for infection)	One dose	25µg/polysaccharide	IPD, Pneumonia
PCV10 *Synflorix®*	Not licensed			
PCV13 *Prevenar13®*	≥ 6 weeks	• 6 weeks-5 yrs.: 4 doses • ≥ 6 yrs.: one dose	2.2µg/polysaccharide (Except serotype 6B: 4.4 µg) individually conjugated to CRM_{197}	• 6 weeks-5 yrs.: IPD, AOM • 6 yrs.-17 yrs.: IPD • ≥ 18 yrs.: IPD, Pneumonia
PCV15 *Vaxneuvance®*	≥ 6 weeks	• 6 weeks-17yrs.: 4 doses • ≥ 18 yrs.: one dose	2.0 µg/polysaccharide (Except serotype 6B: 4.0 µg) individually conjugated to CRM_{197}	IPD
PCV20 *Prevnar20®*	≥ 6 weeks	• 6 weeks-17yrs.: 4 doses • ≥ 18 yrs.: one dose	2.2µg/polysaccharide (Except serotype 6B: 4.4 µg) individually conjugated to CRM_{197}	• 6 weeks-5 yrs.: IPD, AOM • 5 yrs.-17 yrs.: IPD • ≥ 18 yrs.: IPD, Pneumonia

US Food and Drug Administration (fda.gov)

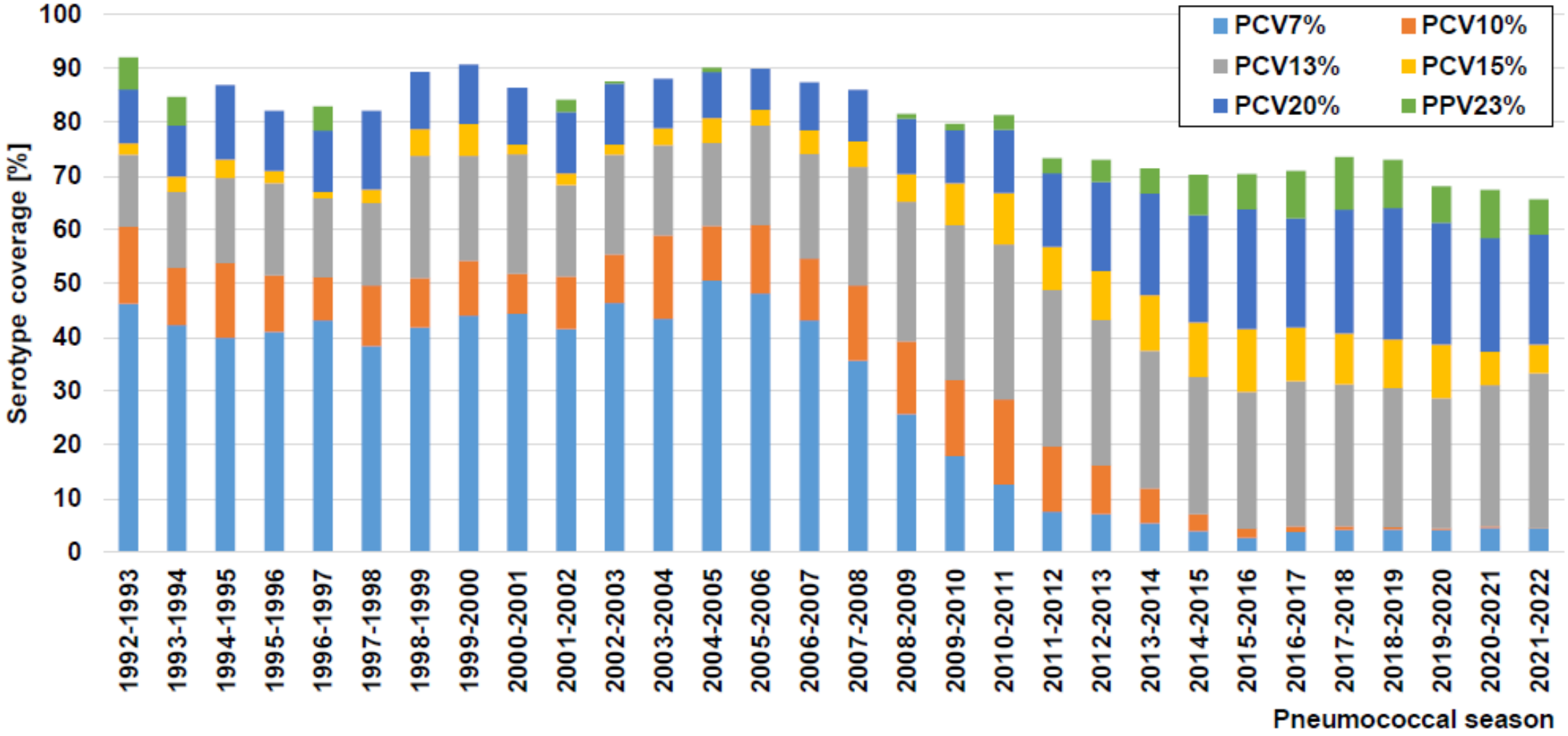
Serotype coverage by different PCVs - IPD isolates, <18 yr

