

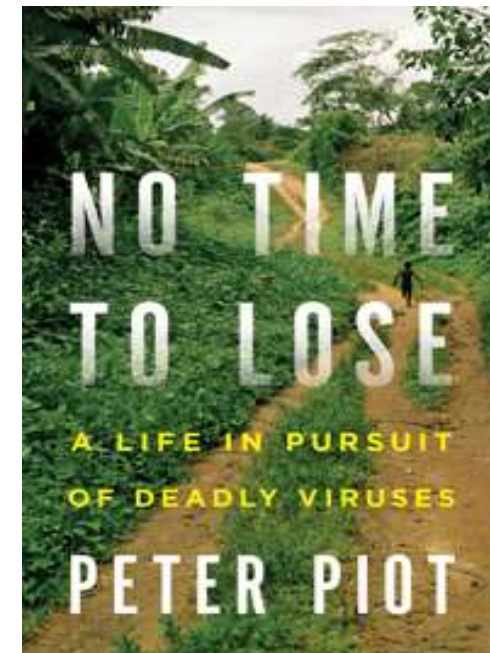
The urgent need for antivirals for epidemic preparedness and control

EU Broad-spectrum Antiviral Workshop

Peter Piot

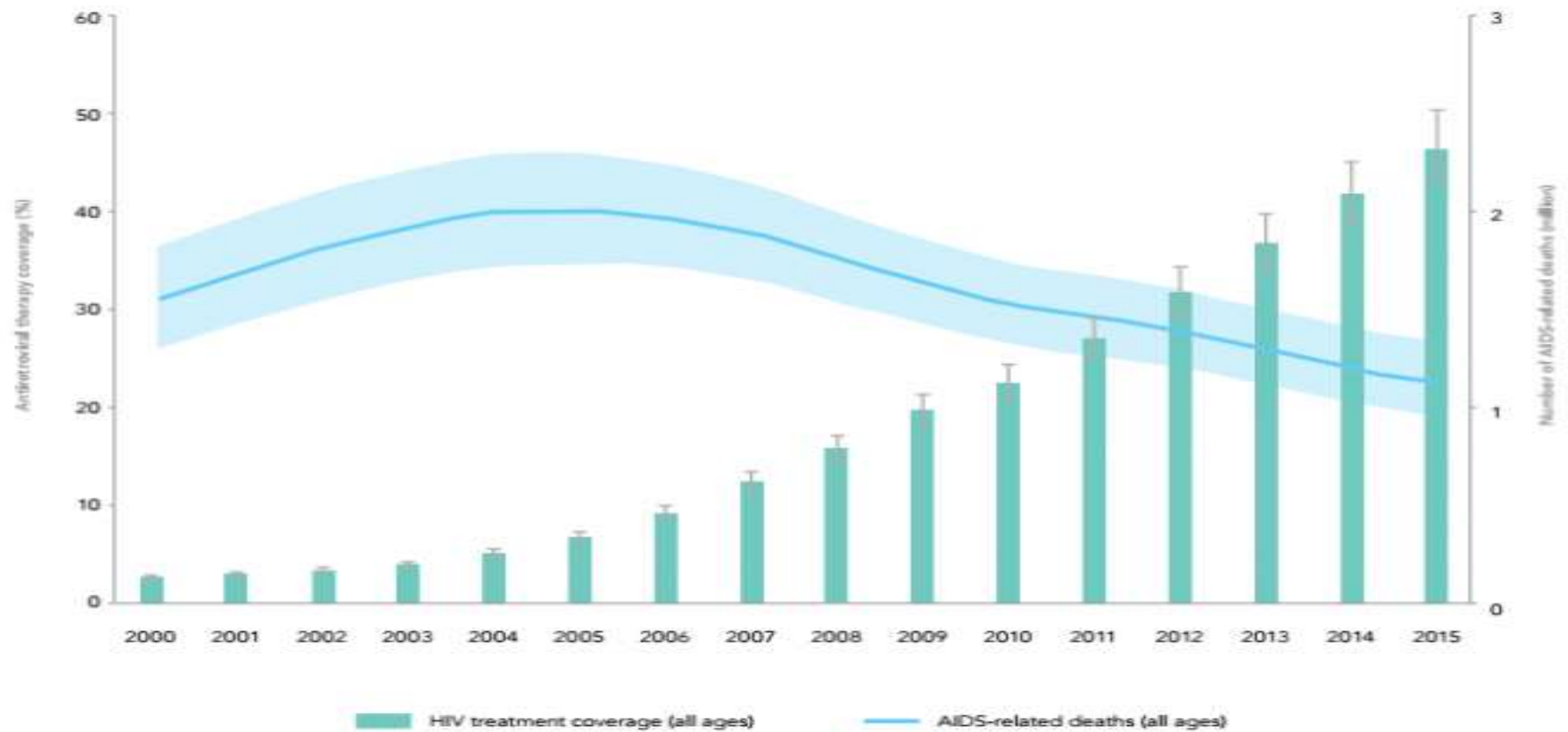
Special Advisor to the EC President

22 Nov 2022



HIV: how antivirals saved millions of lives

Antiretroviral therapy coverage and number of AIDS-related deaths, global, 2000–2015



Sources: GARPR 2016; UNAIDS 2016 estimates.

**TREATMENT OF VIRAL INFECTIONS
(EXAMPLE HIV)**



1990'S

KU LEUVEN

TREATMENT OF VIRAL INFECTIONS (EXAMPLE HIV)



