

Jabbing SG

A health planner's guide to pandemic vaccines

Ben Seet

Deputy GCEO (Education & Research)



Adding years of healthy life

How to buy something the whole world thinks it needs,
at a time when nobody knows what will work,
and when nothing is available for sale anywhere?

And upon securing it, convince everyone that they need it... 3 times!

Disclaimer:

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Today, Singapore is one of world's best vaccinated countries

Total population vaccinated: 93%
(or 96% of eligible population)
Population boosted: 79%

Almost exclusively mRNA vaccines

- Highest neutralising Ab levels
- High vaccine efficacy, including against number of variants of concern
- Very good safety profile

Covid-19 trivia

At the peak, we were vaccinating
~1% of our population every day



What this means for us?



We have begun to live safely with Covid-19...

Singapore announces major easing of Covid-19 rules from April 26: What you need to know



The sweeping changes are the most major since such measures were first introduced in 2020. PHOTOS: DESMOND WEE, GIN TAY, LIM YAOHUI.

e Big Story: 555 of the *Straits Times: Jan 2022*

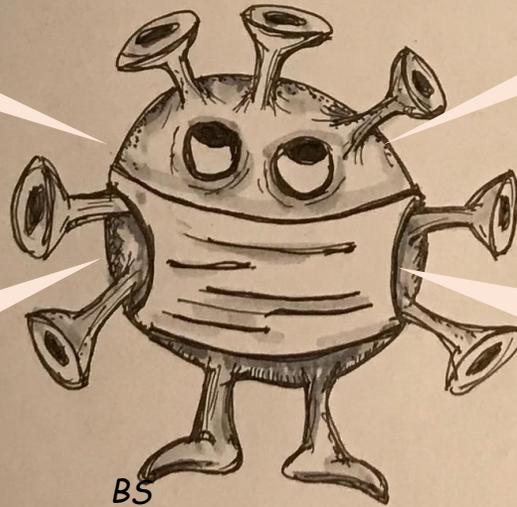
Straits Times: Apr 2022

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What I'm going to talk about today...

How did Singapore decide so quickly?

How did we choose the "best" vaccines?



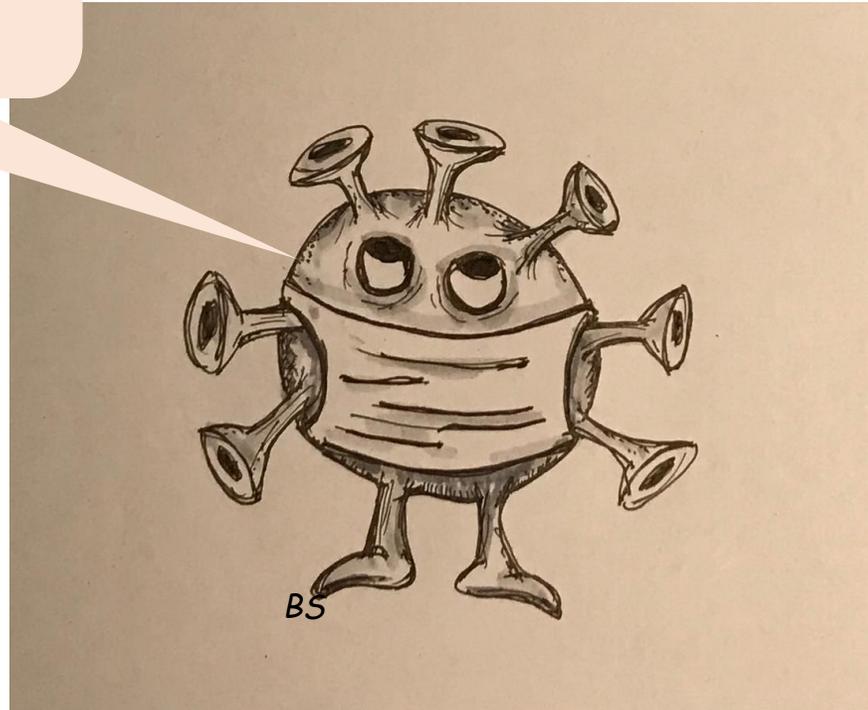
What are we planning next?

How did we persuade the population to step up for the jab?

Jabbing SG

What I'll talk about first...

How did Singapore decide so quickly?



How did Singapore
decide so quickly?

1. Be clear about the Mission

Apr 2020

“When a safe and effective vaccine becomes available, make sure we are one of the first to get it.”

Apr 2021

“Our job is to avert serious illness in the elderly and vulnerable, so as to prevent deaths and preserve hospital capacity.”

“Our job is to avert serious illness in the elderly and vulnerable, so as to prevent deaths and preserve hospital capacity.”



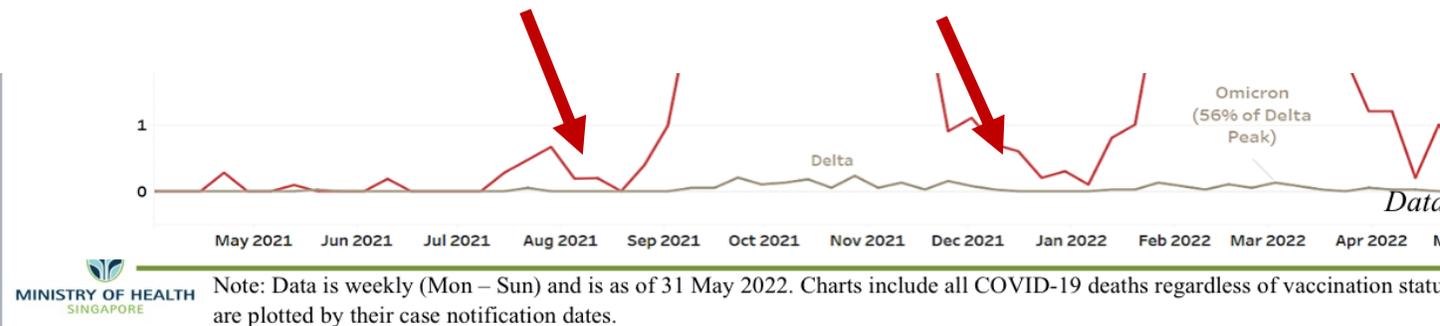
Covid-19 vaccines helped prevent 8,000 deaths in Singapore during Delta wave: MOF report

Averted 33,000 serious infections
Kept 112,000 out of hospital

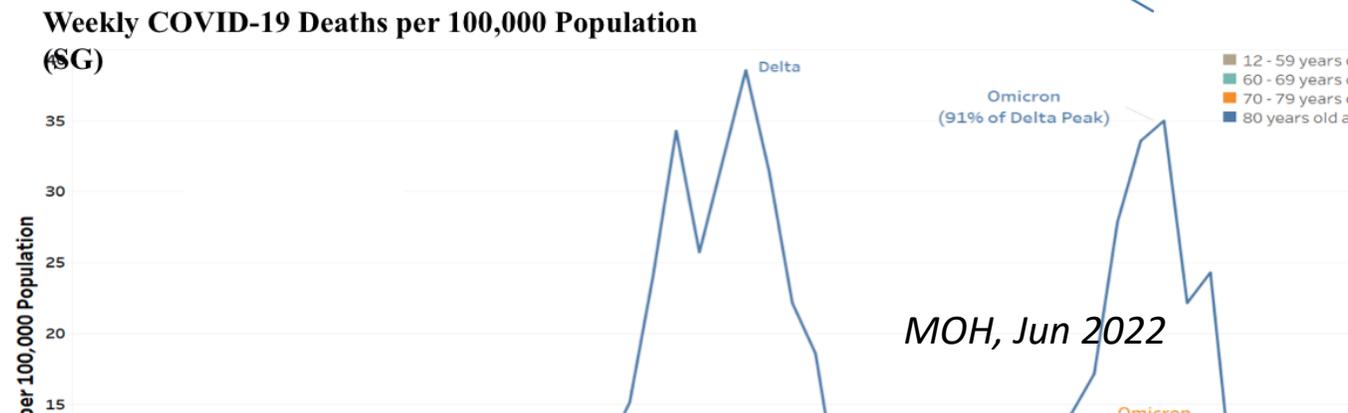
Straits Times, Feb 2022

At peak of Delta wave, our death rate was 1/3 that of the US

At peak of Omicron wave, our death rate was 1/5 that of the US



Breaking down by age groups, highest death rates were for those 80+



How did Singapore
decide so quickly?

1. Be clear about the Mission

kia-su

“When a safe and effective vaccine becomes available, make sure we are one of the first to get it.”

kia-si

“Our job is to avert serious illness in the elderly and vulnerable, so as to prevent deaths and preserve hospital capacity.”

kia-su + kia-si

“We need to be ready for future variants, in case current vaccines no longer do the job.”

How did Singapore
decide so quickly?