Germany, ARI-season 1997-2022



Serotype coverage by different PCVs - IPD isolates, ≥60 yr

Germany, ARI-season 1997-2022



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id-ea.org

PCV15 (*Vaxneuvance*®)vs. PCV13 (*Prevnar13*®)

Serorepsonders in infants post dose 3

Table 9: Proportions of US Participants with IgG Response Rates ≥0.35 mcg/mL at 30 Days Following Dose 3 in Infants Administered VAXNEUVANCE at 2, 4 and 6 Months of Age (Study 8)

Pneumococcal Serotype	VAXNEUVANCE (n=452-455)	Prevnar 13 (n=426-430)	Percentage Point Difference (VAXNEUVANCE – Prevnar 13) (95% CI)* †
	Observed Response Percentage	Observed Response Percentage	
Serotype			
1	93.8	98.6	-4.8 (-7.5, -2.4)
3	93.1	74.0	19.1 (14.4, 24.0)
4	94.7	98.1	-3.4 (-6.1, -1.0)
5	93.4	96.0	-2.6 (-5.7, 0.3)
6A	92.7	99.3	-6.6 (-9.4, -4.2)
6B	86.7	89.9	-3.2 (-7.5, 1.1)
7F	98.7	100.0	-1.3 (-2.9, -0.4)
9V	96.7	97.2	-0.5 (-2.9, 1.9)
14	97.8	98.1	-0.3 (-2.4, 1.7)
18C	96.2	98.1	-1.9 (-4.3, 0.3)
19A	97.4	99.8	-2.4 (-4.3, -1.0)
19F	98.5	100.0	-1.5 (-3.2, -0.6)
23F	89.8	91.4	-1.5 (-5.4, 2.4)
Additional Serotypes			
22F	98.0	‡	8.1 (5.1, 11.5)
33F	84.8	‡	-5.1 (-9.5, -0.7)

FROM: FDA SmPC Vaxneuvance; accessed 2022-09-11

PCV20 – Immunogenicity in infants post primary dose 3 (Phase 2 data)