1990'S

KU LEUVEN

TREATMENT OF VIRAL INFECTIONS (EXAMPLE HIV)



TODAY

KU LEUVEN

A cure for HCV



Hepatitis C



Key facts

- Antiviral medicines can cure more than 95% of persons with hepatitis C infection, but access to diagnosis and treatment is low.

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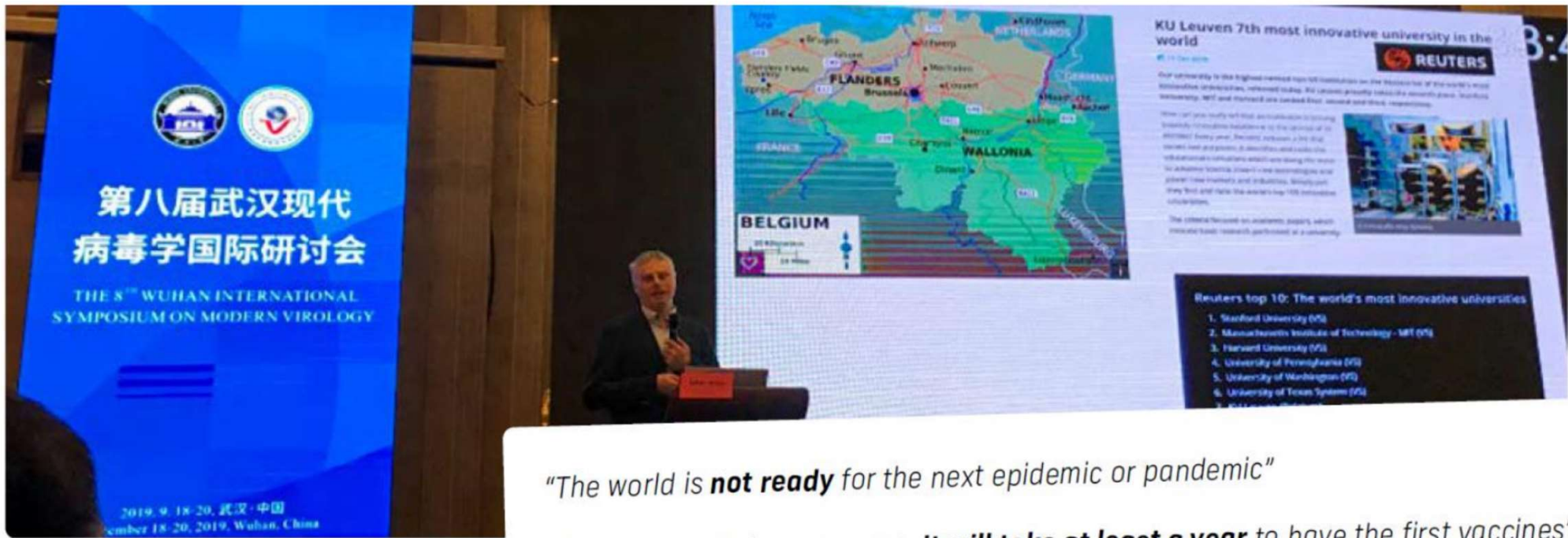


Volume 393, Issue 10179, 6–12 April 2019, Pages 1453–1464

Articles

Clinical outcomes in patients with chronic hepatitis C after direct-acting antiviral treatment: a prospective cohort study