2. Task organise to get the job done

TxVax

Scientific & technical advisory panel for Covid-19 vaccines & therapeutics

PG(V&T): Planning Group for Vaccines & Therapeutics

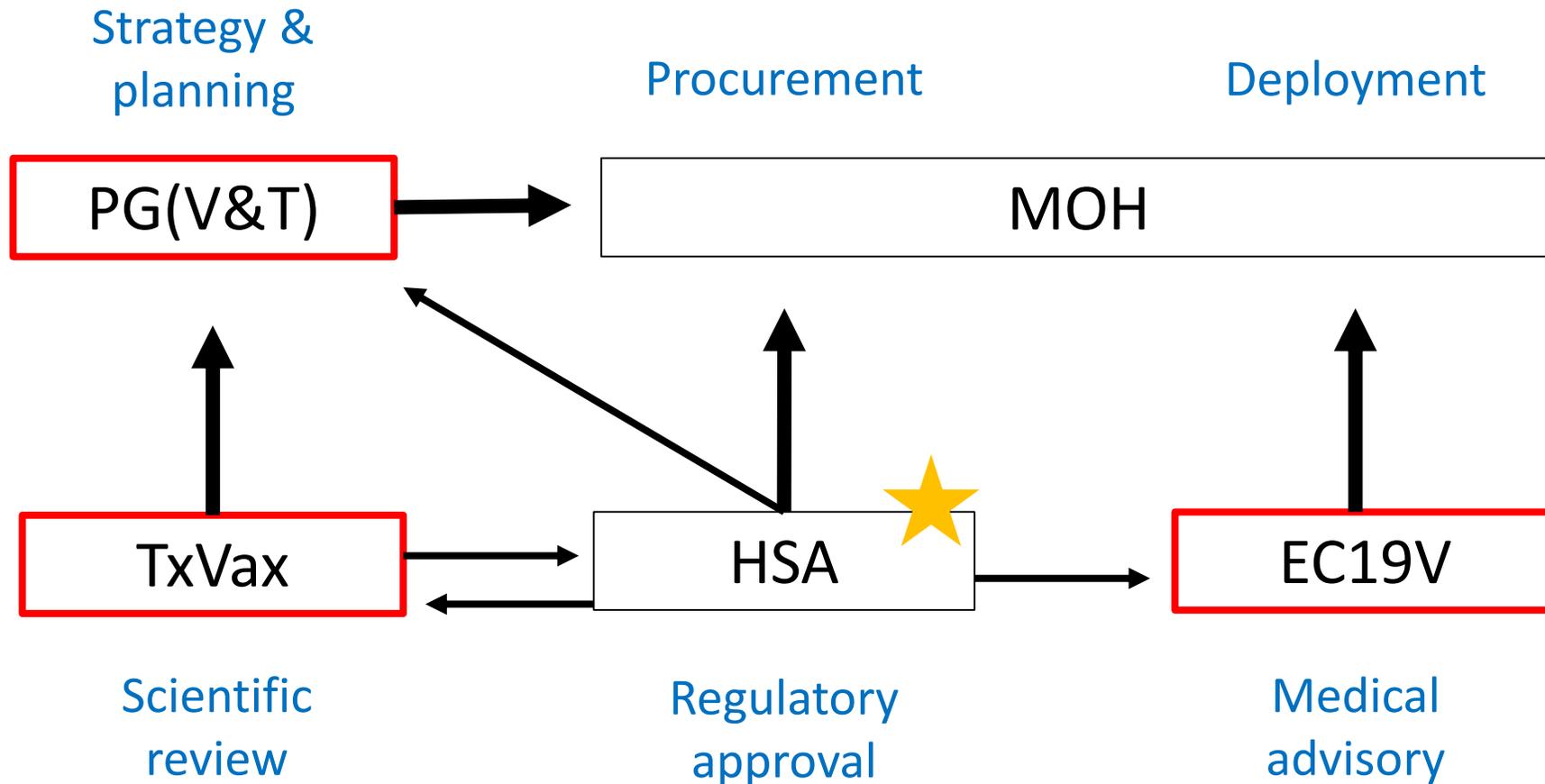
National strategy & planning for vaccine & therapeutics access & portfolio

EC19V: MOH Expert Committee for Covid-19 Vaccines

Medical advisory panel to MOH for deployment of vaccines in national vaccination programme

How did Singapore
decide so quickly?

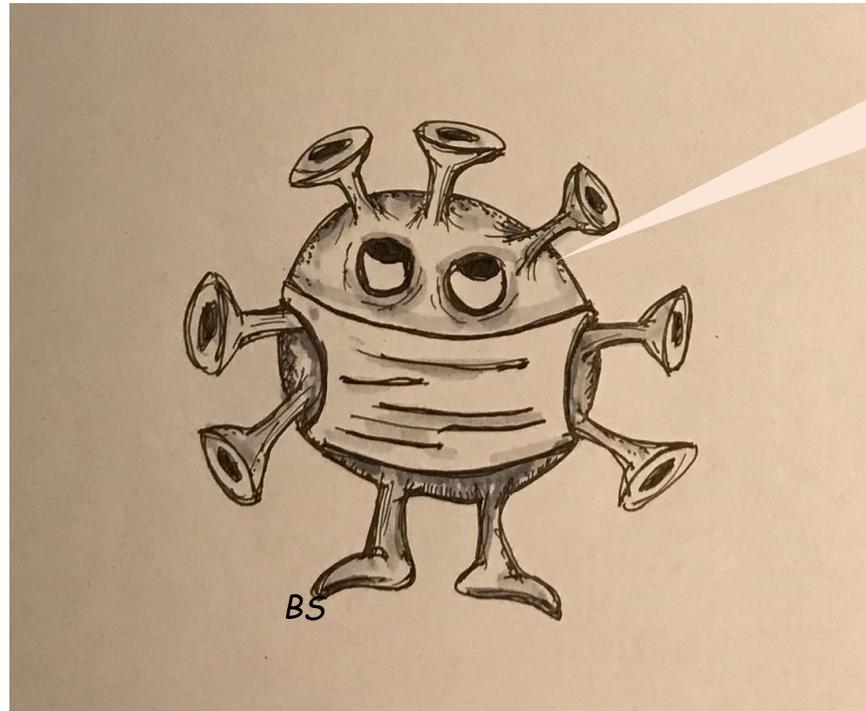
3. Streamline decision making



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What I'm going to talk about next...

How did we choose the "best" vaccines?

