Eerste lessen uit de COVID-19 crisis: Ontwikkeling en distributie van vaccins

Meta Roestenberg

CONTROLLED HUMAN INFECTIONS CENTRE

Leiden University Medical Center

September 2020

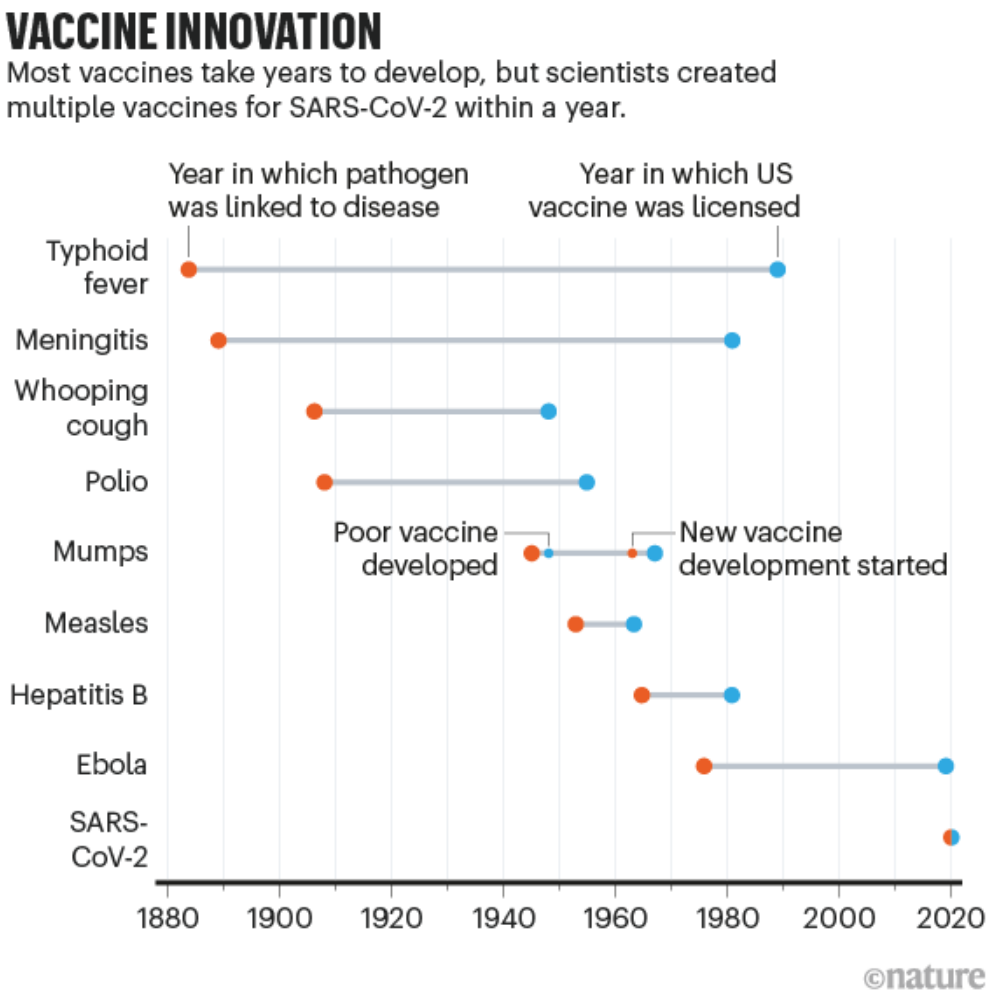
BeReady protocol

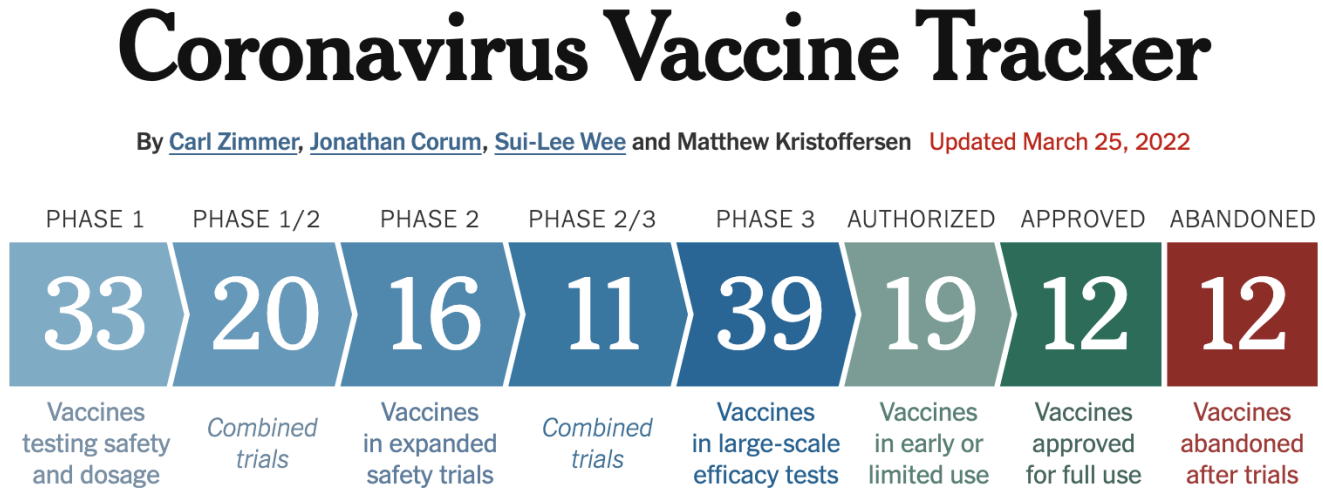
“generiek” protocol voor vroege fase testen van vaccins

Maart 2020 > recruteren van 100 proefpersonen die klaar stonden voor fase 1 klinische testen

september 2020 > 1e vaccin COVID-19

Ongeëvenaarde ontwikkeling van producten





Bouwen op bestaande kennis:

- MERS en SARS1
- mRNA en “viral vector platforms”

The New York Times corona vaccine tracker

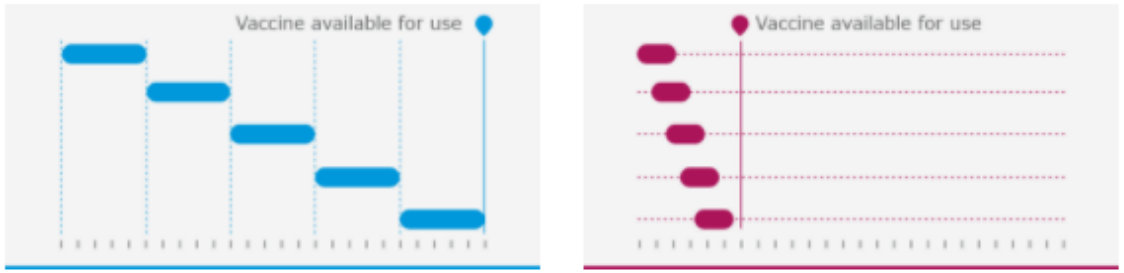
Ball. Nature news feature, December 2020.
https://www.nature.com/articles/d41586-020-03626-1

Bouwen op bestaande kennis en…

Versnelde ontwikkeling

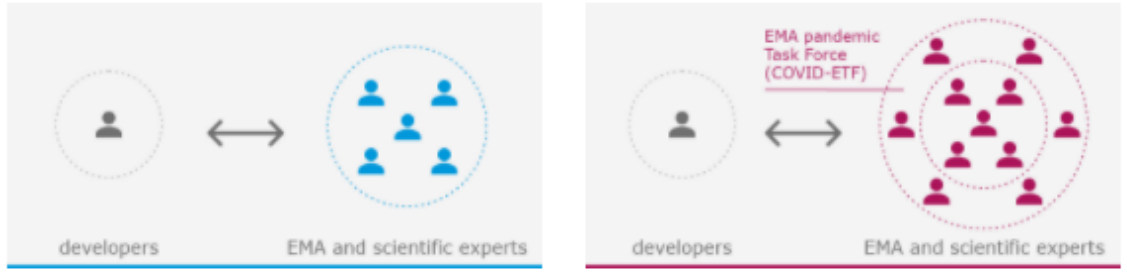
Development

COVID-19 vaccine development is compressed in time, applying the extensive current knowledge on vaccine development.



Continuous dialogue

COVID-19 vaccine development is supported by early, continuous dialogue between developers and a dedicated group of regulatory experts.

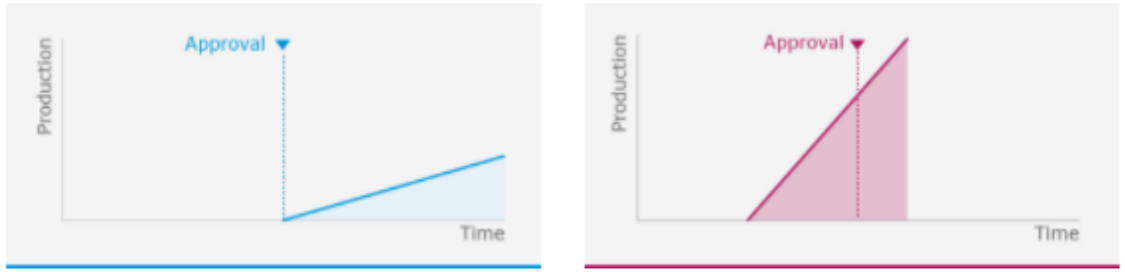


“Rolling review”

Productie voor authorisatie

Manufacturing

Companies are expanding manufacturing and production capacity to ensure efficient vaccine deployment.



Resources

COVID-19 vaccine development mobilises more resources simultaneously.

Mobilisatie van “resources”

En als het dan zo ver is….