Prof Fabrice Carrat PhD ^{a, b, c, d, e}, H  l  ne Fontaine MD ^c, C  line Dorival PhD ^a, M  lanie Simony MS ^e, Alpha Diallo MD ^f, Prof Christophe Hezode MD ^g, Prof Victor De Ledinghen MD ^h, Prof Dominique Larrey MD ⁱ, Georges Haour MSc ^a, Prof Jean-Pierre Bronowicki MD ^j, Prof Fabien Zoulim MD ^k, Prof Tarik Asselah MD ^l, Prof Patrick Marcellin MD ^l, Prof Dominique Thabut MD ^m, Prof Vincent Leroy MD ⁿ, Prof Albert Tran MD ^o, Prof Fran  ois Habersetzer MD ^p, Prof Didier Samuel MD ^q, Prof Dominique Guyader MD ^r, Prof Olivier Chazouilleres MD ^s ... Prof Stanislas Pol MD ^{c, d}



The 8th Wuhan International Symposium on Modern Virology

Keynote by Johan Neyts, Wuhan (Sept 2019)

*"The world is **not ready** for the next epidemic or pandemic"*

*"In case a new virus emerges, **it will take at least a year** to have the first vaccines"*

*"**It may even be impossible** to develop vaccines; cfr. HIV"*

*"**Broader-acting antiviral drugs should be developed** in peace-time against entire virus families"*

*"Such drugs will help, together with quarantine measures, to **contain the outbreak** in the first weeks and will be essential to **provide the global population protection** in case the virus would eventually spread and before vaccines become available"*

Current Ebola outbreak in Uganda – a case in point

Misinformation hampers Uganda's battle against new outbreak of Ebola

Despite 53 deaths, people are still in denial of the danger as doctors race to develop an effective vaccine against Sudan strain of disease



📹 Villagers in Mubende district look on as Red Cross workers don PPE before burying a three-year-old boy who was thought to have Ebola. Photograph: Luke Dray/Getty Images

- **Misinformation** - “I hear someone’s grandmother died of old age, and they said that it was Ebola. Lies,”

Stigma – ostracization of survivors

Sudan ebolavirus – Two existing Ebola vaccines (rVSV-ZEBOV (Ervebo) by Merck and Ad26.ZEBOV/MVA-BN-Filo (Zabdeno/Mvabea) by J&J) protective against **Zaire ebolavirus**.

WHO recommends for treatment of Zaire ebolavirus: **Inmazeb** (3 monoclonals, Regeneron) & **Ansuvimab / Ebanga** (single mAB, Ridgeback Biotherapeutics)

Ideal to have **broad-spectrum antivirals** and vaccines that protect against multiple filoviruses – (Ebola viruses Marburg)

Covid-19 treatments approved by EMA (as of 21.11.2022)



Currently under rolling review

No treatments currently under rolling review



Marketing authorisation application submitted

- **Lagevrio**
(molnupiravir)
- **Olumiant**
(baricitinib)*



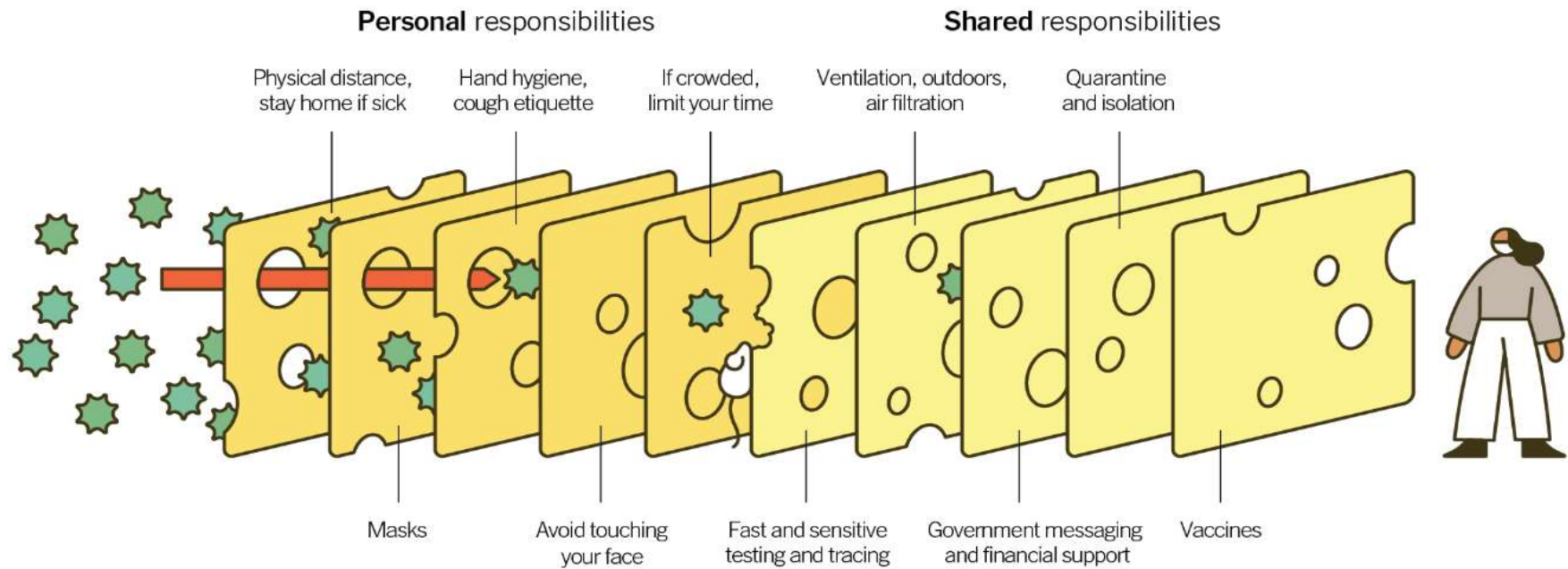
Authorised for use in the European Union