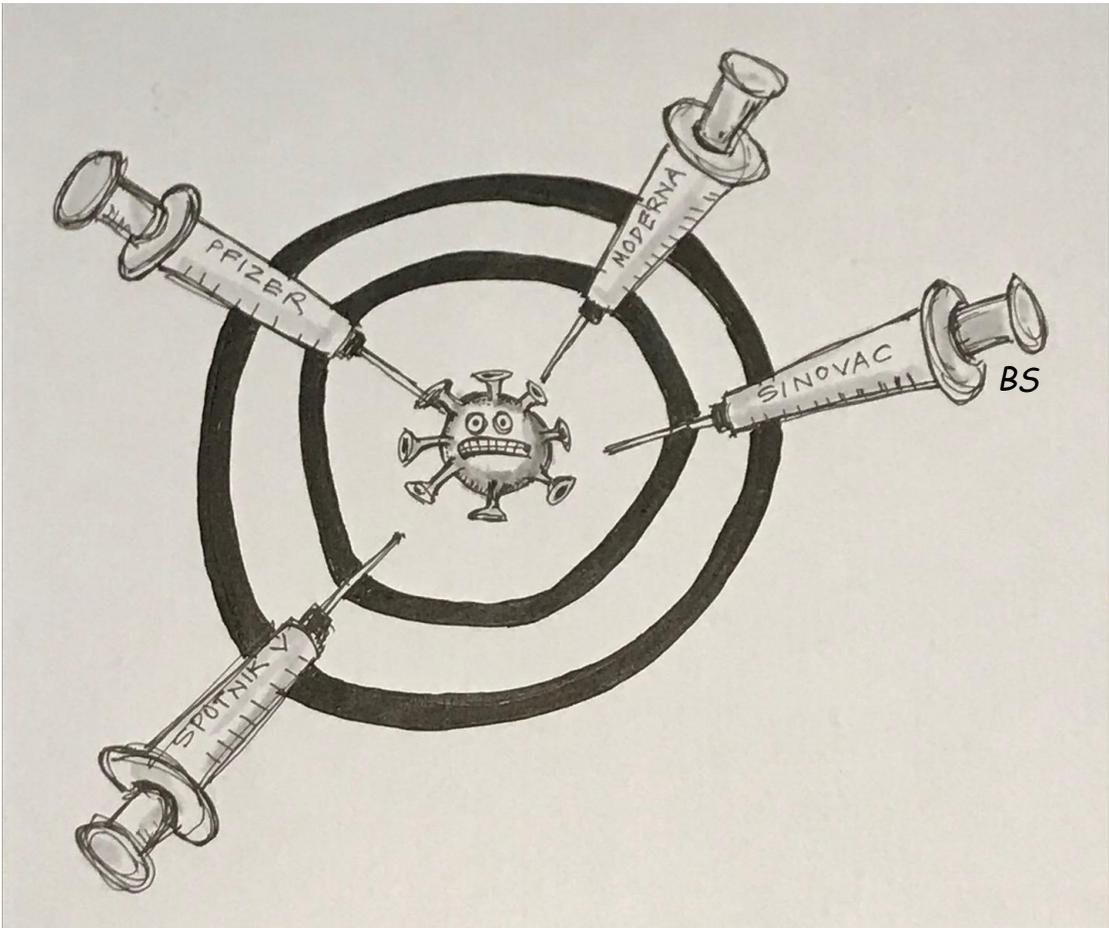
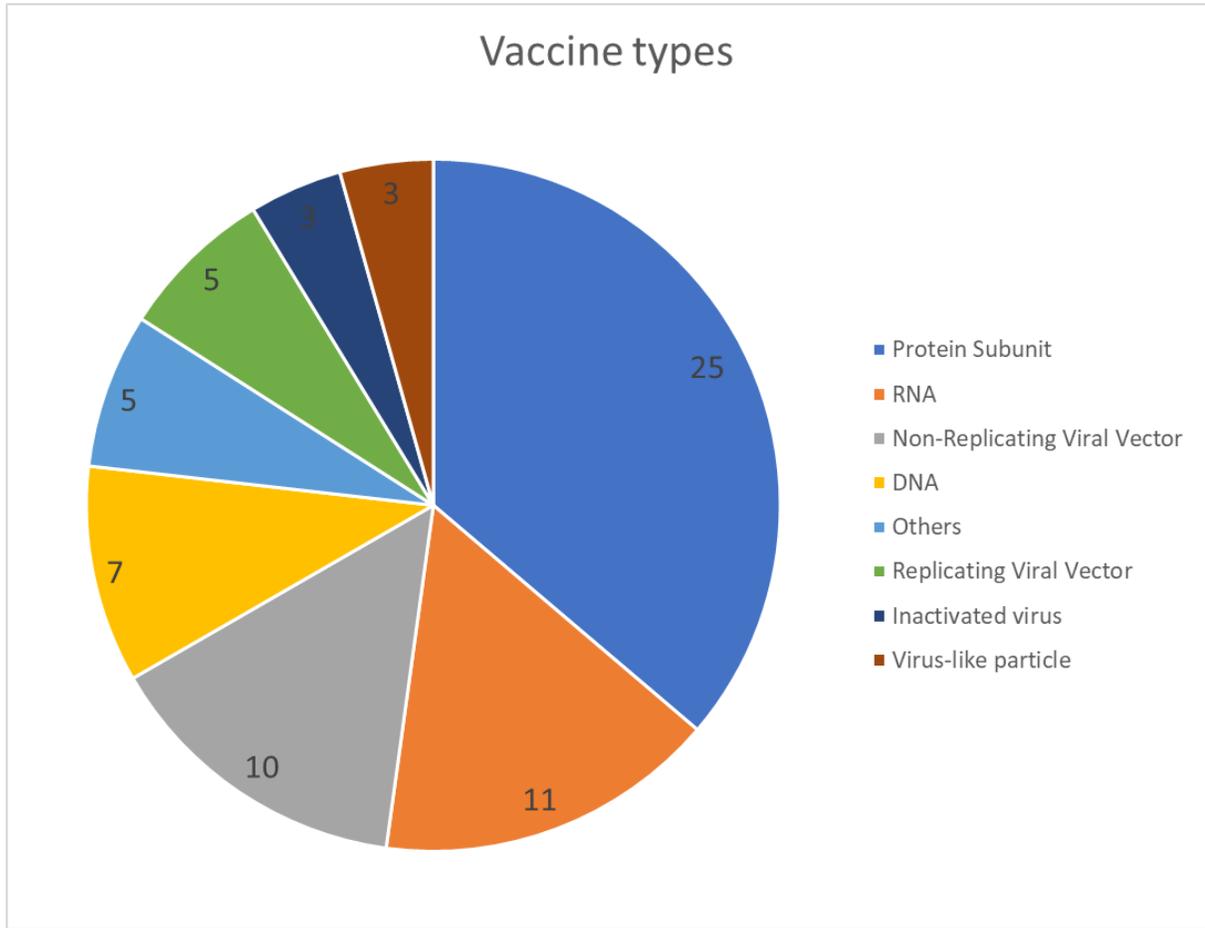


Covid-19 vaccine landscape

In Apr 2020, ~70 known projects
Historically, 1:10 chance of successful vaccine

How did we choose the "best" vaccines?

By Jul 2021, ~290 projects, 105 in clinical trial, 8 with WHO Emergency Use Listing (EUL)



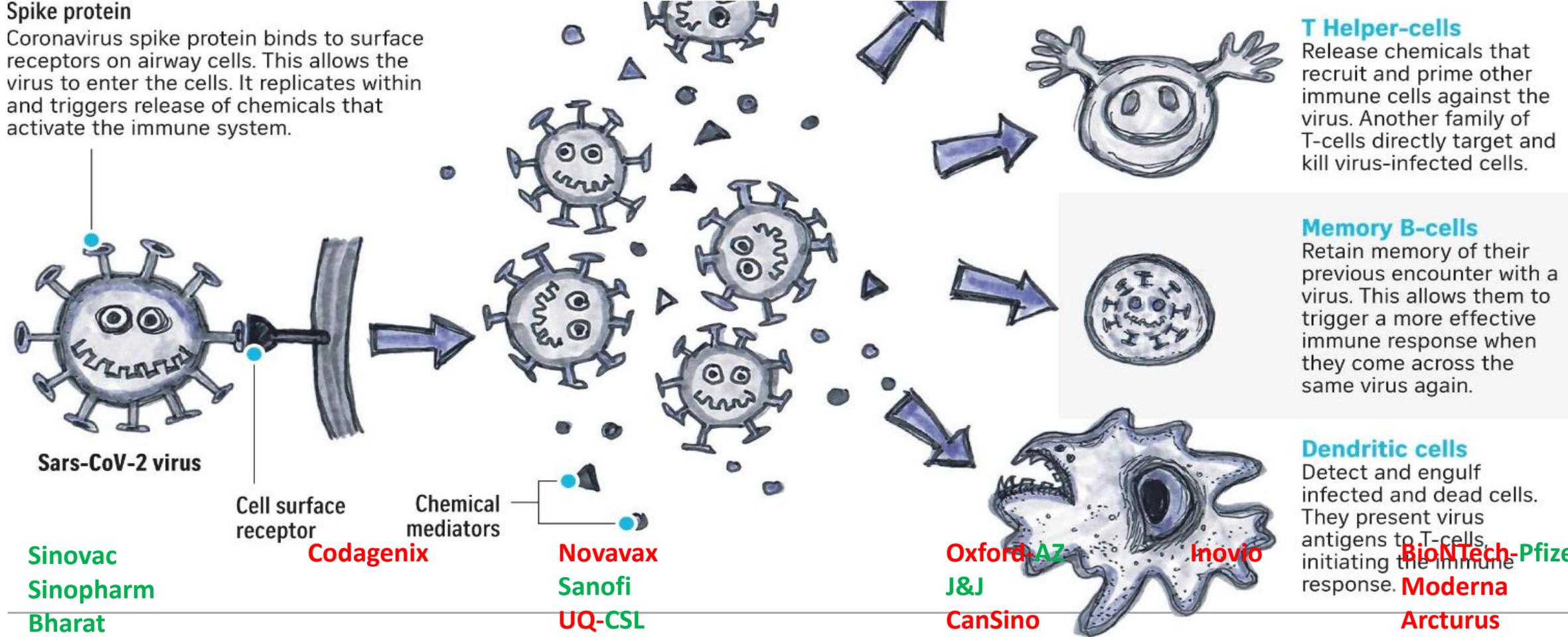
How did we choose the "best" vaccines?

Covid-19 vaccine landscape

~10 different vaccine formats, more than half of which had never been previously used in man. More than half of vaccine companies had never made or sold vaccines.

Spike protein

Coronavirus spike protein binds to surface receptors on airway cells. This allows the virus to enter the cells. It replicates within and triggers release of chemicals that activate the immune system.