Sero-responders

IgG GMC

Immune Measurement	Group	Serotype 1	3	4	5	6A	6B	7F	9V	14	18C	19A	23F
	PCV20 (n† = 189)	87.8 (82.3–92.1)	65.1 (57.8–71.9)	87.8 (82.3–92.1)	87.8 (82.3–92.1)	93.7 (89.2–96.7)	86.8 (81.1–91.3)	98.9 (96.2–99.9)	89.4 (84.1–93.4)	94.2 (89.8–97.1)	92.6 (87.9–95.9)	98.4 (95.4–99.7)	79.9 (73.5–85.4)
	PCV13 (n† = 187)	87.7 (82.1–92.0)	75.4 (68.6–81.4)	89.8 (84.6–93.8)	92.5 (87.8–95.8)	90.4 (85.2–94.2)	97.9 (94.6–99.4)	89.3 (84.0–93.3)	95.7 (91.7–98.1)	95.2 (91.1–97.8)		97.9 (94.6–99.4)	81.8 (75.5–87.1)
IgG GMCs 1 month	PCV20 (n† = 189)	0.92 (0.81–1.05)	0.43 (0.38–0.48)	0.93 (0.79–1.11)	2.28 (1.94–2.67)	0.63 (0.49–0.80)	2.15 (1.92–2.40)	1.22 (1.05–1.42)	3.15 (2.69–3.70)	1.59 (1.37–1.84)		0.85 (0.74–0.96)	0.94 (0.78–1.14)
	PCV13 (n† = 187)	1.16 (1.00–1.33)	0.56 (0.49–0.64)	1.13 (0.96–1.34)	2.57 (2.16–3.05)	0.99 (0.77–1.27)	2.59 (2.28–2.93)	1.45 (1.24–1.70)	3.6 (3.07–4.21)	2.05 (1.76–2.38)		1.02 (0.89–1.17)	1.26 (1.03–1.55)

Immune Measurement	Group	Serotype 8	10A	11A	12F	15B	19A	33F
Participants achieving prespecified IgG concentration* 1 month after Dose 3, % (95% CI‡)	PCV20 (n† = 189)	99.5 (97.1–100.0)	87.8 (82.3–92.1)	97.4 (93.9–99.1)	82.5 (76.4–87.7)	98.9 (96.2–99.9)	98.9 (96.2–99.9)	92.1 (87.2–95.5)
	PCV13 (n† = 187)	3.7 (1.5–7.6)	1.1 (0.1–3.8)	1.6 (0.3–4.6)	0.5 (0.0–2.9)	4.3 (1.9–8.3)	1.1 (0.1–3.8)	1.6 (0.3–4.6)
IgG GMCs 1 month after Dose 3, % (95% CI§)	PCV20 (n† = 189)	2.09 (1.90–2.30)	1.67 (1.35–2.08)	1.94 (1.70–2.21)	0.86 (0.72–1.01)	5.86 (5.11–6.72)	4.62 (3.99–5.35)	2.21 (1.87–2.61)
	PCV13 (n† = 187)	0.04 (0.03–0.04)	0.03 (0.03–0.03)	0.01 (0.01–0.01)	0.02 (0.02–0.02)	0.04 (0.04–0.05)	0.01 (0.01–0.01)	0.05 (0.04–0.05)

Vaxneuvance®(PCV15), Appexnar®(PCV20): Use in Infants

USA: PCV15/PCV13 interchangeable as 3+1 (1 dose as of 3 yr)

- **Licenses for children in Europe**
  Based on non-inferior immunogenicity & safety vs. PCV13
  Schedule 3+1 or 2+1 or (off label in EU) in the UK: 1+1Cave: immune responses decline with number of additional serotypes

- **Decision criteria –for discussion** **(same price, 10 doses: € 767,35)**
  Does lower titer make a difference? Is herd protection more relevant?
  Impact/effectiveness against serotypes 3 and 19A
  Magnitude of local strain coverage and protection regarding:
  22F, 33F (PCV15) *PLUS* 8, 10A, 11A, 12F, 15B (PCV20)

We will only know 1-5 years after licensure

The most infectious diseases the WHO has identified to date:

- ✓ **Nipah virus Check out GHC 33**
- ✓ **Crimean-Congo hemorrhagic fever Check out GHC 34**
- ✓ **Lassa fever Check out GHC 35**
- ✓ **Rift Valley fever Check out GHC 36**
- ✓ **Zika Check out GHC 37**
- ✓ **Ebola and Marburg Check out GHC 38**
- Middle East respiratory syndrome (MERS)
- Severe acute respiratory syndrome (SARS)

Disease X (any unknown pathogen that could cause a future outbreak)