- **Evusheld**
(tixagevimab / cilgavimab)
- **Kineret**
(anakinra)*
- **Paxlovid**
(PF-07321332 / ritonavir)
- **Regkirona**
(regdanvimab)
- **RoActemra**
(tocilizumab)*
- **Ronapreve**
(casirivimab / imdevimab)
- **Veklury**
(remdesivir)
- **Xevudy**
(sotrovimab)

“Swiss Cheese” Model of Pandemic Defence

Multiple Layers Improve Success

The Swiss Cheese Respiratory Pandemic Defense recognizes that no single intervention is perfect at preventing the spread of the coronavirus. Each intervention (layer) has holes.



Source: Adapted from Ian M. Mackay (virologydownunder.com) and James T. Reason. Illustration by Rose Wong

NA

Source: <https://www.nytimes.com/2020/12/05/health/coronavirus-swiss-cheese-infection-mackay.html>

Use of Paxlovid and other antivirals in the US versus UK

- Paxlovid supply far outstripped demand in the United States, UK, Japan, and South Korea (Reuters, Apr 2022)
- As of April, U.S. has **distributed around 1.5 million courses** and pharmacies still have **over 500,000 available**. (Ditto)
- The **UK** has deals for **2.75 million Paxlovid courses**, given to more than **6,000 patients** as of April 9.
- **UK's National Institute for Health and Care Excellence (NICE)** recommended against prescription of 5 Covid treatments, including molnupiravir for high-risk patients, citing cost-effectiveness concerns. It recommended three treatments for Covid in adults, including **Paxlovid, baricitinib, and tocilizumab**.

Lower vaccine efficacies with immunosuppression and immunosenescence

- A meta-analysis of 82 studies: seroconversion rates after Covid vaccination were **significantly lower in immunocompromised patients**, (*Lee et al. BMJ 2022*)
- Columbian study: vaccine effectiveness at preventing death was 22.6% **lower in adults > 80** (68.4%) compared with 60 - 69 years (91.0%). (*Arregocés-Castillo et al. Lancet HL 2022*)
- **Elderly** people in Brazil: **significant decline** in vaccine effectiveness against symptomatic covid-19 with increasing age, from 59.0% in those aged 70-74 year to 32.7% in those aged **≥80 years**. (*Ranzani et al. BMJ 2021*)

Efficacy of covid-19 vaccines in immunocompromised patients: systematic review and meta-analysis

BMJ 2022 ; 376 doi: <https://doi.org/10.1136/bmj-2021-068632> (Published 02 March 2022)

Cite this as: *BMJ* 2022;376:e068632

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Healthy Longevity

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ARTICLES | VOLUME 3, ISSUE 4, E242-E252, APRIL 01, 2022

Effectiveness of COVID-19 vaccines in older adults in Colombia: a retrospective, population-based study of the ESPERANZA cohort

Leonardo Arregocés-Castillo, DrPH • Julián Fernández-Niño, PhD • Maylen Rojas-Botero, PhD •