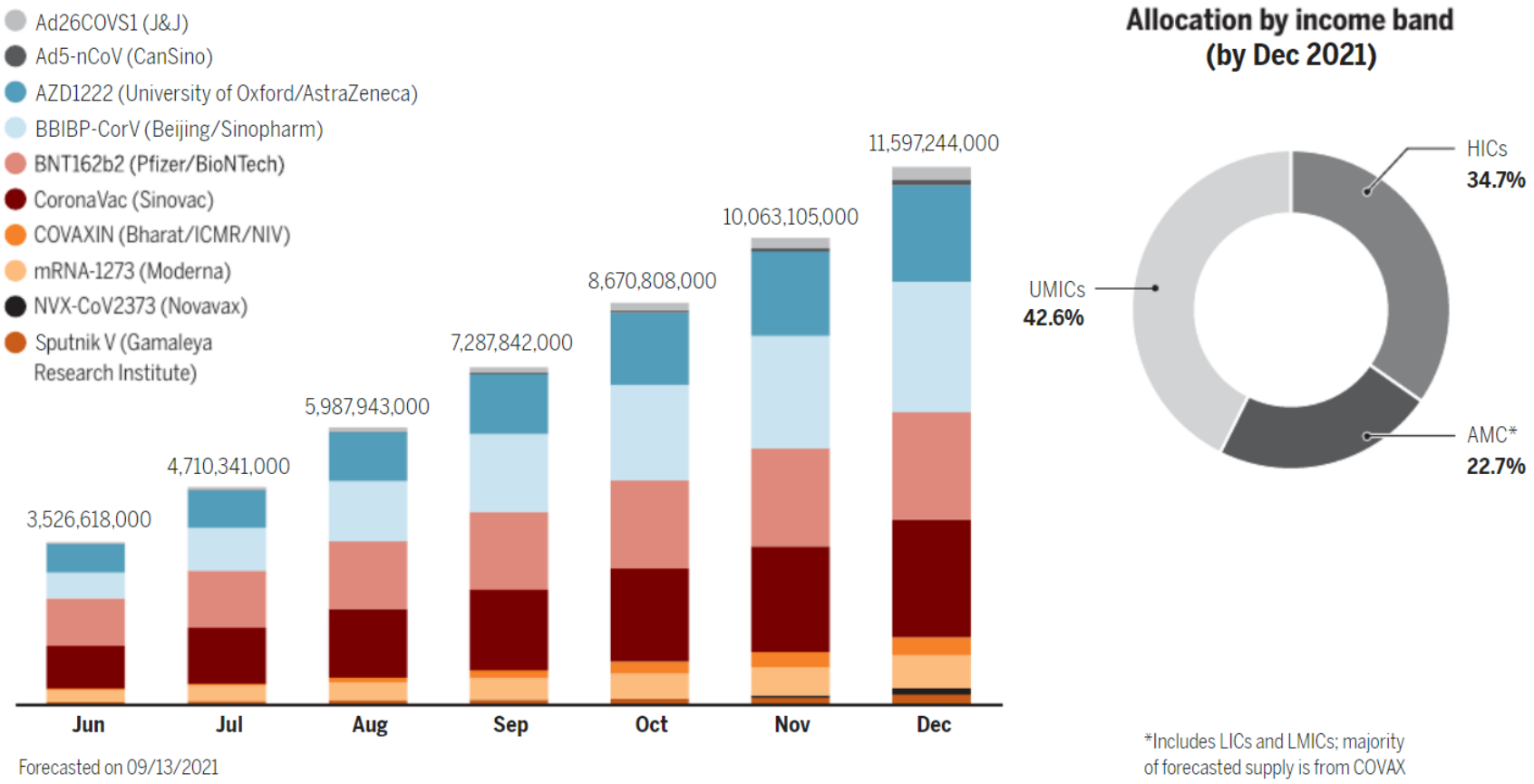


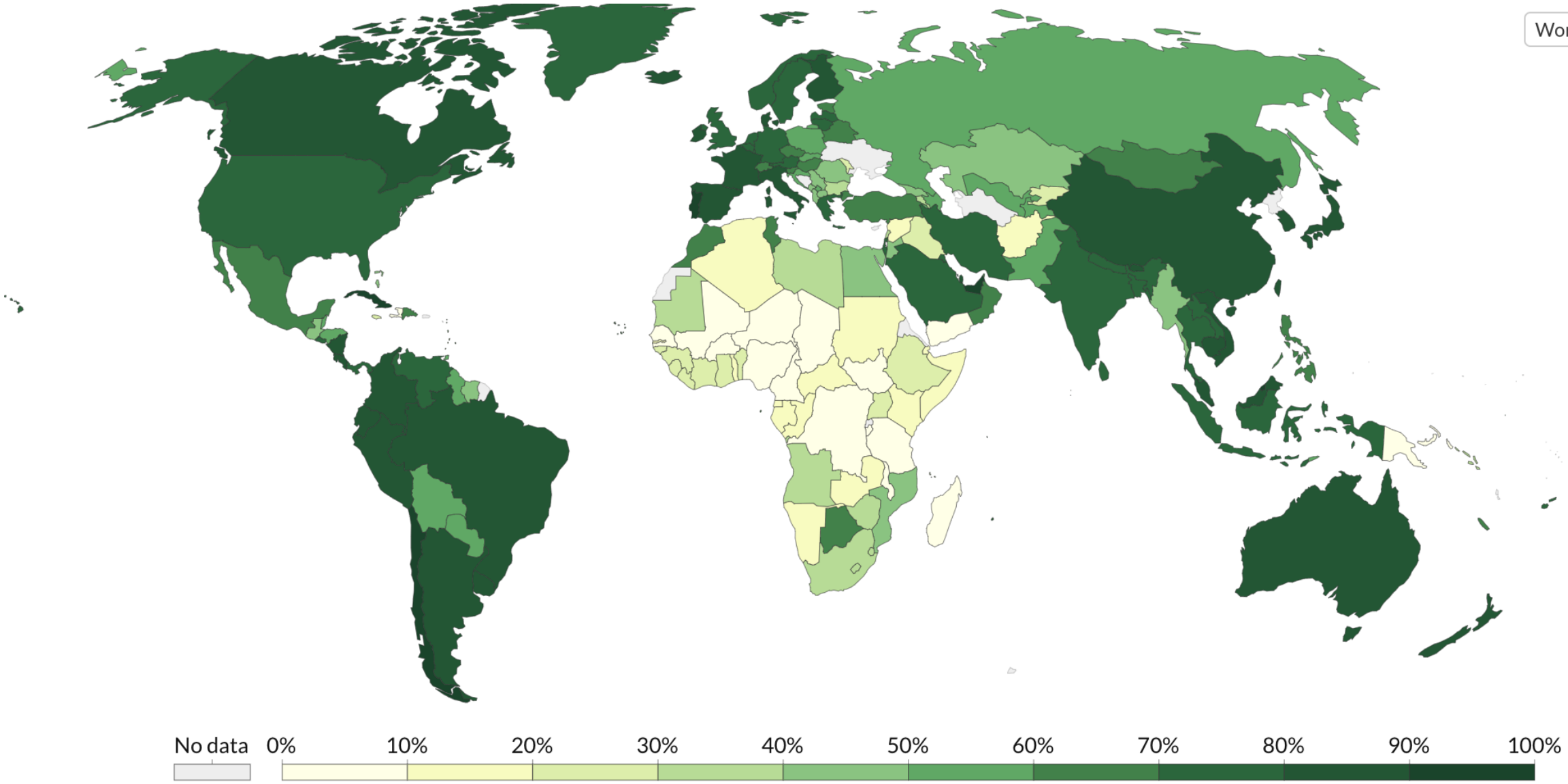
Fig. 1. COVID-19 Vaccine Global Supply Forecast. The graph shows the cumulative number of doses of currently approved COVID-19 vaccines (plus Novavax, which is pending approval) that are estimated be produced by major manufacturers each month until the end of 2021. The circle chart indicates how those vaccine doses are forecasted to be distributed across countries according to economic income band. HICs, high-income countries (as defined by Organisation for Economic Co-operation and Development); LICs, low-income countries; LMICs, low- and lower middle-income countries; UMICs, upper middle-income countries; AMC, Advance Market Commitment. The AMC segment of the circle chart represents countries (primarily LICs and LMICs) that are eligible for COVAX advance market commitment vaccine doses. Source: Airfinity.

Share of people who received at least one dose of COVID-19 vaccine, Apr 3, 2022

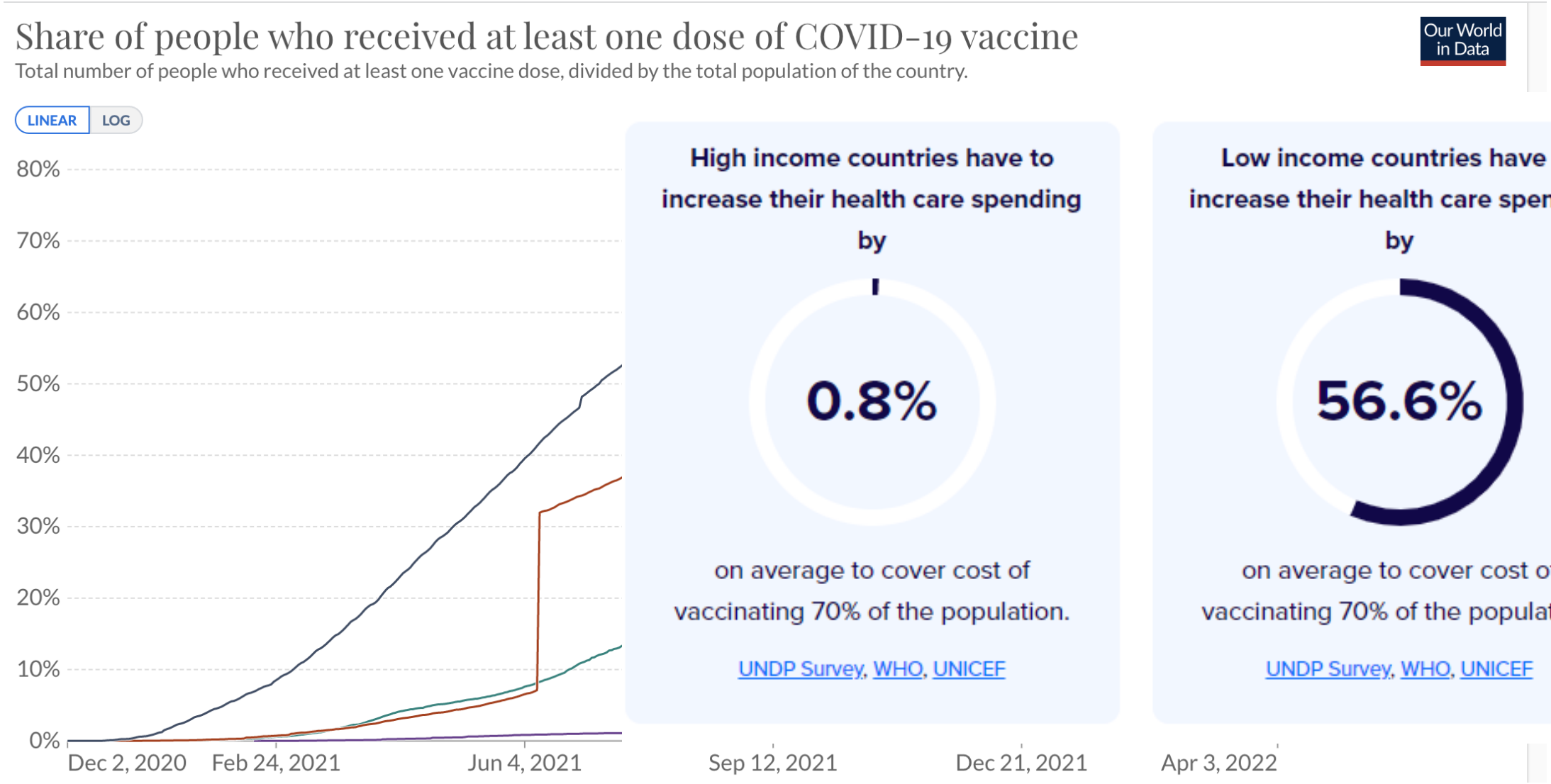
Total number of people who received at least one vaccine dose, divided by the total population of the country.