Sars-CoV-2 virus

Cell surface receptor

Chemical mediators

- Sinovac
- Sinopharm
- Bharat
- Valneva

Codagenix

- Novavax
- Sanofi
- UQ-CSL
- Vaxine
- Clover

- Oxford-AZ
- J&J
- CanSino
- Gamelaya
- ReiThera

Inovio

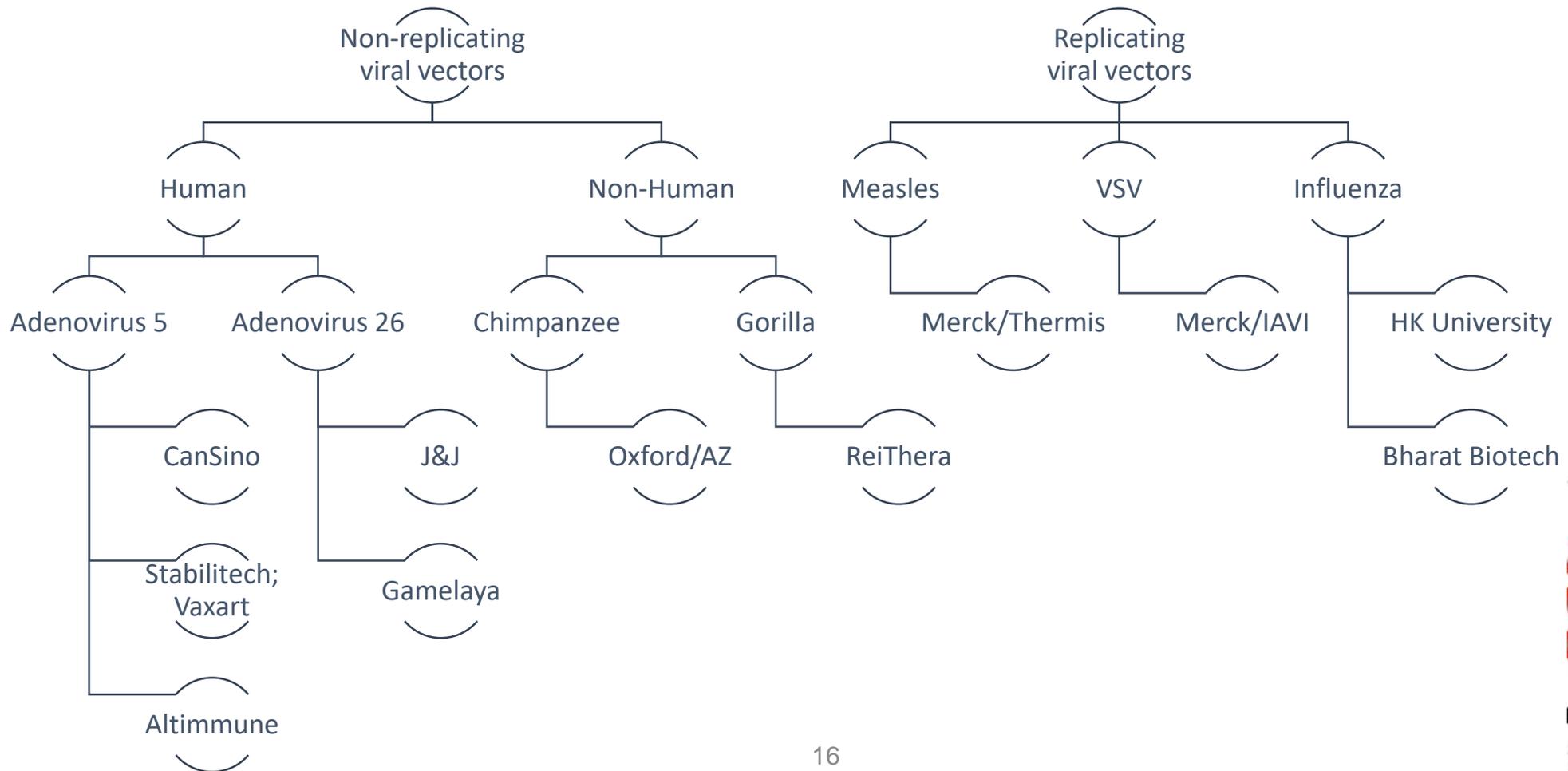
- BioNTech-Pfizer
- Moderna
- Arcturus
- Imperial College
- Curevac

POSSIBLE COVID-19 VACCINES COULD COME IN VARIOUS FORMS, BUT EACH IS DESIGNED TO TEACH THE IMMUNE SYSTEM HOW TO RECOGNISE AND FIGHT OFF THE VIRUS:

Covid-19 vaccine landscape

How did we choose the "best" vaccines?

Even within a single vaccine format, there were different technology platforms. In Jun 2020, this was the spread of viral vector Covid-19 vaccines:



**ACTIVATED
ING VIRUS INF
CINATION:**

n
spike protein binds to
n airway cells. This all
er the cells. It replicat
release of chemical

What TxVax looked at:

How did we choose the “best” vaccines?

When we first started:

- Vaccine design, adjuvant, vector, formulation
- Safety: preclinical, clinical
- Preclinical efficacy: in vitro, in vivo
- Clinical endpoints: immunogenicity, vaccine efficacy
- Accessibility by Singapore

As we learnt more:

- Size of company / track record
- Clinical trial experience
- Regulatory experience
- Scalability of production
- Robustness of supply chain

Today:

- Immune-bridging vs real world efficacy
- VE against variants, boosters
- Rare severe adverse events
- Paeds formulations
- Multivalent & pan-coronavirus vaccines

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As we learnt more:

Covid-19 trivia

TxVax has conducted ~250 meetings with some 50 companies & academic groups from the time it was formed

- Scalability of production
- Robustness of supply chain

Today:

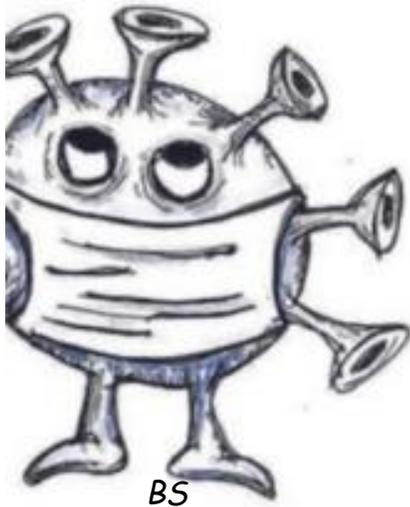
- Immune-bridging vs real world efficacy
- VE against variants
- Rare severe adverse events
- Boosters, paediatric formulations, variant-specific vaccines
- Multivalent & pan-coronavirus vaccines

Hedging risks

How did we choose the “best” vaccines?

We took investment portfolio approach:

- Diversified our bets across different risk categories
- Reviewed & rebalanced portfolio every time new data became available



BS

Risk categories

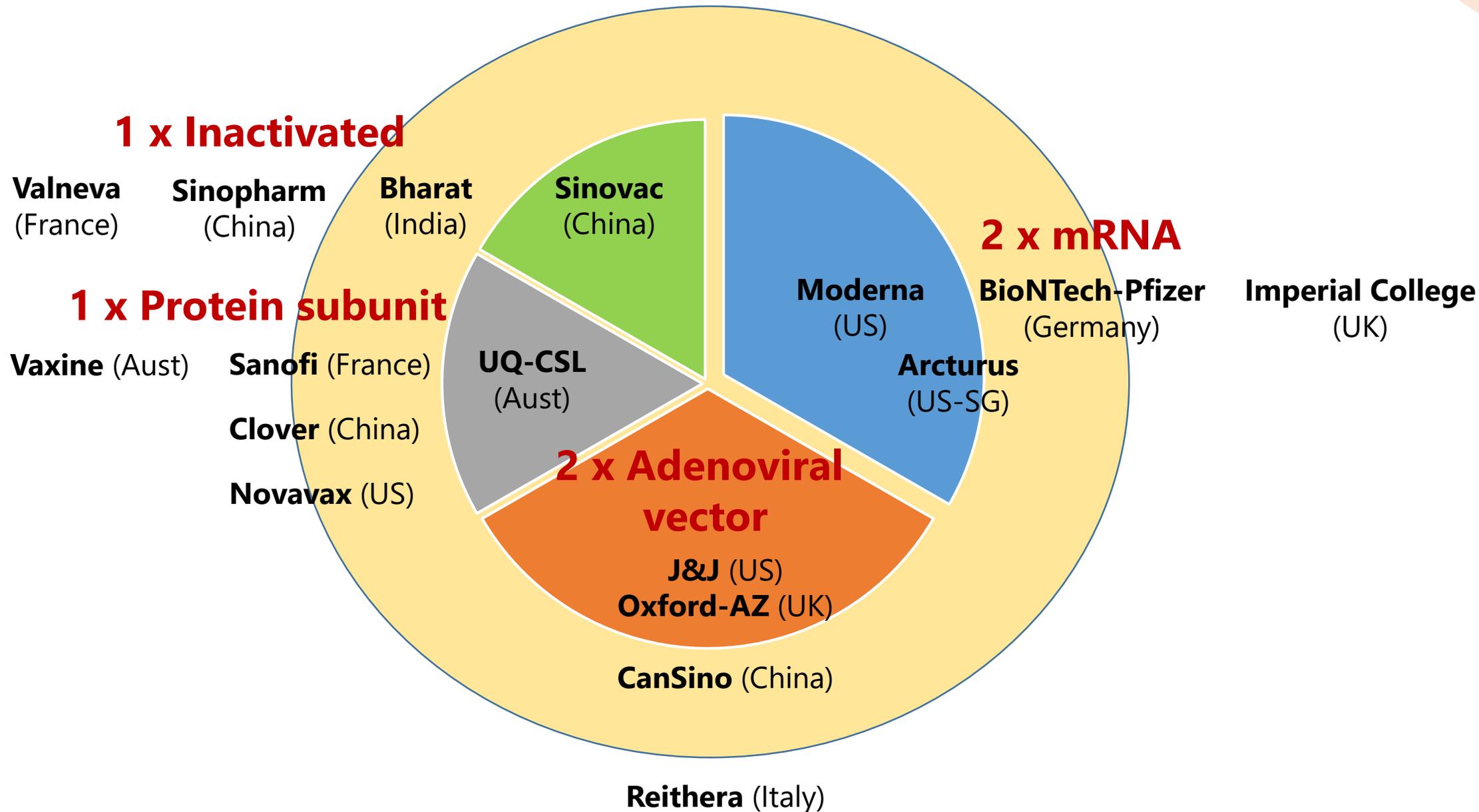
- Vaccine format
- “1st to gate” vs “Best-in-class”
- Big vs small company
- Supply chain uncertainty