Andrés Palacios-Clavijo, MSc • Maryory Galvis-Pedraza, MSc • Luz Rincón-Medrano, MSc • et al. Show all authors

Open Access • Published: March 21, 2022 • DOI: [https://doi.org/10.1016/S2666-7568\(22\)00035-6](https://doi.org/10.1016/S2666-7568(22)00035-6)

Effectiveness of the CoronaVac vaccine in older adults during a gamma variant associated epidemic of covid-19 in Brazil: test negative case-control study

BMJ 2021 ; 374 doi: <https://doi.org/10.1136/bmj.n2015> (Published 20 August 2021)

Cite this as: *BMJ* 2021;374:n2015

Impact of antiviral and vaccination on long-Covid

The New York Times


Paxlovid May Reduce Risk of Long Covid in Eligible Patients, Study Finds

The research looked at patients who qualified for the antiviral through age or health conditions. Those who took it shortly after infection were 26 percent less likely to have symptoms 90 days later.

Give this article



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Nirmatrelvir and the Risk of Post-Acute Sequelae of COVID-19

Yan Xie, Taeyoung Choi, Ziyad Al-Aly
doi: <https://doi.org/10.1101/2022.11.03.22281783>

Participants who took Paxlovid within five days after their infection were 26 percent less likely to have a wide range of post-Covid symptoms 90 days after infection. Joe Raedle/Getty Images



By Pam Belluck

Nov. 7, 2022



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Danish study shows 3rd booster dose reduces risk of long-COVID

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By Nidhi Saha, BD

Reviewed by Daniel

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Post-acute symptoms four months after SARS-CoV-2 infection during the Omicron period: a nationwide Danish questionnaire study

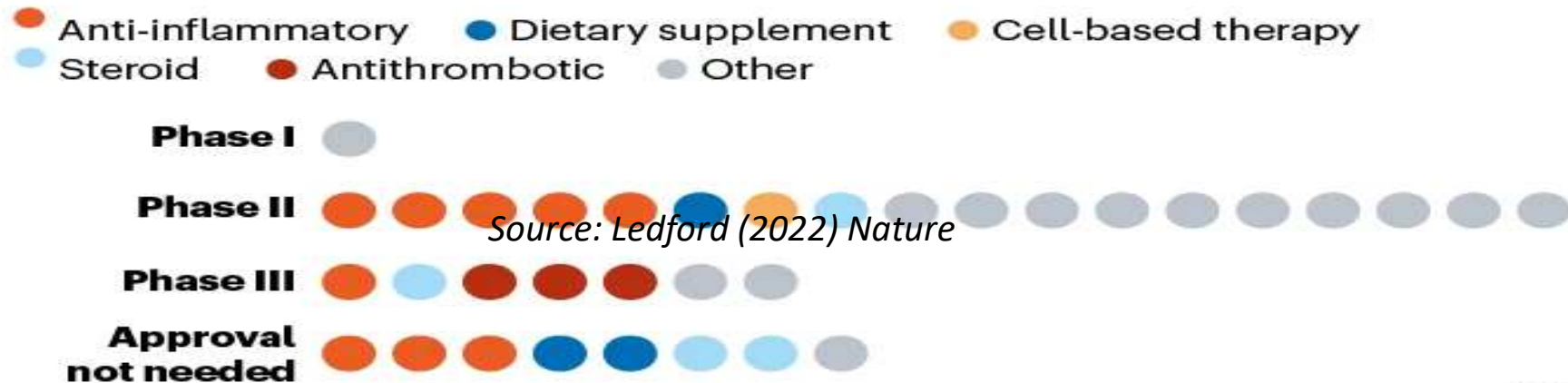
Lampros Spiliopoulos, Anna Irene Vedel Sorensen, Peter Bager, Nete Munk Nielsen, Jørgen Vinsløv Hansen, Anders Koch, Inger Kristine Meder, Poul Videbech, Steen Ethelberg, Anders Hviid

doi: <https://doi.org/10.1101/2022.10.12.22280990>

Treatment of long-Covid

TRIALS TAKE OFF

At least 26 randomized trials are under way to test therapies for long COVID. Many candidates target symptoms such as inflammation or clots. Some, such as the antidepressant fluvoxamine, act on different symptoms. Some researchers are repurposing drugs already approved for other conditions.