Our World in Data

World



LIC hebben nauwelijks toegang tot de markt, en moeten relatief meer investeren



COVAX voorraden…

COVAX Facility Supply Forecast

Ranged forecasts under low, most likely, and high scenarios

PRELIMINARY AND SUBJECT TO ASSUMPTIONS

35 vaccines **approved for use** by at least one national regulatory authority [1]

10 vaccines in WHO's **Emergency Use Listing**

17.8bn doses **secured globally**

$2 – $40 reported vaccine **price range per dose**

2.8bn doses **COVAX has secured, optioned, or received as donations**

1.41bn doses **shipped through COVAX to 145 countries**

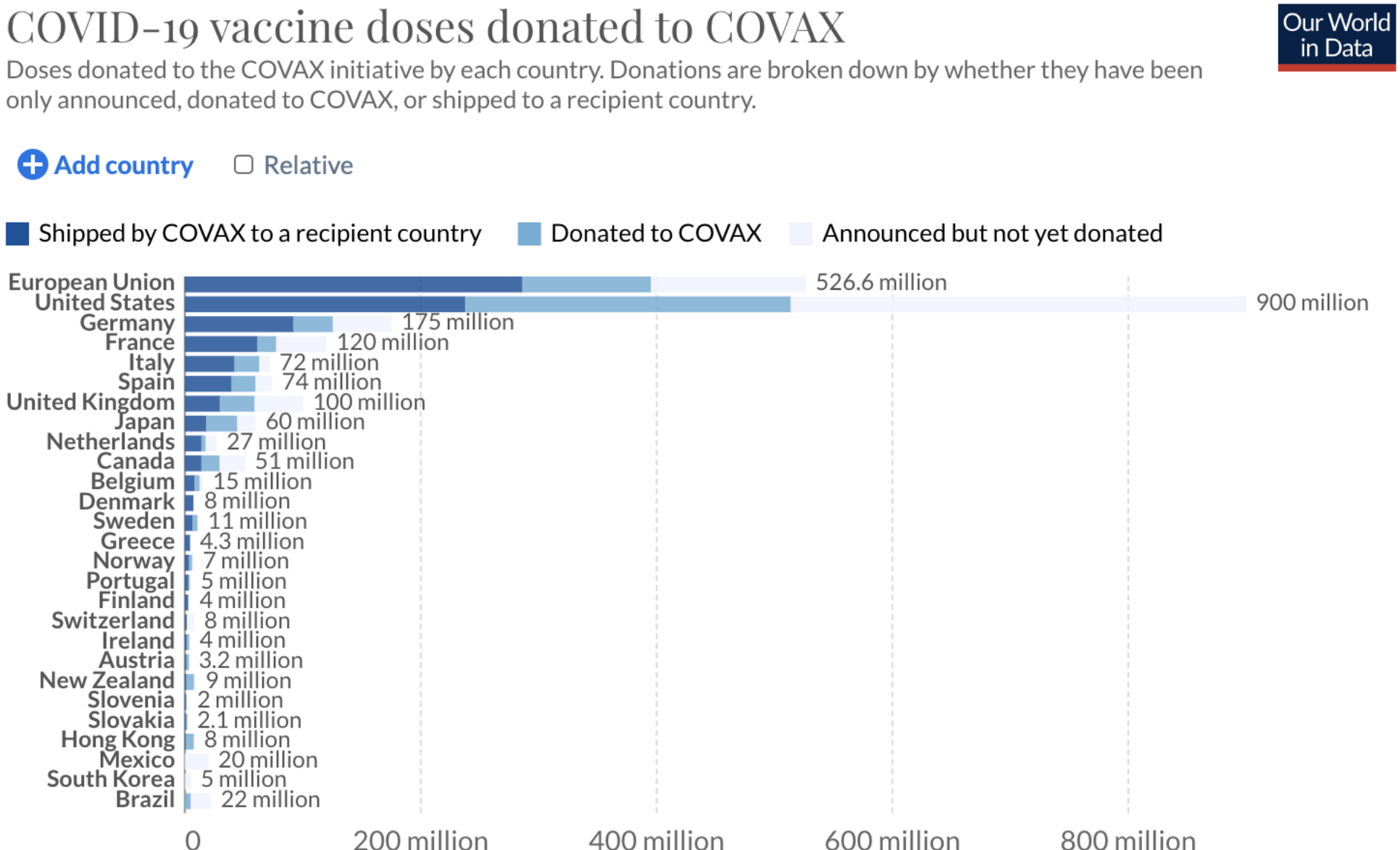
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec | Jan Feb Mar

2021 | **2022**

developed by Novavax, SII-Novavax, and Clover.

1 Timing of available supply is based on anticipated date of release by manufacturer, at which point doses become available for delivery. Timing of delivery to countries will be lagged due to need for local regulatory approvals, supply agreements, country readiness, export licenses, logistics, etc. Volumes for expected single-dose regimen candidates doubled to ensure comparability across vaccines. Volumes include dose donations that are committed to being delivered through COVAX. Volumes have been rounded to nearest 5M.
2 Final SFP volumes may be lower than forecasted based on opt-out and dose-sharing behavior. Volumes only account for current SFP demand based on Commitment Agreements.
3 Coverage refers to proportion of total population in AMC91 Participants that could be fully vaccinated with available volumes, assuming India receives 20% of AMC-funded volumes.
4 Scenarios are based on best available information from manufacturers and analysis from Gavi and UNICEF on the impact and likelihood of potential mitigation efforts.