HEALTHCARE GROUP/ILLUSTRATIONS: BENJAMIN SEET

VACCINE FACTS, FALLACIES AND HOAXES

What we kept warm on the plate (Sep 2020):

How did we choose the "best" vaccines?



How did we choose the “best” vaccines?

What was done differently?

- Hedging risks with portfolio
- Pooling risks (COVAX)
- Advance procurement agreements
- Rolling regulatory review
- Immune-bridging data
- Real world evidence
- From mouse to man?

... this isn't how drugs are typically developed, approved or procured in the highly regulated medical industry.

Vaccine milestones for Singapore

How did we choose the "best" vaccines?



Pfizer-BioNTech
First shipment of Covid-19 vaccine arrives in S'pore on SIA flight from Brussels



Moderna
First shipment of Moderna's Covid-19 vaccine arrives in Singapore on Feb 17



Novavax applies for approval to use its Covid-19 vaccine in S'pore

Apr 2020
TxVax formed

Jun 2020
1st APA signed

Sep 2020
2nd APA signed

Dec 2020

Feb 2021

May 2022

Senior staff nurse at NCID receives first Covid-19 vaccine in Singapore



Sinovac
China's Sinovac Covid-19 vaccine arrives in Singapore, but is not yet approved for use

It wasn't just vaccines...

- Regen-COV (Regeneron)
- Remdesivir (Gilead)
- Sotrovimab (Vir-GSK)
- Molnupiravir (Merck)
- Evusheld (AZ)
- Paxlovid (Pfizer)
- (Hydroxychloroquine)
- (Ivermectin)



Singapore inks deal for antiviral pill to treat Covid-19 and its variants

Straits Times, Jan & Feb 2022

How did we choose the "best" vaccines?



First batch of Pfizer's Paxlovid pill for Covid-19 treatment arrives in S'pore

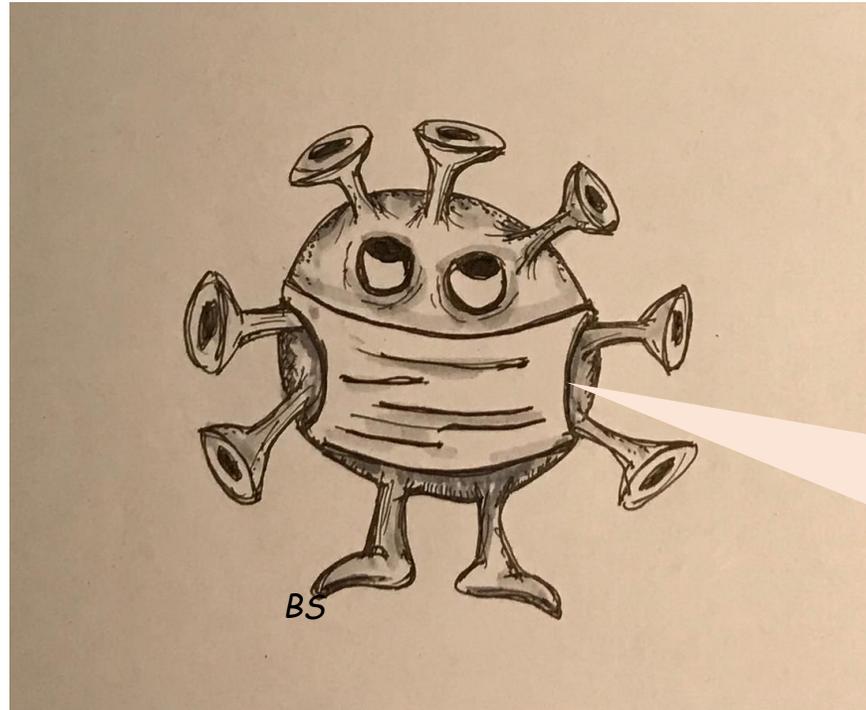


Kok Yufeng
Transport Correspondent
The Straits Times



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What I'm going to talk about next...



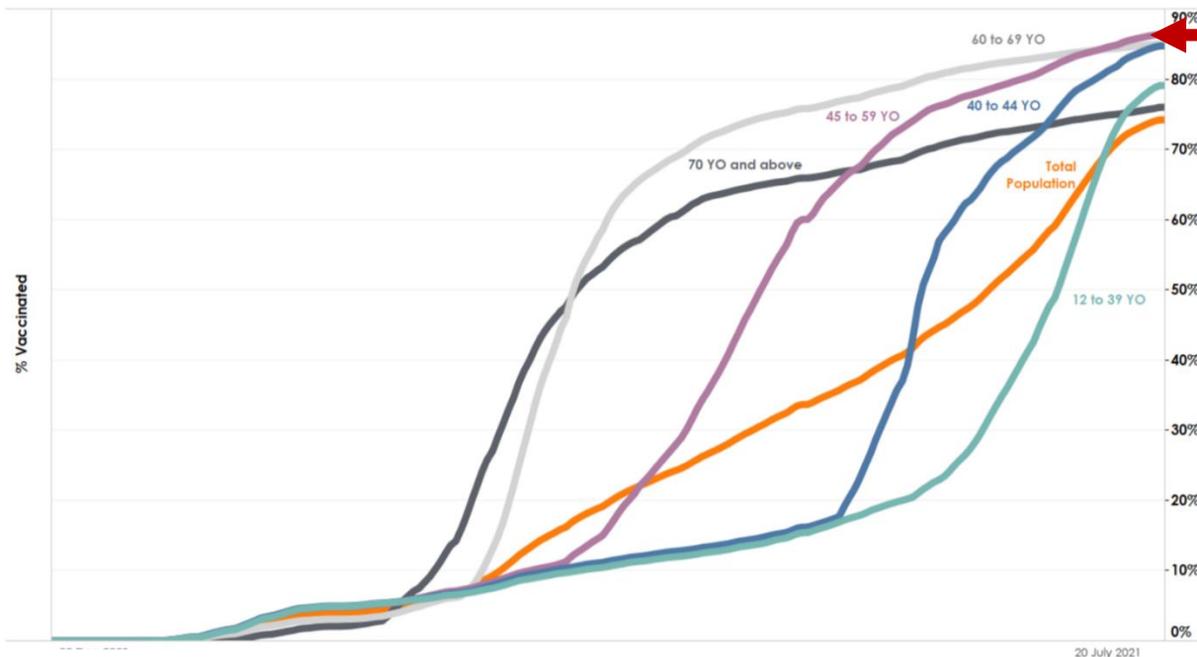
How did we persuade the population to step up for the jab?

It was easy to get started...

but a large number of vulnerable elderly held out:
Did not trust mRNA vaccines, vaccine-hesitant, anti-vaxers, unable to access vaccination centre

How did we persuade the population to step up for the job?

Figure 13: Percentage of Vaccinated Individuals who Received At Least First Dose by Age Group⁵



Source: MOH, 20 July 2021



Number of unvaccinated seniors aged 60 and above now 177,000: Ong Ye Kung

Straits Times: Jul 2021

Cheryl Tan

Figure 14: Percentage of Individuals who Completed Full Regimen⁶ of COVID-19 Vaccine by

Public education & policy

- Provide facts, Counter fake news
- Medical expert opinion
- Social & alternative media

- Facilitate access to vaccines
- Provide vaccine choices
- Vaccine differentiated measures
- Concept of living with Covid-19
- Travel bug

How did we persuade the population to step up for the job?