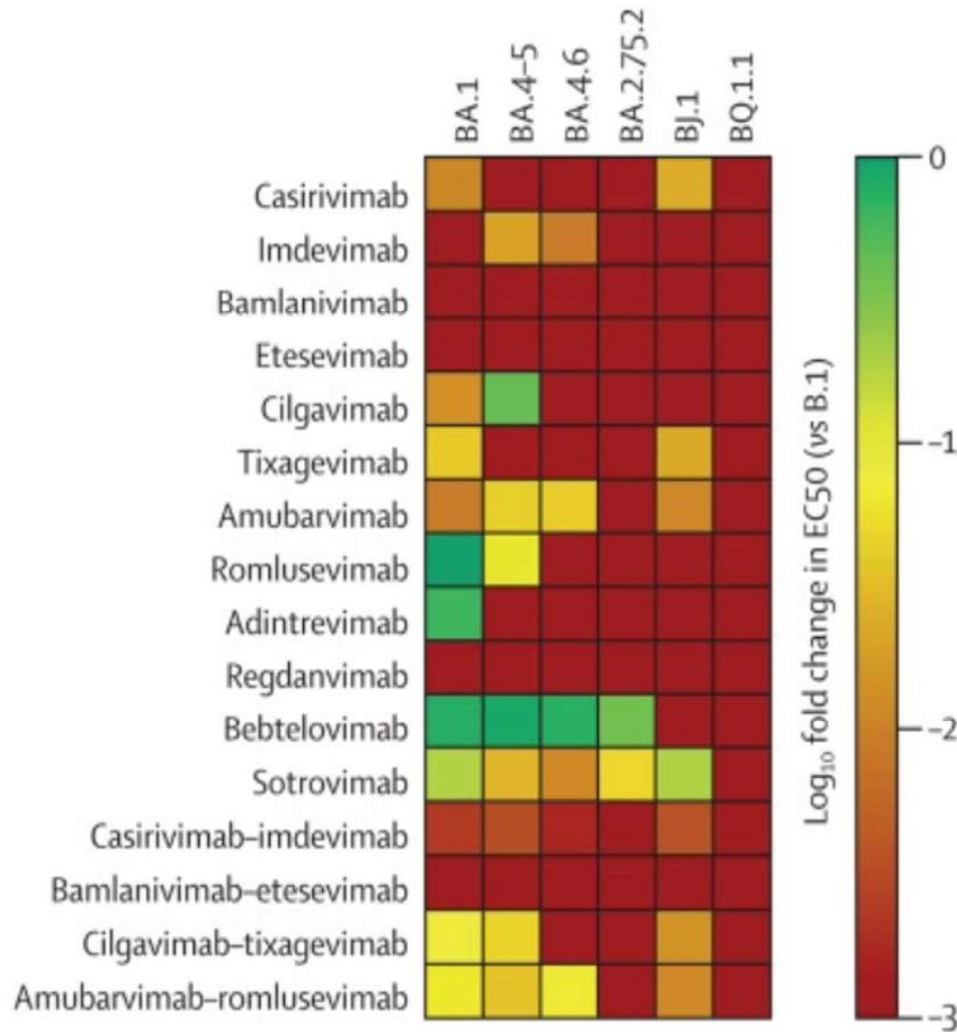
Source: Ledford (2022) Nature

©nature

- **Trials** could **yield results for drugs** that target the immune system, blood clots or lurking fragments of the coronavirus itself.