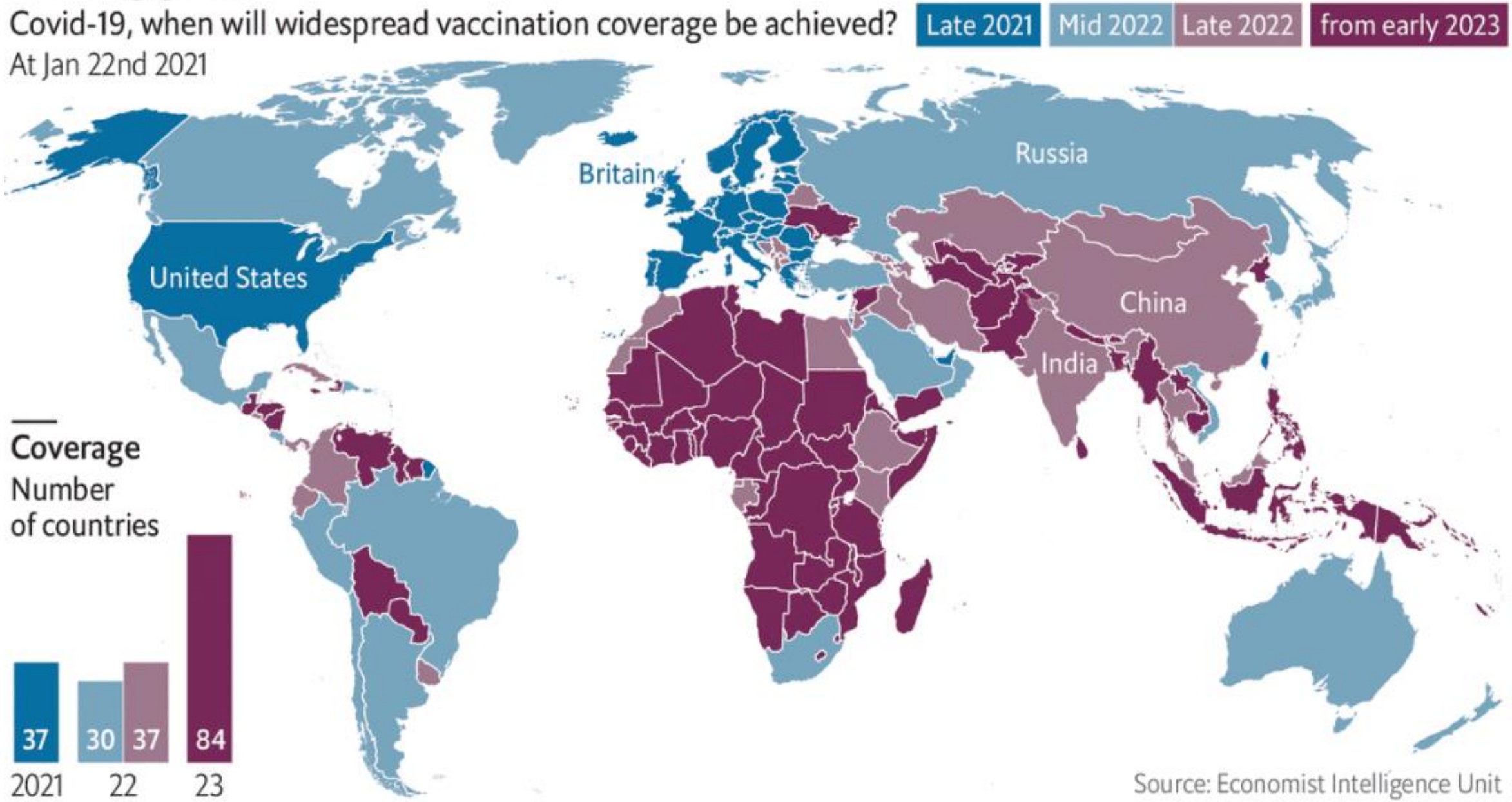
Beloften worden niet waargemaakt



Waiting game

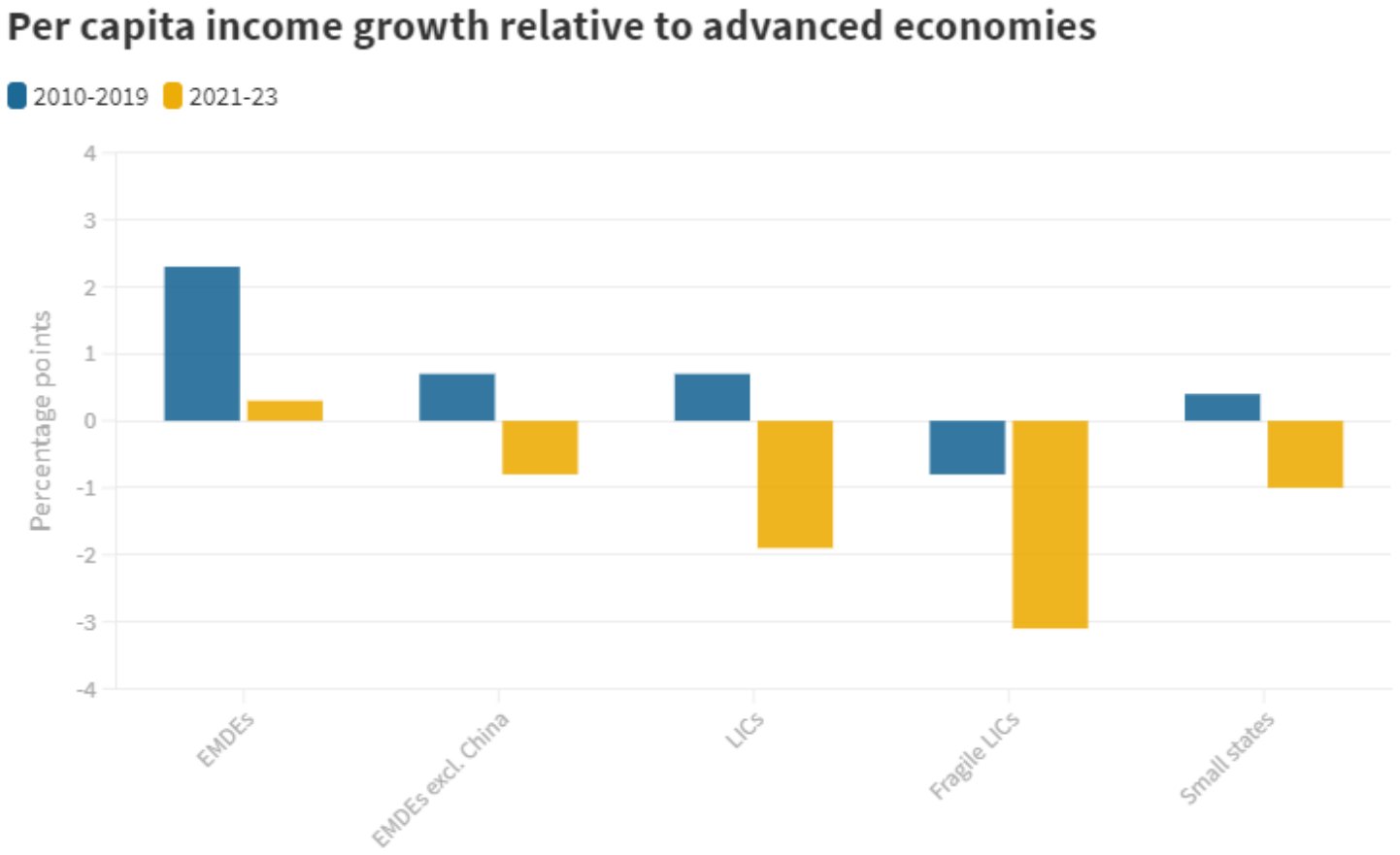
Covid-19, when will widespread vaccination coverage be achieved?

At Jan 22nd 2021



Source: Economist Intelligence Unit

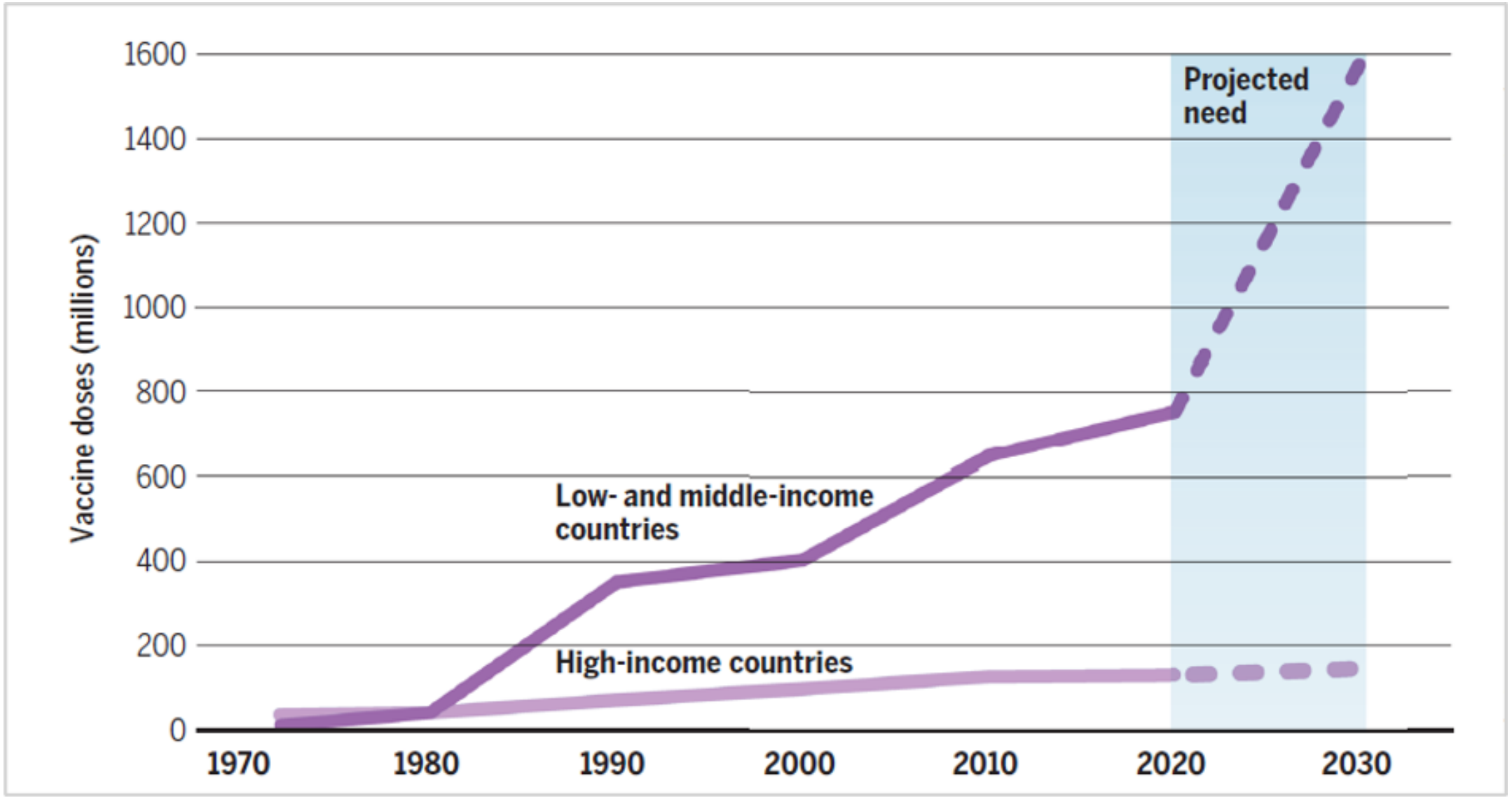
Economische consequenties van vertraagde vaccin leveringen



Source: World Bank
Note: EMDEs = emerging market and developing economies; LICs = low-income countries; Fragile LICs = fragile and conflict-affected LICs. Relative per capita income growth is computed as a difference in per capita GDP growth between respective EMDE groups and advanced economies. For more information on "Small states," see: https://www.worldbank.org/en/country/smallstates/overview.