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- **Middle East respiratory syndrome (MERS)**
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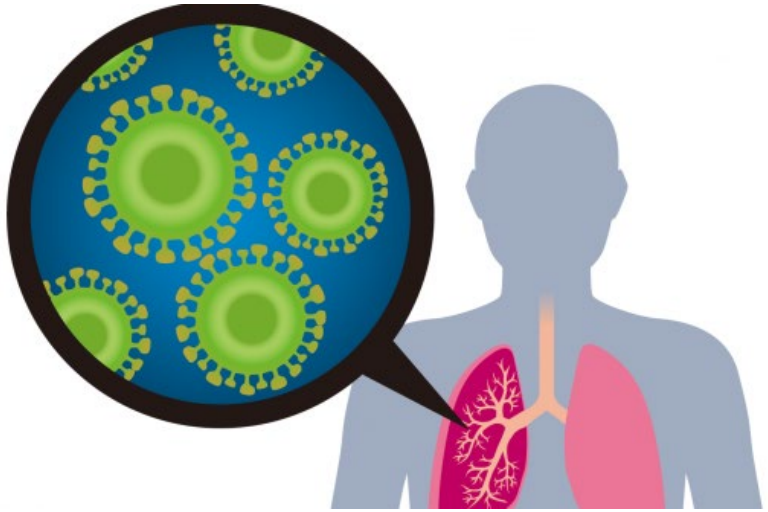

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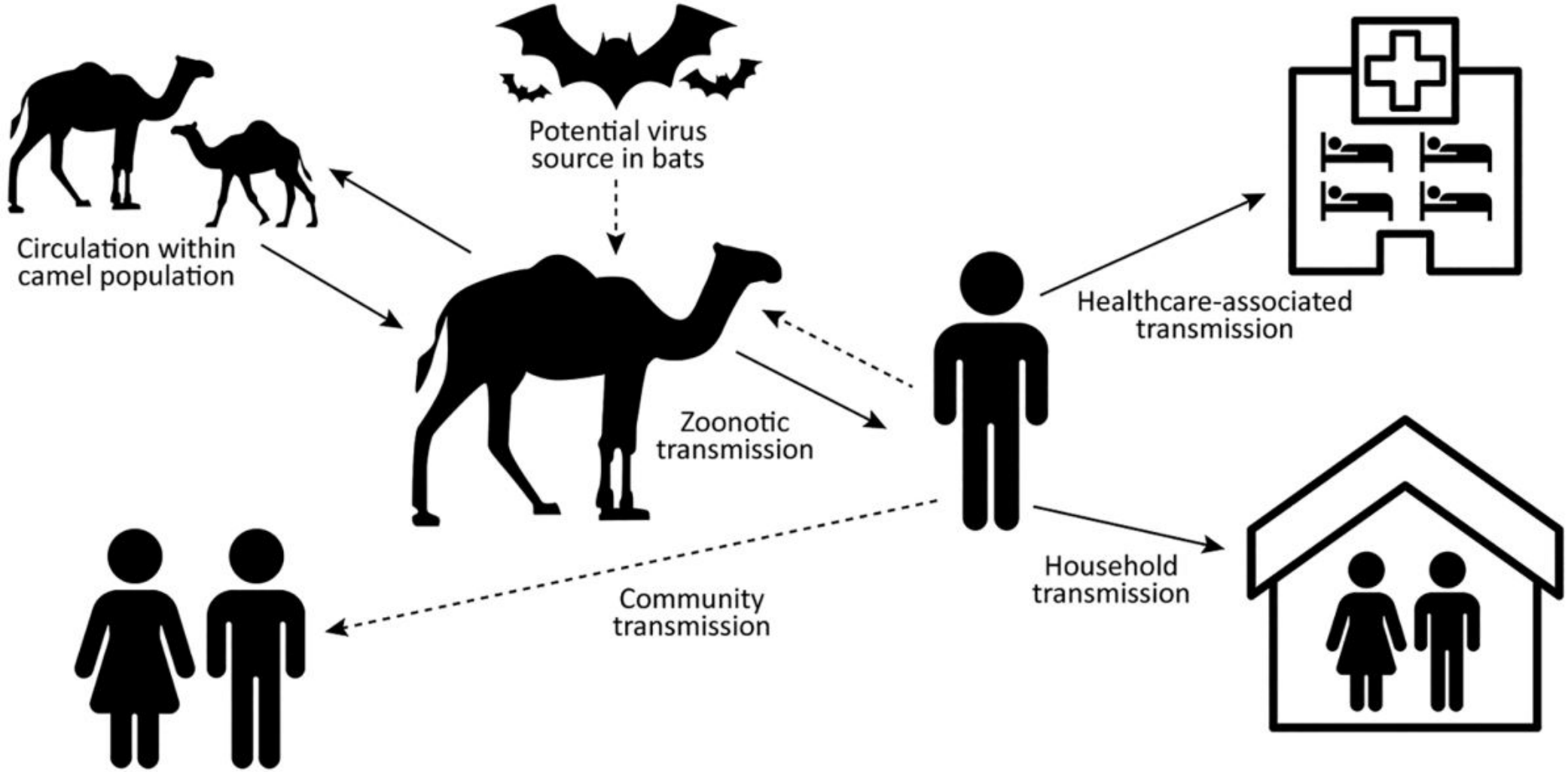