Omicron sublineage BQ.1.1 resistance to monoclonal antibodies

Arora, et al. *Lancet ID* 18 Nov 2022

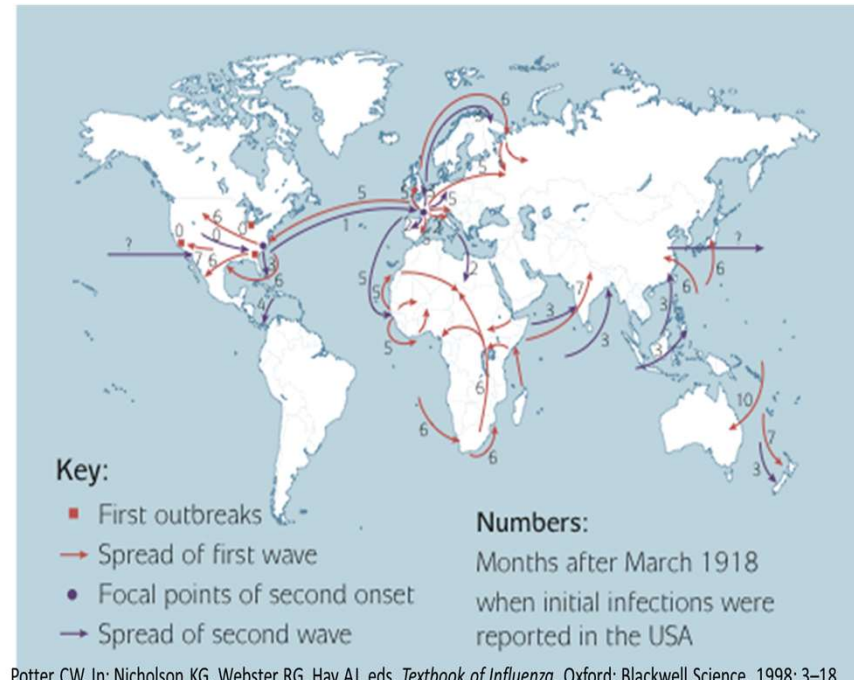


Heatmap indicating the fold change in EC₅₀ compared with B.1 pseudovirus particles

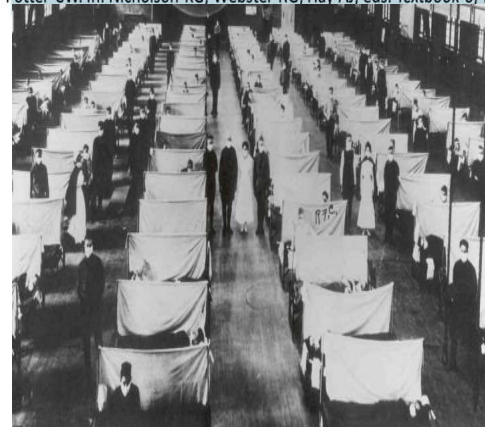
The next Big One: Influenza?

What's available as tools?

- ❖ **Diagnostics**
- ❖ **Vaccines**
- ❖ **Therapeutics/prophylactics**
(?)
 - Oseltamivir (oral)
 - Zanamivir (inhaled power)
 - Peramivir (IV)
 - Baloxavir (oral)

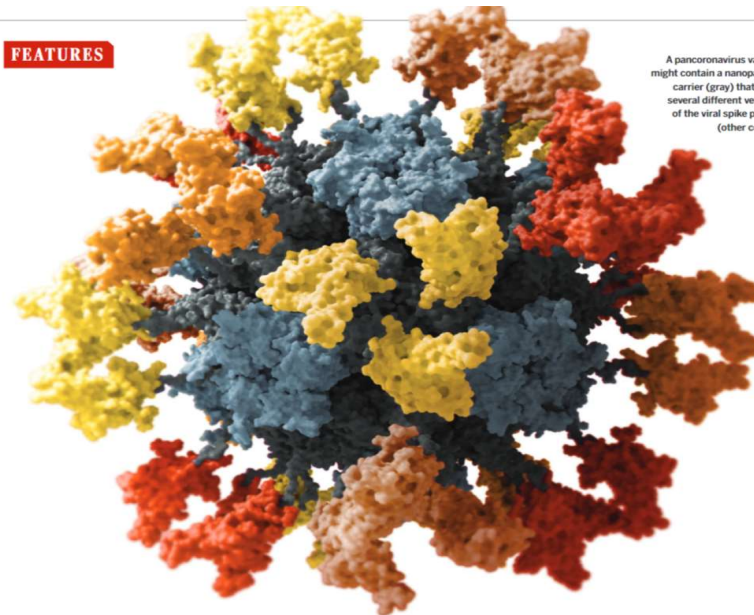


Potter CW. In: Nicholson KG, Webster RG, Hay AJ, eds. *Textbook of Influenza*. Oxford: Blackwell Science, 1998; 3-18



The DREAM THERAPEUTIC?!