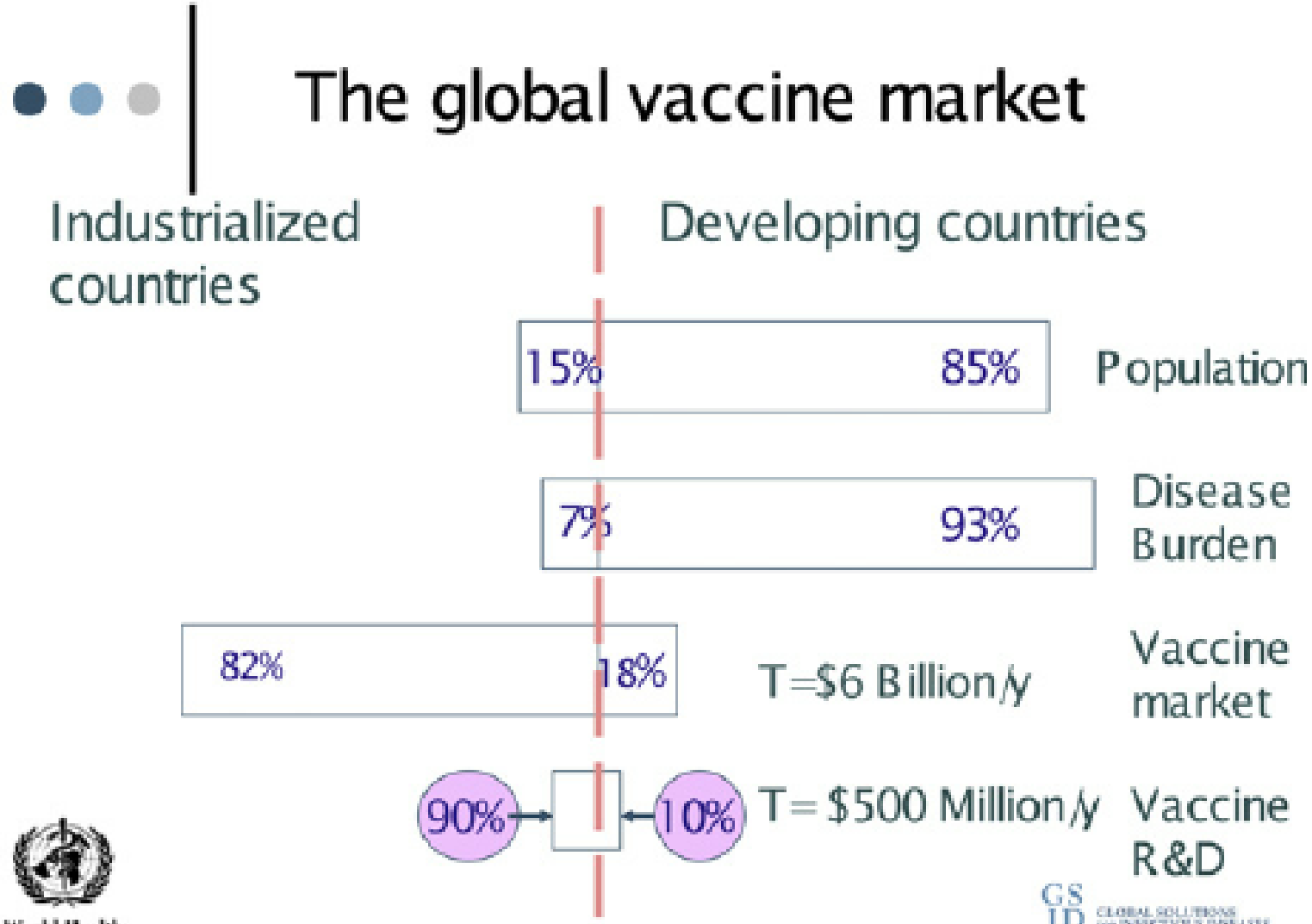
Uniek voor COVID-19?

Projected vaccine needs



Shulman et al. Understanding global vaccine economics R&D

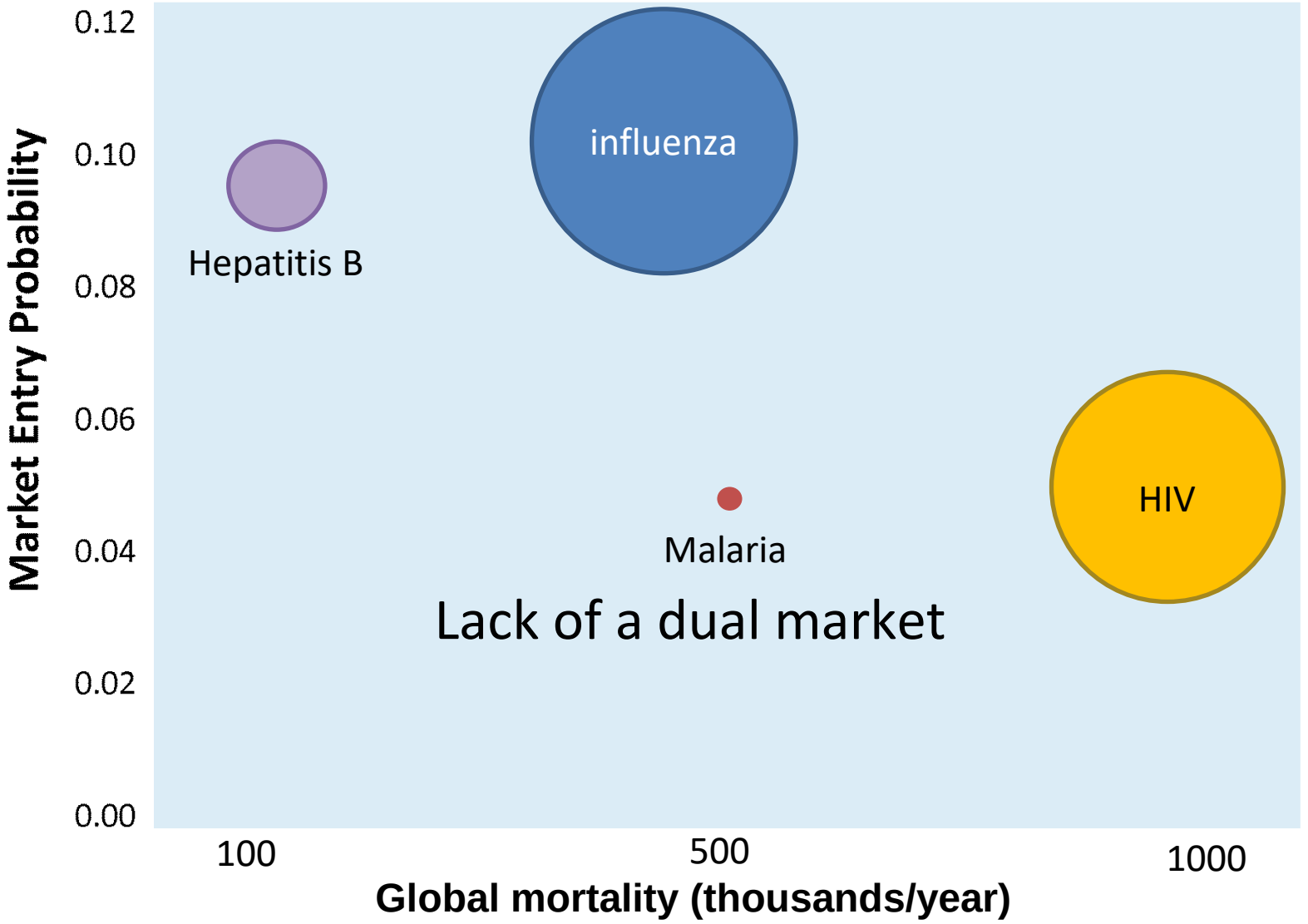
De markt faalt…



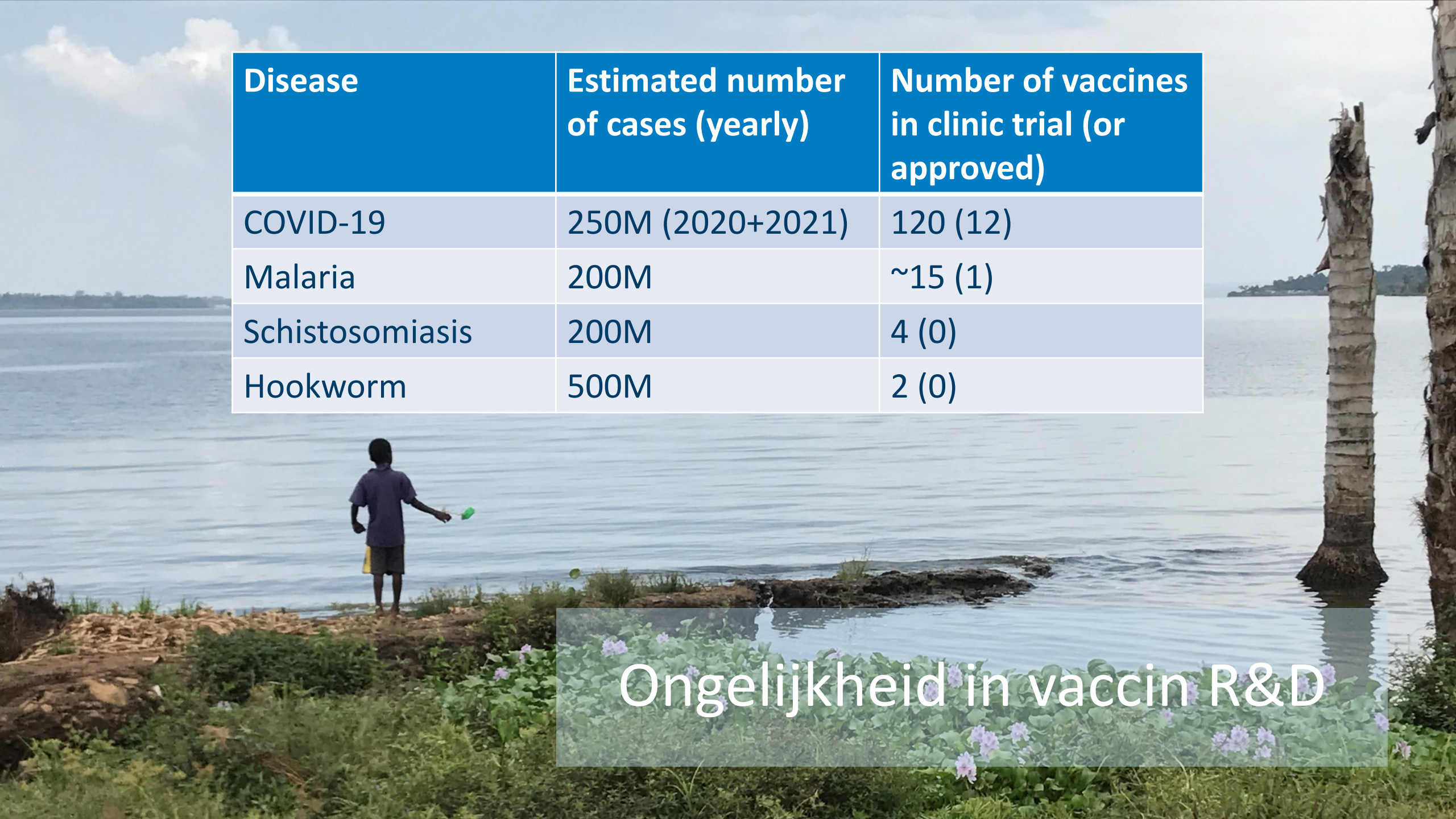
World Health Organization

GS ID GLOBAL SOLUTIONS for INFECTIOUS DISEASES

Risico is hoog, verdiensten laag



Adapted from: Pronker et al. PLoS ONE 2013 8(3): e57755.