Figure. Summary of Middle East respiratory syndrome coronavirus transmission pathways. Solid lines indicate known transmission pathways; dashed lines indicate possible transmission pathways for which supporting evidence is limited or unknown.

MERS-CoV Middle East respiratory syndrome coronavirus

Have you travelled from the Middle East?

Symptoms of MERS-CoV

a fever (38°C and over)

difficulty in breathing

a cough

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MERS-CoV Middle East respiratory syndrome coronavirus

Information for those travelling to the Middle East

Consult doctor before travelling if you have chronic disease

Ensure you have had the mandatory and recommended vaccinations

Cover mouth when coughing or sneezing, use tissue or upper sleeve. Wash hands with soap and water regularly

Carry and drink plenty of water to avoid dehydration and get urgent help if you develop heat-related illness (eg cramps, dizziness, fever, collapse)

Avoid close contact with camels, drinking camel milk or camel meat

If you have a fever (38°C and over), cough or difficulty in breathing contact your nearest healthcare service

Apply sun cream to any exposed skin

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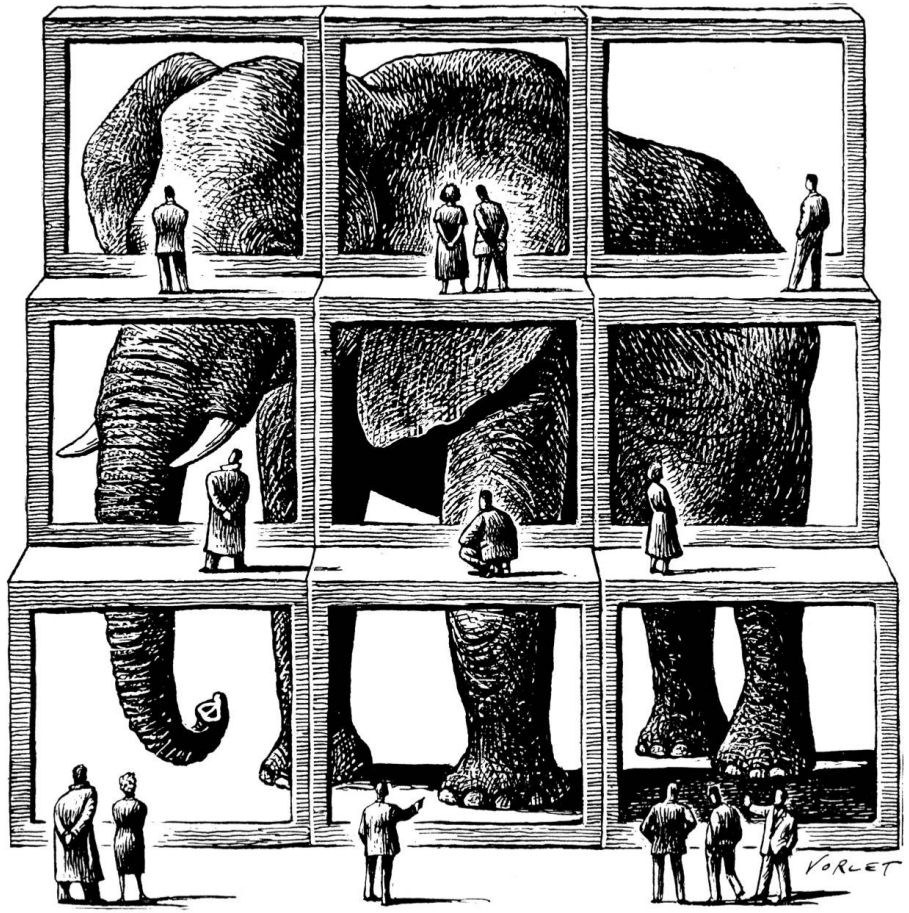
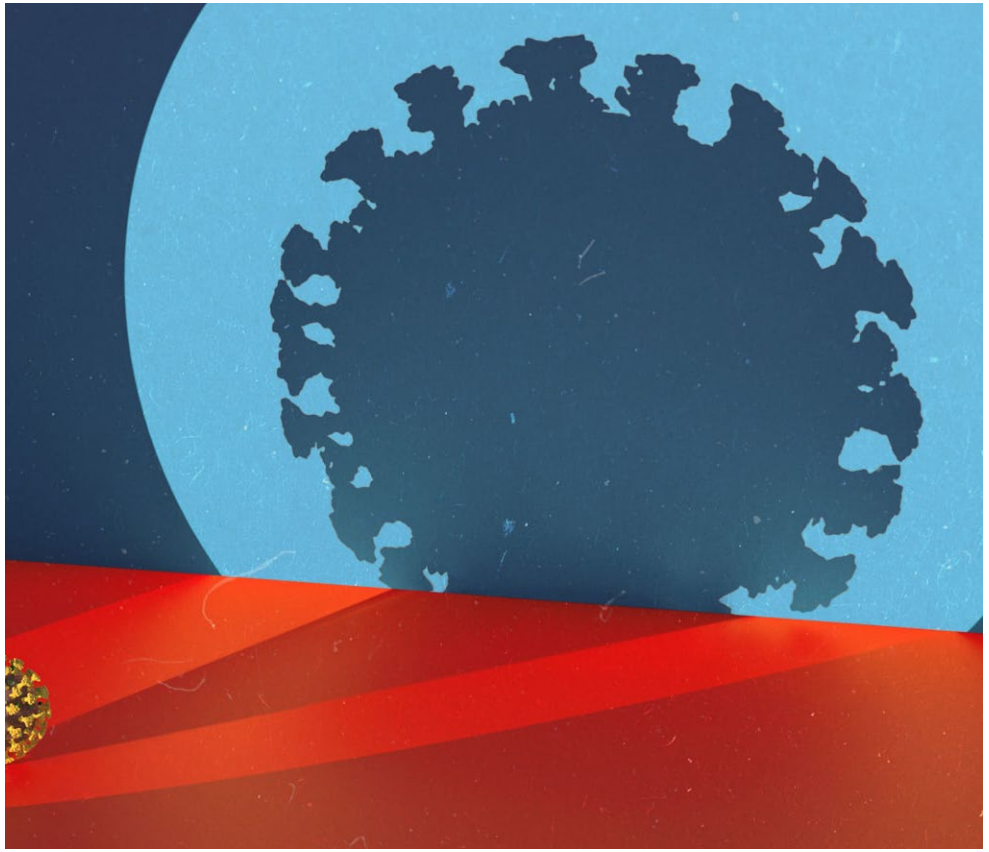

VORLET



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