FEATURES

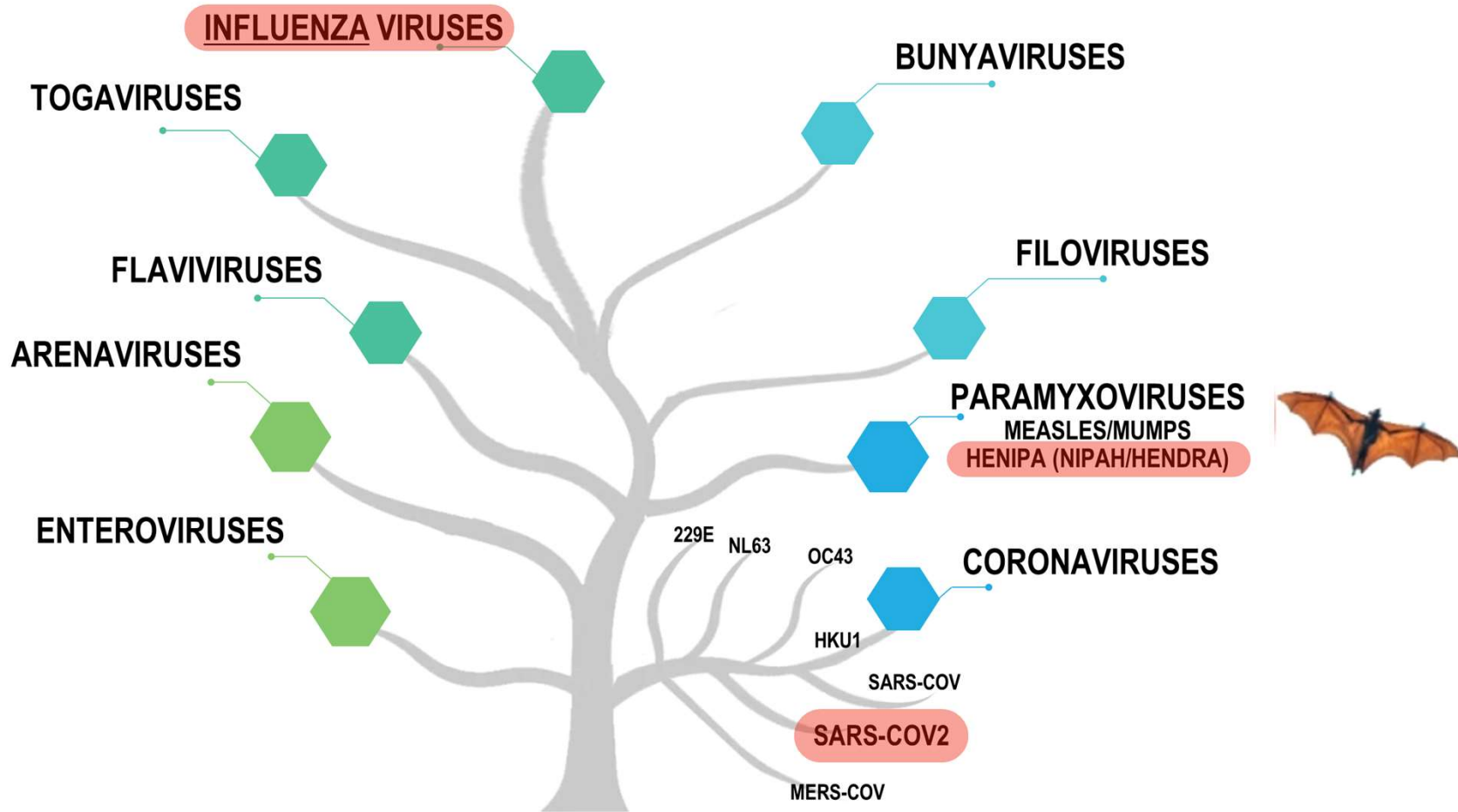


A pancoronavirus vaccine might contain a nanoparticle carrier (gray) that holds several different versions of the viral spike protein (other colors).

THE DREAM VACCINE

Why stop at just SARS-CoV-2? Vaccines in development aim to protect against many coronaviruses at once

THE FAMILY TREE OF VIRUSES



MORE VIRUS FAMILIES EXIST BUT ARE NOT DEPICTED HERE



What does it take to develop broad antivirals?

- **Scientific excellence, infrastructure, models, data sharing**
- **Development: academia, biotech, pharma**
- **Incentives, removal of obstacles & risk reduction**
- **Proactive clinical trials networks with pre-agreed protocols, ethics review and approvals**
- **Close collaboration with regulators**
- **Manufacturing: capacity & incentives**
- **Long term view & funding**
- **Ambition & risk taking!**



Making Antivirals available

- **Policy & indications**
- **Manufacturing & availability**
- **Effectiveness & adverse effects**
- **Mode of administration**
- **Affordability & public funding**
- **Acceptance by prescribers**
- **People's acceptance and education**
- **Equitable global access**

How to use antivirals in epidemic context??

- **Treatment in hospital & community**
- **Individual and community prophylaxis eg immunocompromised, elderly, household contacts, events**
- **Outbreak containment**