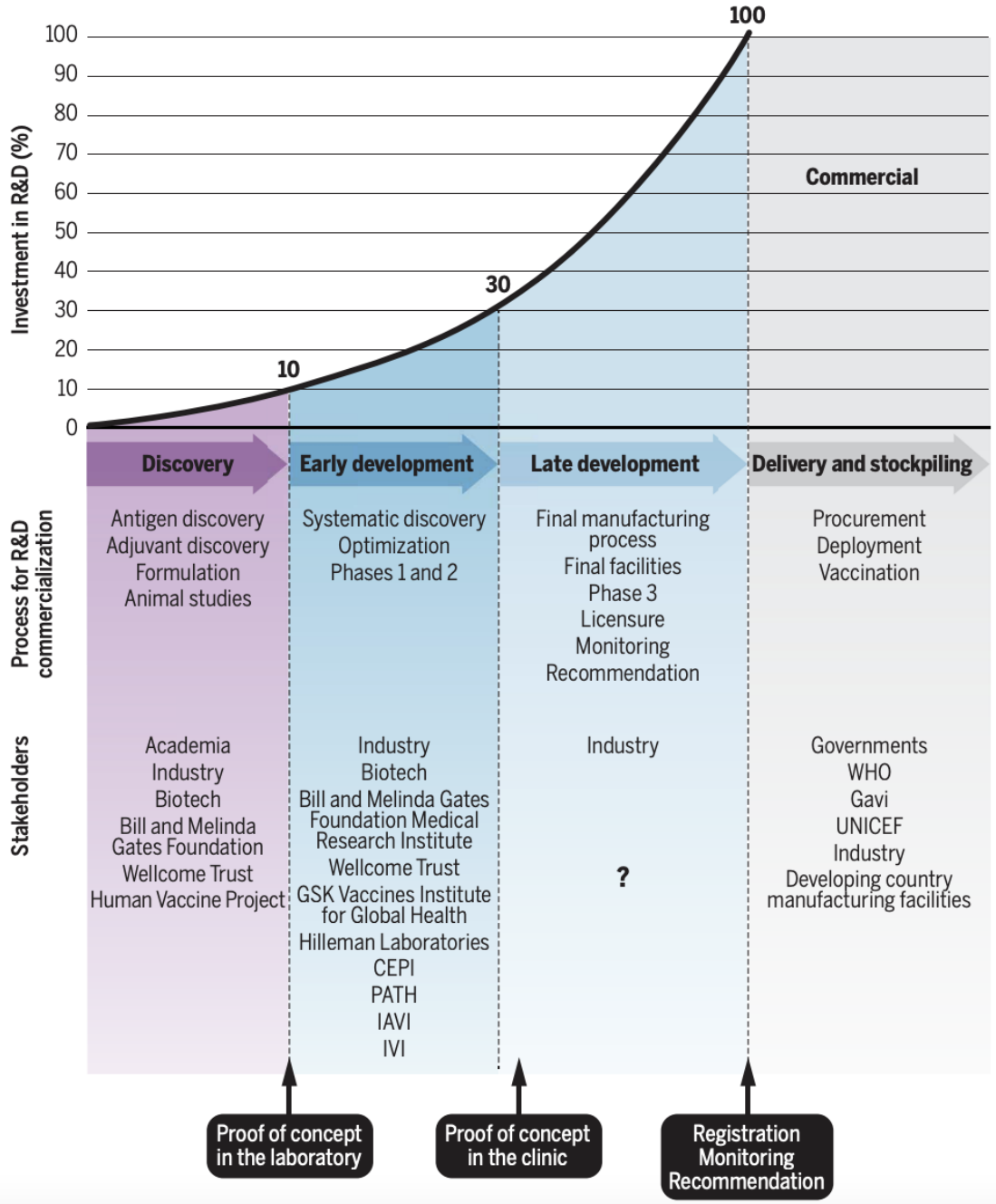


Disease	Estimated number of cases (yearly)	Number of vaccines in clinic trial (or approved)
COVID-19	250M (2020+2021)	120 (12)
Malaria	200M	~15 (1)
Schistosomiasis	200M	4 (0)
Hookworm	500M	2 (0)

Ongelijkheid in vaccin R&D

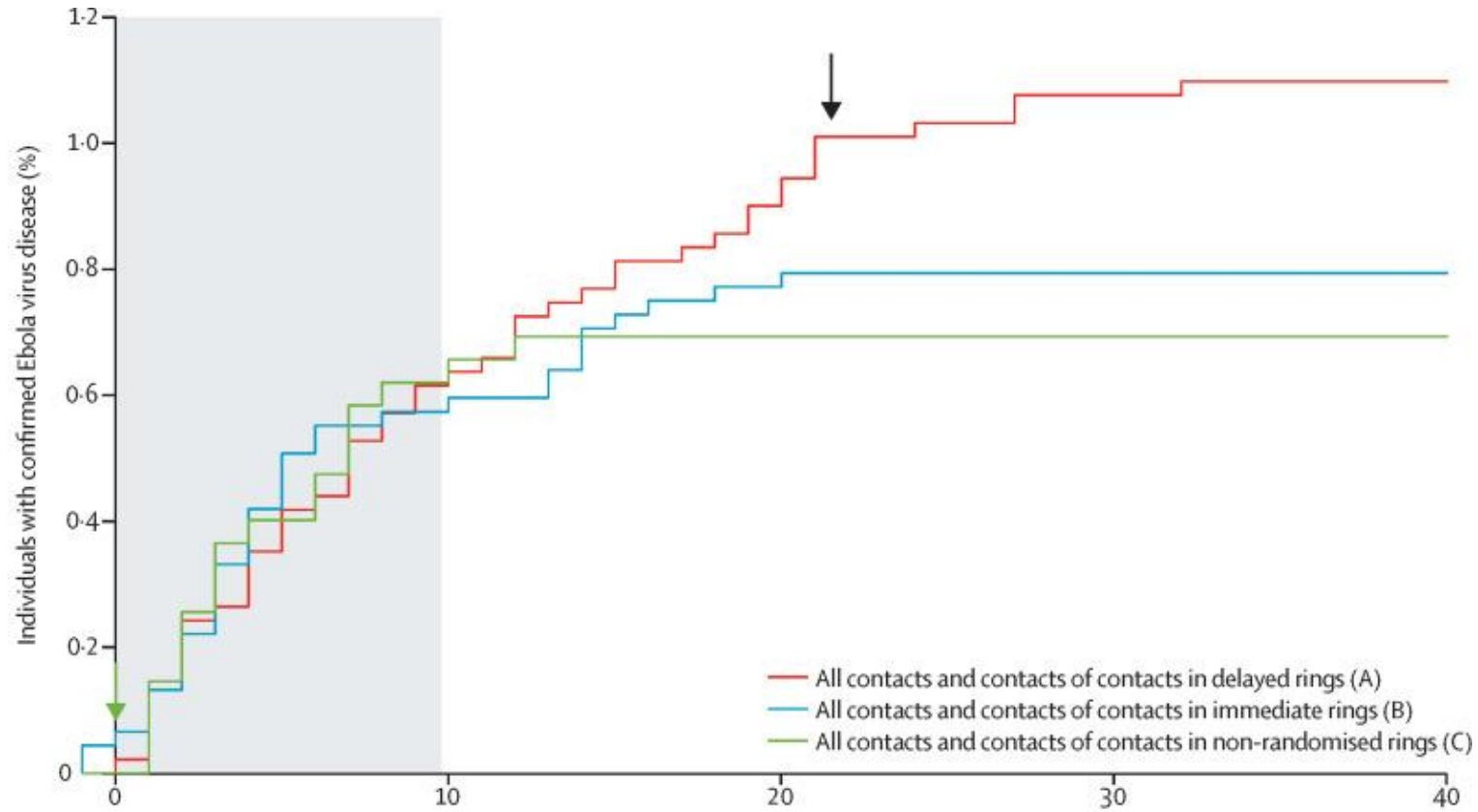
Mogelijke oplossing

- Advanced market commitments
- Product development partnerships
- Innovating and de-risking R&D