BEAT COVID-19
PREVENT ANOTHER WAVE
GET VACCINATED
TO PROTECT OUR COMMUNITY

We can achieve community protection when enough of us are vaccinated

Added layer of protection for ourselves

- Continue to be safe after vaccination
- Practise safe distancing
- Clean hands frequently
- Mask up

Community vaccination protects everyone, including those who cannot get vaccinated:

- People with severely weakened immune systems
- Seniors in ill health
- Pregnant women
- Children below 16
- Those with serious allergies

STAY PREPARED **TEMASEK FOUNDATION**

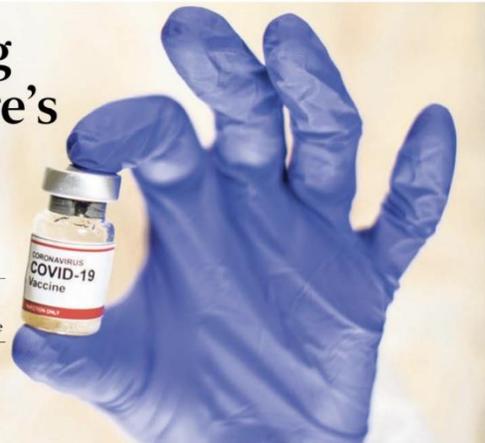
Writing & posting about vaccines...

How did we persuade the population to step up for the job?

Benjamin Seet and Ren Ee Chee
For The Straits Times

With more than 200 potential Covid-19 vaccines being developed globally, the world is inundated each day with news of the latest developments.
How to sift through the vast amount of information, to guide the pressing decisions on which vaccines to buy or use?
To put together Singapore's Covid-19 vaccine portfolio, an expert committee reviewed more than 40 vaccine candidates over the past seven months. This involved more than a hundred meetings with companies and academics, and a detailed study of thousands of pages of scientific papers, industry reports and protocols.

Choosing Singapore's Covid-19 vaccines



An expert panel reviewed over 40 vaccine candidates over 7 months to put together portfolio for S'pore

BALANCING A VACCINE PORTFOLIO

Covid-19 fuelled the development of an unprecedented number of vaccine platforms, some of which have never been approved for use in humans.
These include traditional and well-tested approaches using inactivated whole viruses or fragments of virus protein, newer technologies employing nucleic acids (DNA or RNA) and viral vectors (riding on another virus to deliver a payload of coronavirus RNA to the immune system).
From the outset, it was important to address multiple concerns. This includes which technologies make better vaccines, which are safer, which will become available earlier, and which are easier to manufacture, given that billions of doses are needed to protect the population.
There are already front runners attaining regulatory approval for conditional or emergency use. These, however, may not eventually end up as the "best-in-class" in terms of safety or efficacy.
There are also concerns of vaccine nationalism, and fears that the export of vaccines may be stopped by governments and redirected to deal with their domestic situation.
Any vaccine portfolio has to be based on robust scientific and clinical evidence, and be adequately di-

Singapore's final vaccine portfolio balances considerations of safety, efficacy, timeliness, accessibility and implementability, while mitigating risks of failure, say the writers. This required close scrutiny of what was published, reading between the lines of what was not, and making tough calls based on the best available evidence. PHOTO: REUTERS

of thousands of people need to receive the vaccine before this happens.
So there is a need to weigh the risks of infection from Covid-19 against the rare likelihood of harm from vaccination.
Another important consideration is how well the vaccine works. One way to measure this is the potency of antibody response. Antibodies are proteins produced by the body that target and neutralise the virus. It is generally thought that the higher the level of

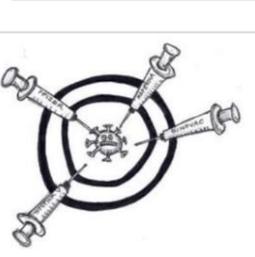
About the writers
Professor Benjamin Seet is deputy group CEO (education and research) of the National Healthcare Group and adjunct professor at the Yong Loo Lin School of Medicine, National University of Singapore.
Professor Ren Ee Chee is an immunologist and principal investigator at the Singapore Im-

munoNetwork, under the Agency for Science, Technology and Research, and adjunct associate professor at the Yong Loo Lin School of Medicine, National University of Singapore.
Both writers are members of the Ministry of Health's expert committee on Covid-19 vaccination.

Real-world evidence shows what's next in the Covid-19 fight



While good vaccine cover provides light at the end of the Covid-19 tunnel, there are still gaps that we have to mind. ST PHOTO: CHONG JUN LIANG



It is also important to find out how long the protection lasts. Many recovered Covid-19 patients continue to have antibodies in their blood even six months later.
To determine how long the vaccine protection lasts, clinical trials need to continue for at least two years.
Finally, clinical trials evaluate how well a vaccine works across different age groups, particularly the elderly, as well as patients with pre-existing diseases.
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Finally, clinical trials evaluate how well a vaccine works across different age groups, particularly the elderly, as well as patients with pre-existing diseases.

With the need to administer millions of doses, each additional step creates its own set of challenges. We also need to consider logistics.
A number of vaccines are unstable at room temperature and have to be shipped and stored at temperatures as low as minus 70 deg C. This requires the set-up of an ultra-low-temperature freezer farm to house the vaccines, and highly coordinated truck runs to distribute them to vaccination sites.

ten sub-unit vaccines, and do not make use of viruses, dead or live.
Q Is it better to get immunity from a natural infection rather than through vaccination?
A Both scenarios can produce high-quality immune protection. However, with natural infection, there is a risk of developing serious and potentially life-threatening illness, particularly for the elderly and those with pre-existing diseases like diabetes.
A small number of individuals may also develop "long Covid", where they experience chronic symptoms including shortness of breath, headaches and even damage to the heart, lungs and kidneys. This condition is not fully understood, and there is no standard treatment.
It is also unlikely for entire populations to achieve herd immunity through natural infection.
Even in hard-hit communities, studies have shown that less than 10 per cent of people show immunity against Covid-19, which means that the remainder continue to be vulnerable.

Q If I get vaccinated, does it mean that I no longer need to wear a mask?
A It is important to continue wearing a mask to protect the people around you. Being vaccinated greatly reduces your risk of developing symptomatic Covid-19 disease, as well as the chance of get-

SINGAPORE



FOR SUBSCRIBERS

Science Talk How S'pore was able to roll out Covid-19 vaccines early

Benjamin Seet for The Straits Times

VACCINE FACTS, FALLACIES AND HOAXES

While Covid-19 has infected about 65 million people worldwide, misinformation, fake news and conspiracy theories about the virus have probably spread to billions. Benjamin Seet and Ren Ee Chee clear the air about vaccines.
Q Can Covid-19 vaccines cause long-term complications?
A It is too early to tell. Some complications are so rare that they are seen only once every one million to two million vaccinations, sometimes as long as one to two years later.

To date, only about 200,000 people have taken part in late-stage clinical trials for different Covid-19 vaccines worldwide, with the longest follow-up not exceeding four months. So it is still too early to draw firm conclusions.
What we do know is that major vaccine companies have been very transparent with their data, and have taken the unprecedented step of publishing their clinical trial protocols and interim results.
These are submitted to health regulators who assess the data with

tough guidelines also applied to other vaccines.
There are no shortcuts when it comes to establishing the safety of a vaccine. We should expect no less with Covid-19 vaccines, despite their compressed development timelines.
Q Can an RNA vaccine change my DNA?
A There are some who claim that ribonucleic acid (RNA) vaccines can manipulate and change human deoxyribonucleic acid or DNA, result-

ing in a genetically modified human.
Biologically, it just does not work that way. DNA uses one set of molecules for its genetic code, while RNA is made up of a different set of molecules.
The genetic information flow is one-way: DNA contains information that cells use to make messenger RNA (mRNA), which in turn provides a template to assemble proteins the body needs. The mRNA in Covid-19 vaccines cannot change human DNA.

Besides, the half-life of mRNA vaccines is very short. Once injected, it is quickly taken up by the body's cells and broken down after 48 hours. The influenza virus is an RNA virus. When you catch the flu, you are in fact getting a massive dose of virus RNA. It can make you sick, but it does not change your DNA.
Q Does Covid-19 vaccination inject live viruses into your body?
A There are different types of Covid-19 vaccines.
One common vaccine is made up

of dead viruses that have been chemically inactivated and are no longer infectious. These include the vaccines produced by Sinovac, Sinopharm and Valveva.
Another type of vaccine makes use of a common virus, called adenovirus, to transport a small fragment of SARS-CoV-2 gene into cells.
Such viral vectors are weakened so that they pose little risk of causing illness compared with a natural infection. Examples of vaccines that employ adenoviruses include the ones produced by AstraZeneca, Johnson & Johnson and CanSino, and the Russian Sputnik V vaccine.
Other leading programmes from Pfizer/BioNTech, Moderna, Novavax and Sanofi use biotechnology to manufacture either RNA or pro-

teins that can produce a protective immune response.
In more sensational versions of this hoax, there are claims that 5G networks and artificial intelligence will send signals to these microchips to control human behaviour.
While we are unable to establish the origins of this falsehood, it predates Covid-19 by almost a decade. Hoaxers tend to look for old stories and adapt them to the current situation to make the lies seem more convincing.
What we know is that certain vaccines contain metal salts, typically aluminium phosphate or aluminium hydroxide, to enhance the immune response. Such adjuvants - added to vaccines to improve immune response - have been used safely in vaccines for more than 60 years.
Vaccine adjuvants cannot be tracked or controlled by 5G.
In fact, mobile phones make better tracking devices that already control human behaviour.