Rappuoli et al., Sci. Transl. Med. 2019

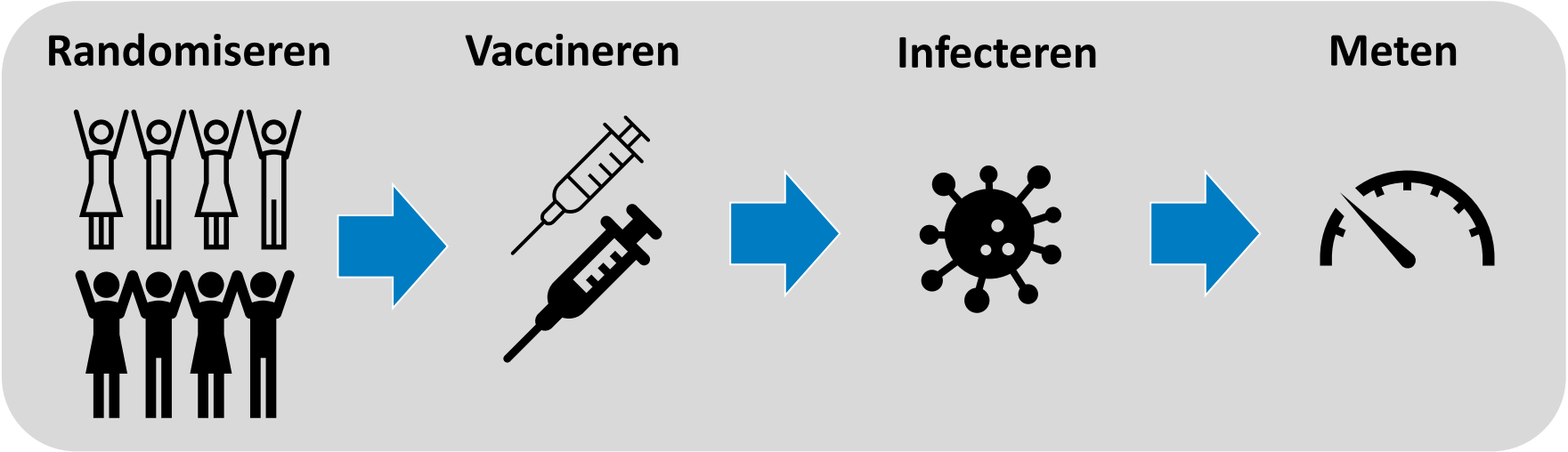
Platform technologie, slimmere “design” van trials



Number at risk					
All contacts and contacts of contacts in delayed rings	4556	4528	4514	4508	4507
All contacts and contacts of contacts in immediate rings	4536	4512	4503	4503	4503
All contacts and contacts of contacts in non-randomised rings	2745	2727	2726	2726	2726

Henao-Restrepo et al Lancet 2017

Gecontroleerde humane infectie modellen



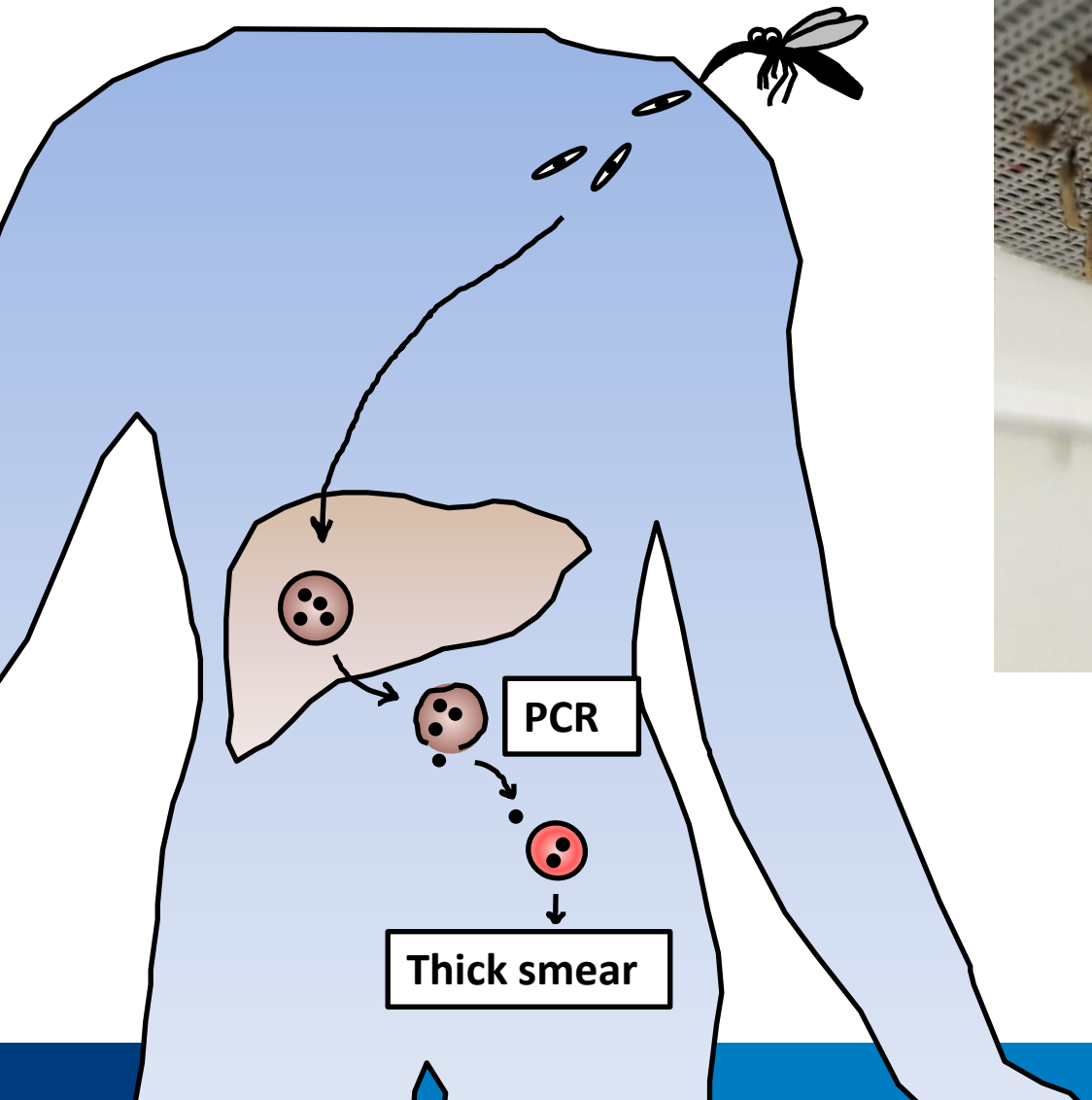
Doel:

- Effectiviteitsdata (tijdens “lockdown”)
- Correlaten van bescherming
- Transmissie in gevaccineerde vs ongevaccineerde populatie

Uitdagingen:

- Veiligheidsrisico’s = beperkend
- Geen 100% effectieve behandeling
- Regulatoire acceptatie
- Technisch (BSL3 GMP omgeving)