Writing & posting about vaccines...

How did we persuade the population to step up for the jab?

Going viral...



David Lye

7 June 2021 at 01:02 · 🌐

"Why fake science and anti-vaccine groups are dangerous in a pandemic"

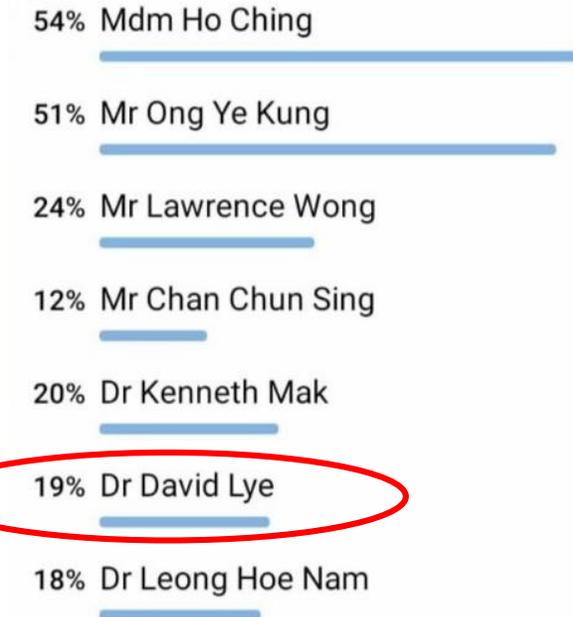
This public post is by me, an infectious disease specialist. You can find it on my Facebook. No need to contact me to check 😊. After the unintended attention from the "social bubble" Facebook post, I have stayed low. But I must now correct misinformation on COVID vaccination.

Please feel free to share widely to inform the Singapore public (eg high school, JC, university, medical classmates, family, work, hobby or religious chat groups on WhatsApp or Telegram; social media eg Facebook or Twitter).

Healing The Divide Channel

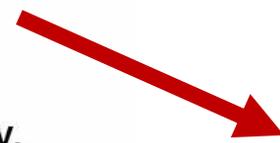
We are doing a survey on who to sue next? This poll would guide us who to bring to Court next after we brought SPH to Court earlier.

Anonymous Poll



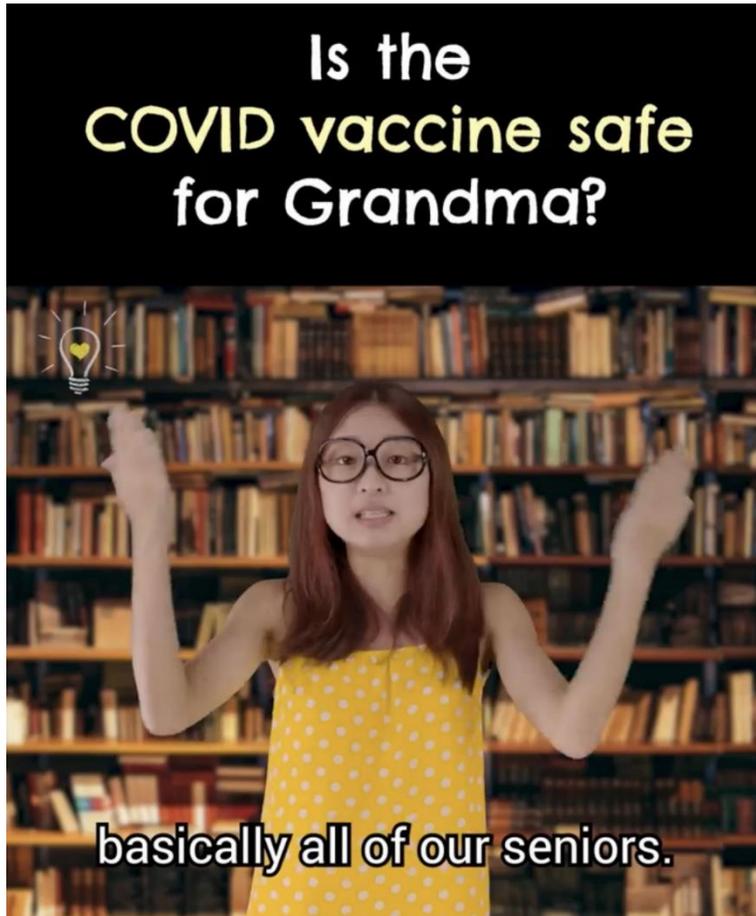
631 votes

👁 2.6K 5:51 PM



Working with social media influencers

How did we persuade the population to step up for the job?

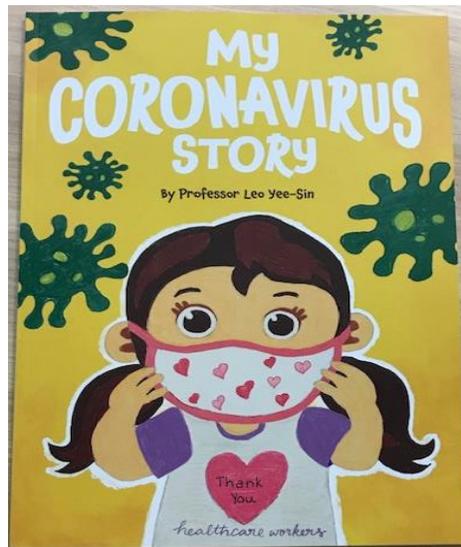


WITH A BIG THANK YOU TO
DR BEN SEET AND DR DANNY SOON
FOR FACT-CHECKING THIS PRODUCTION.



Communicating through art

How did we persuade the population to step up for the job?

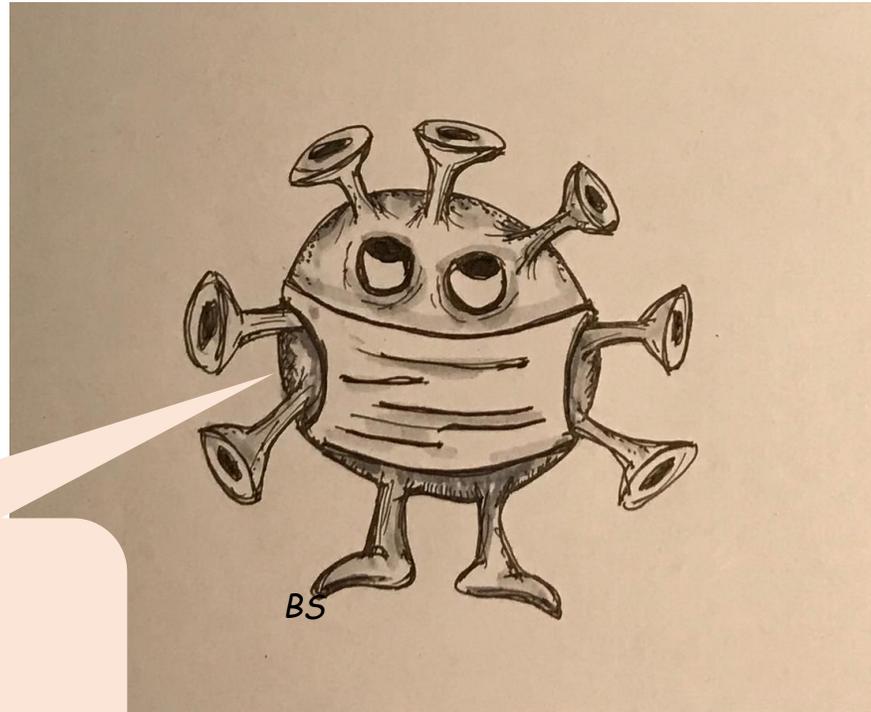


“Paid a visit to the Heroes Of Our Time exhibition at Ion Orchard this evening. Found a familiar scene! Fitting, with the recent vaccine news!”

MCI, Mar 2021

Jabbing SG

And finally...