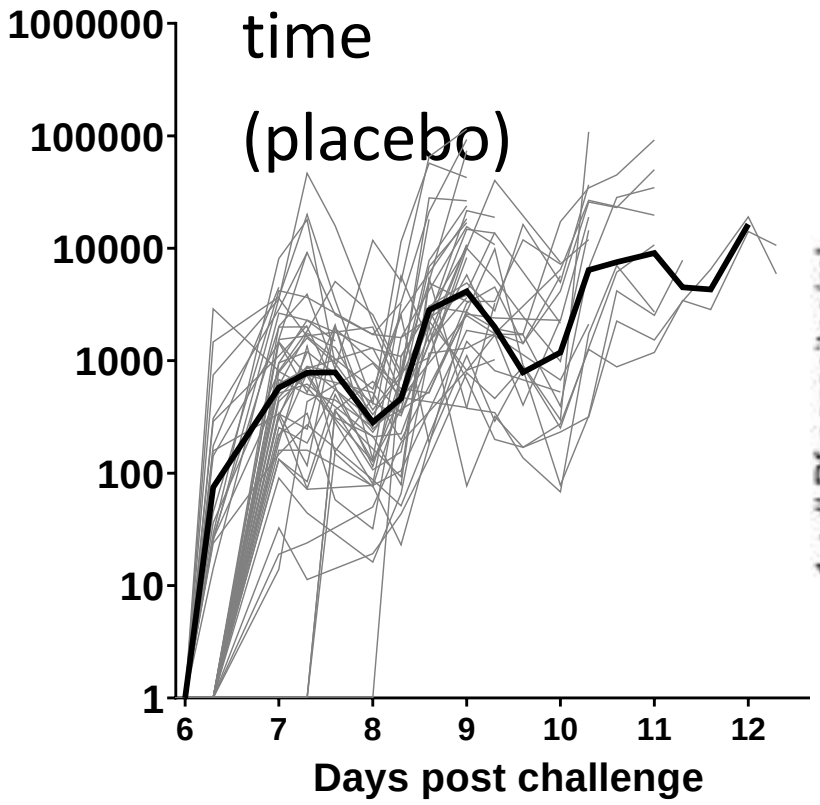
Malaria

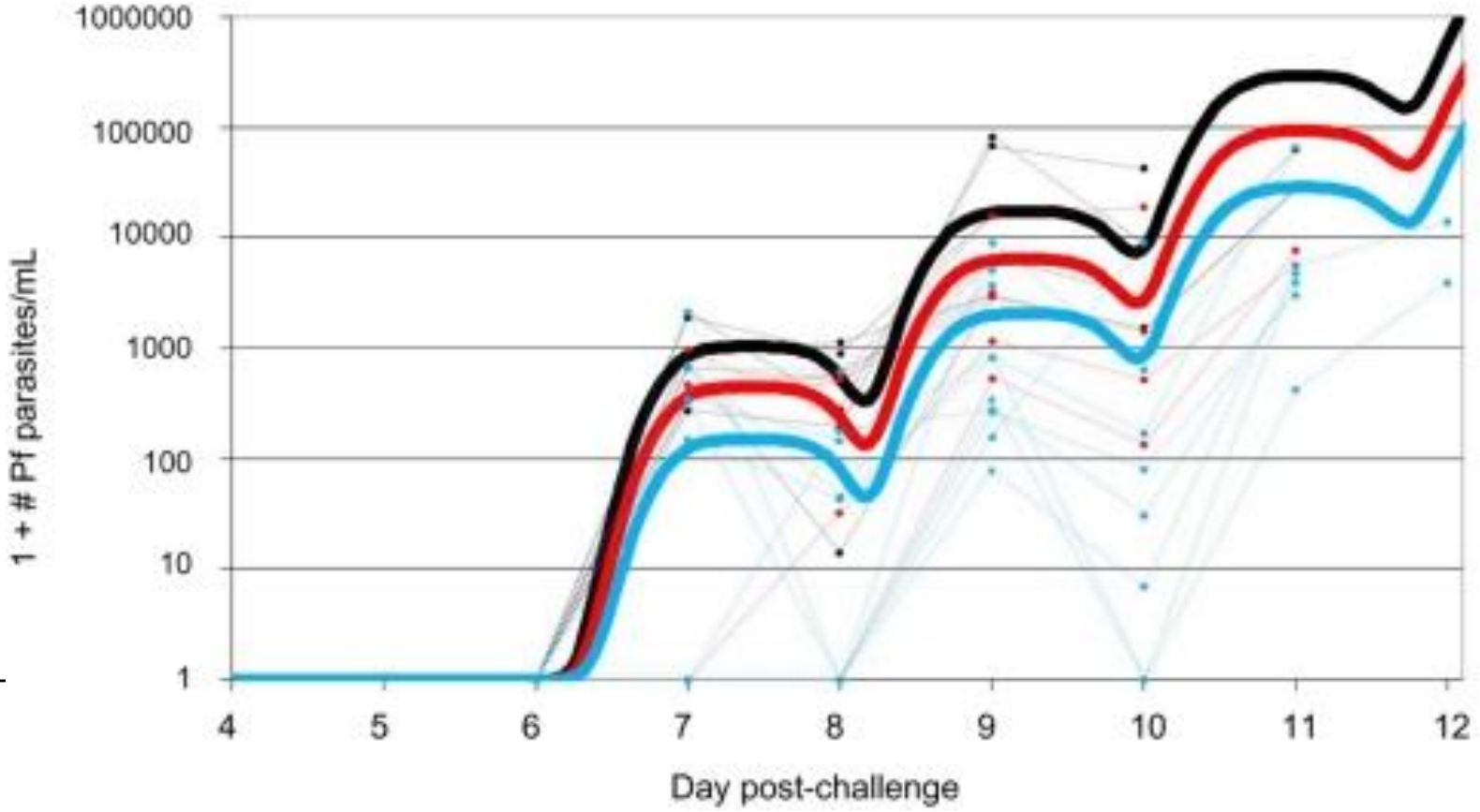

PCR
Thick smear


SANARIA
MALARIA ERADICATION THROUGH VACCINATION

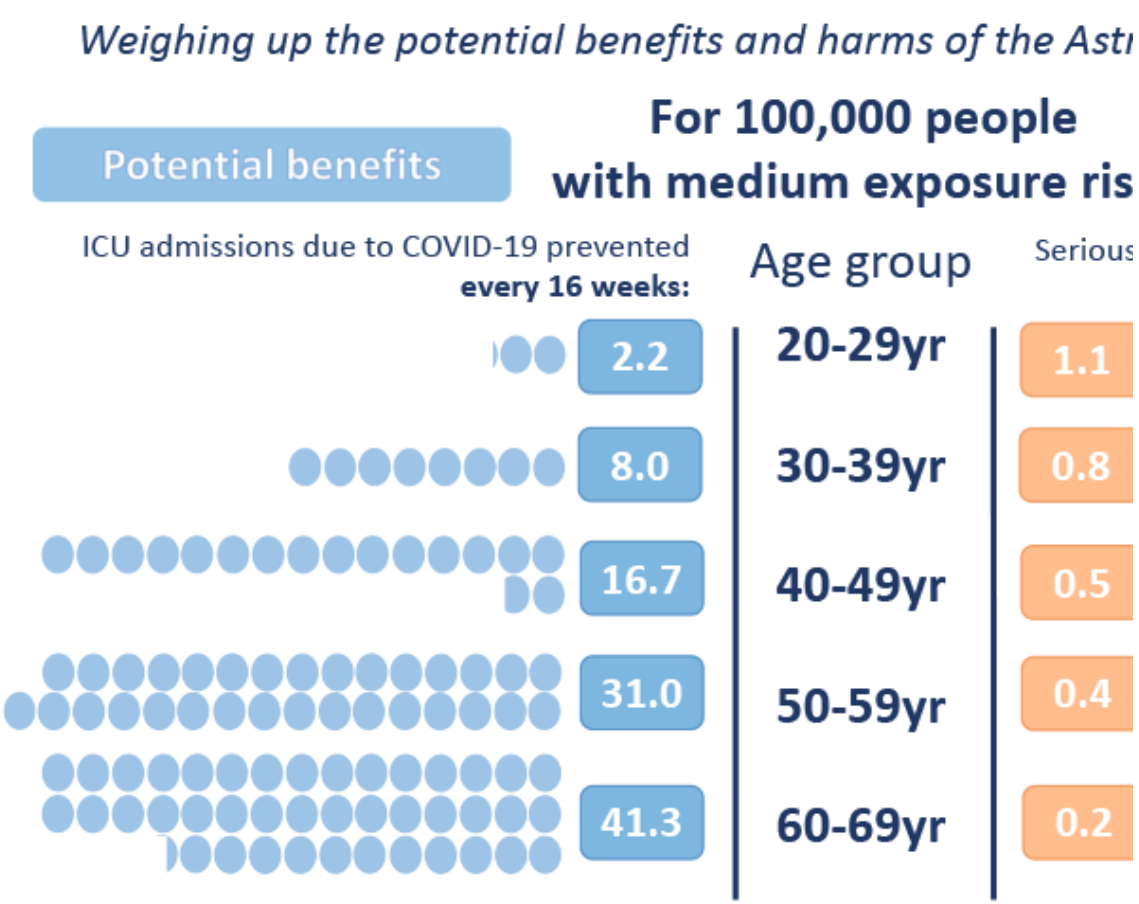
Malaria vaccine efficacy trial

Parasitemia over time (placebo)





Publiek debat



Wi

* Based on coronavirus incidence of 6 per 10,000: roughly UK in February

Table 1
Estimated morbidity and mortality costs of delayed vaccine introduction [a].

Vaccine	Diseasedeaths/ year	Vaccine efficacy	Potential maximum impact on lives lost per year of delay in vaccine introduction
Malaria: RTS,S in Sub-Saharan Africa	**407,000** deaths/ year	57.7% (95% CI: 16.2–80.6)	**234,000**(95% CI: 65,934 –328,042)
Human papillomavirus: One dose vaccine schedule in Sub-Saharan Africa given current supply constraints	**81,687** deaths/ year in a population of 372,000 women at risk with 119,284 new cases per year	95.89% (95% CI: 86 –100) against vaccine strains	**8, 662**[b] (95% CI: 7,768–9,032)
Human papillomavirus: Accelerated 2-dose vaccine introduction in LMICs	**226,100** deaths/year in LMICs	95.89% (95% CI: 86 –100) against vaccine strains	**151,687**[c] (95% CI: 136,112–158,270)
Tuberculosis: M72/AS01$_E$ globally	**1,700,000** deaths/year	54.0% (95% CI: 2.9–78.2)	**918,000**(95% CI: 49,300 –1,329,400)

Black et al. Seminars in immunology 2020

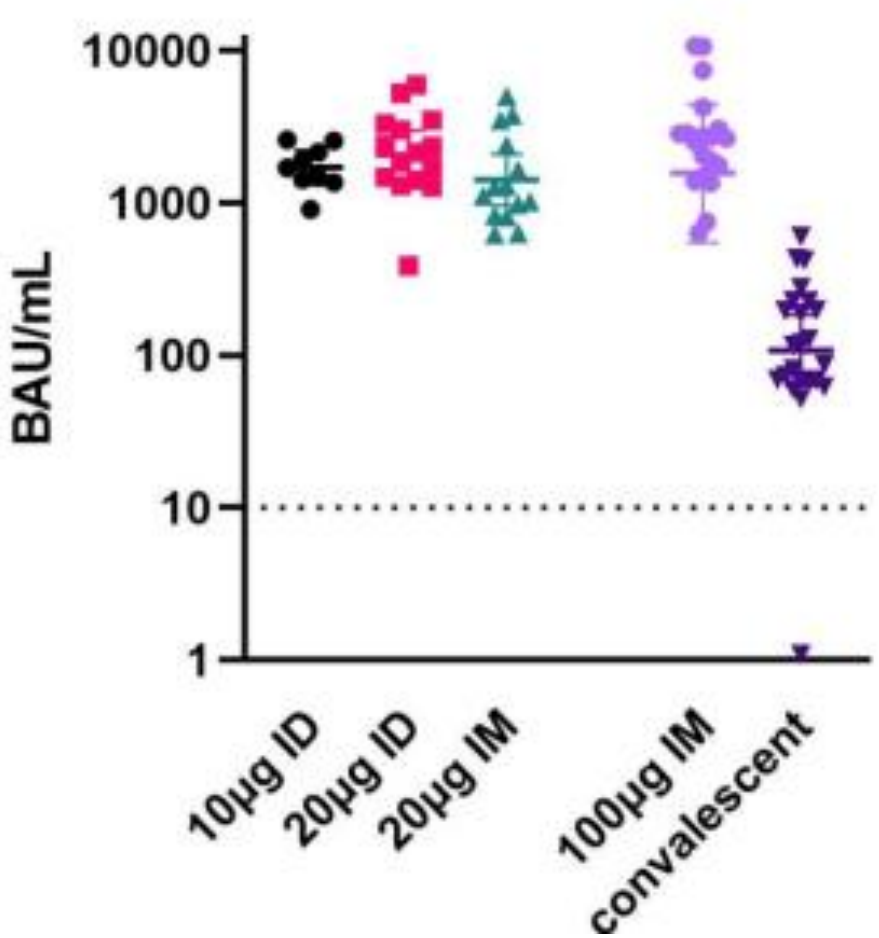
Innovatie na registratie

Combineren van verschillende vaccins

Fractionele dosering

Intradermale vaccinatie

> Publieke domein



Anna Roukens

Lancet Glob Health. 2022 Apr;10(4):e570-e573.

https://www.medrxiv.org/content/10.1101/2021.07.27.21261116v1.full.pdf

Conclusie – onderzoeksinfrastructuur in pandemie

- Resources en infrastructuur: snel schakelen, benutten van kennis – private-publieke samenwerking/hybride
- Investeren in innovatie: anticiperen in plaats van reactief
- Publieke gezondheid = publiek debat = wetenschapscommunicatie

No one is safe until everyone is safe

Gogiveone.org