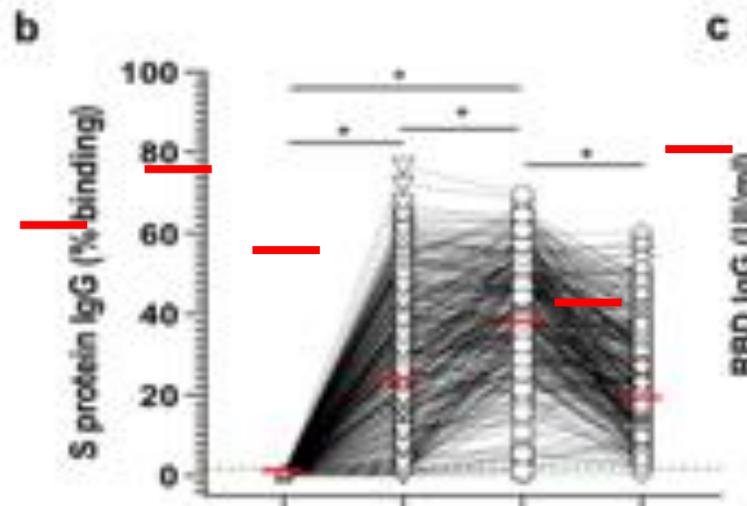
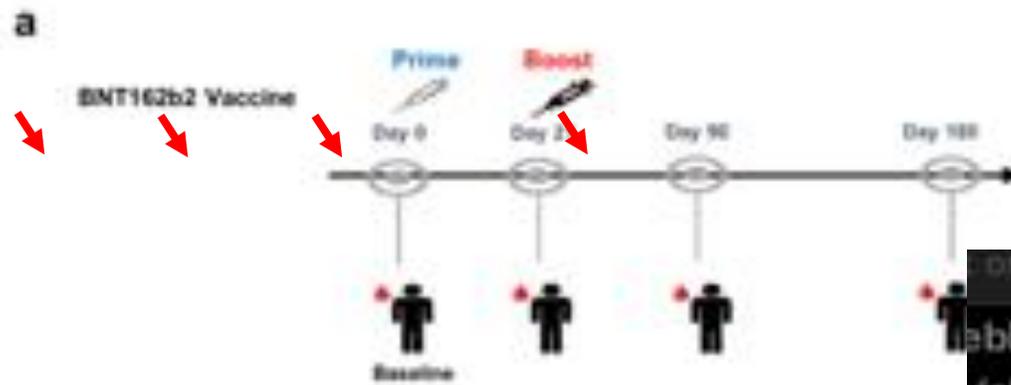


What are we
planning next?

What's next?

- Waning immunity: Boosters & dosing intervals

BNT 162b2 vaccine



c



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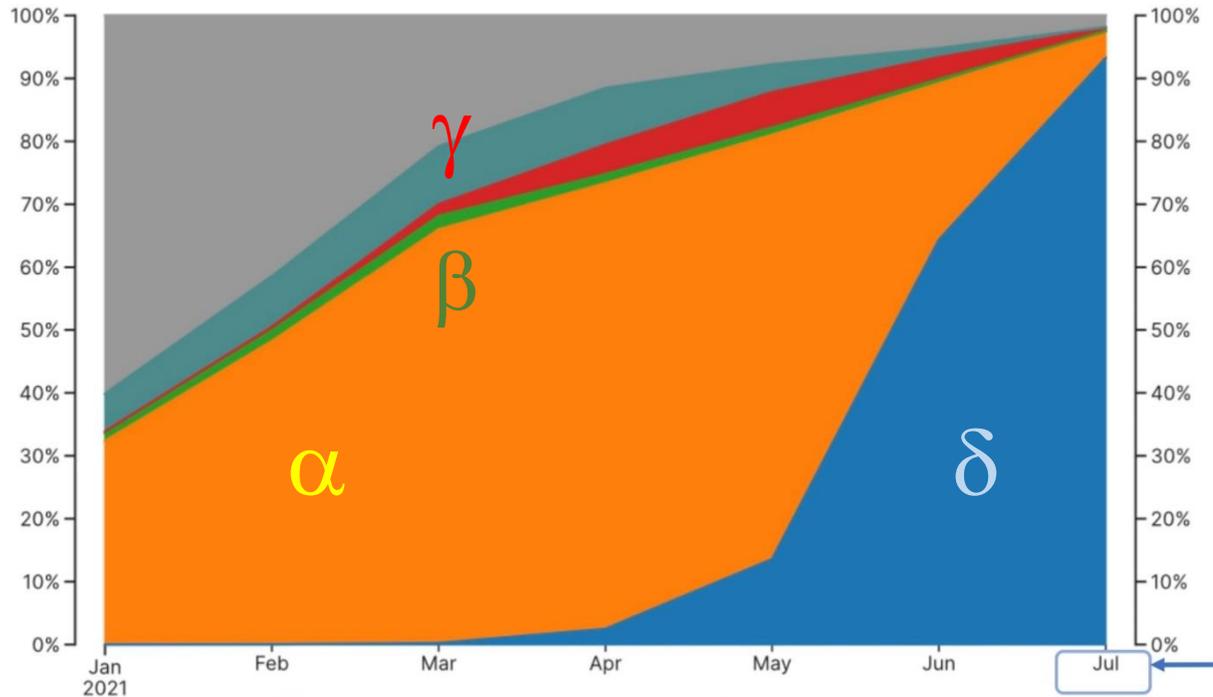


Renia et al, Nature Communications, July 2022

Dealing with variants

3

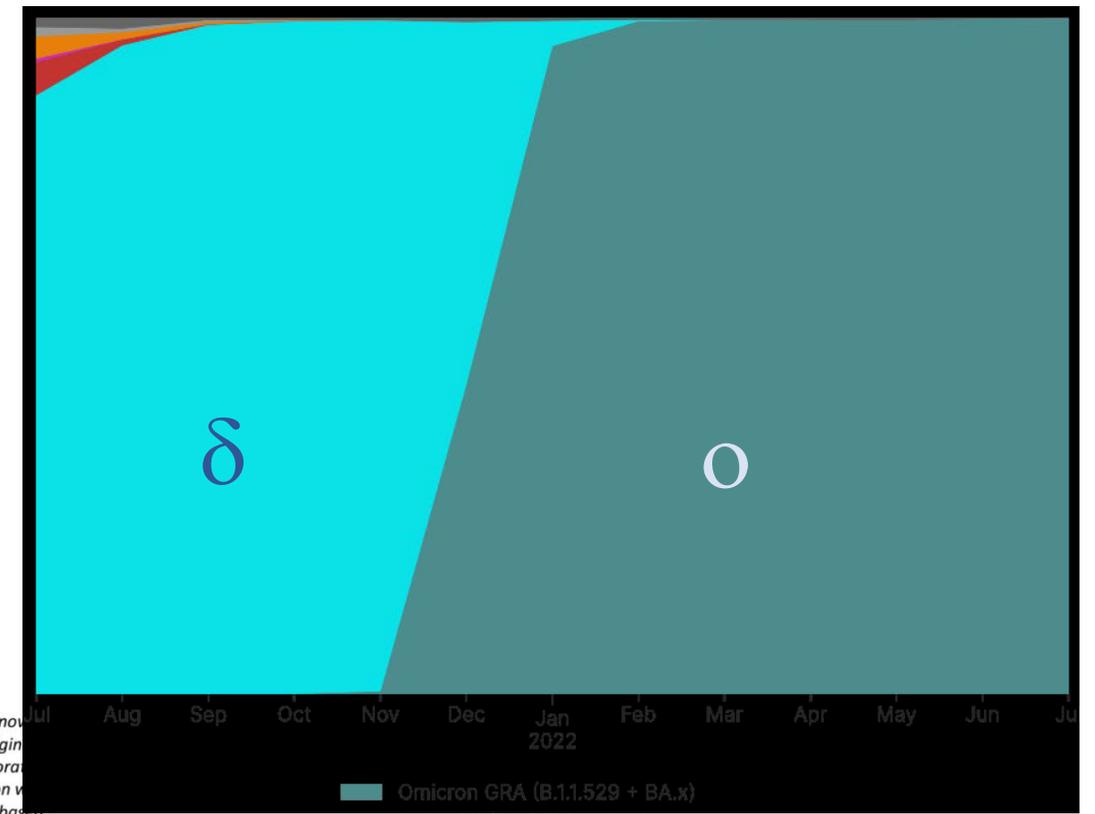
July 2021



- VOC Delta G/478K.V1 (B.1.617.2+AY.1+AY.2) first detected in India
- VOC Alpha B.1.1.7 (GRY/501Y.V1) first detected in United Kingdom
- VOC Beta GH/501Y.V2 (B.1.351) first detected in South Africa
- VOC Gamma GR/501Y.V3 (P.1) first detected in Brazil/Japan
- Variants of Interest
- Others

We gratefully acknowledge the authors from Original Publications for Submitting laboratory sequence data on which this analysis is based.

July 2022



Omicron GRA (B.1.1.529 + BA.x)



What are we planning next?

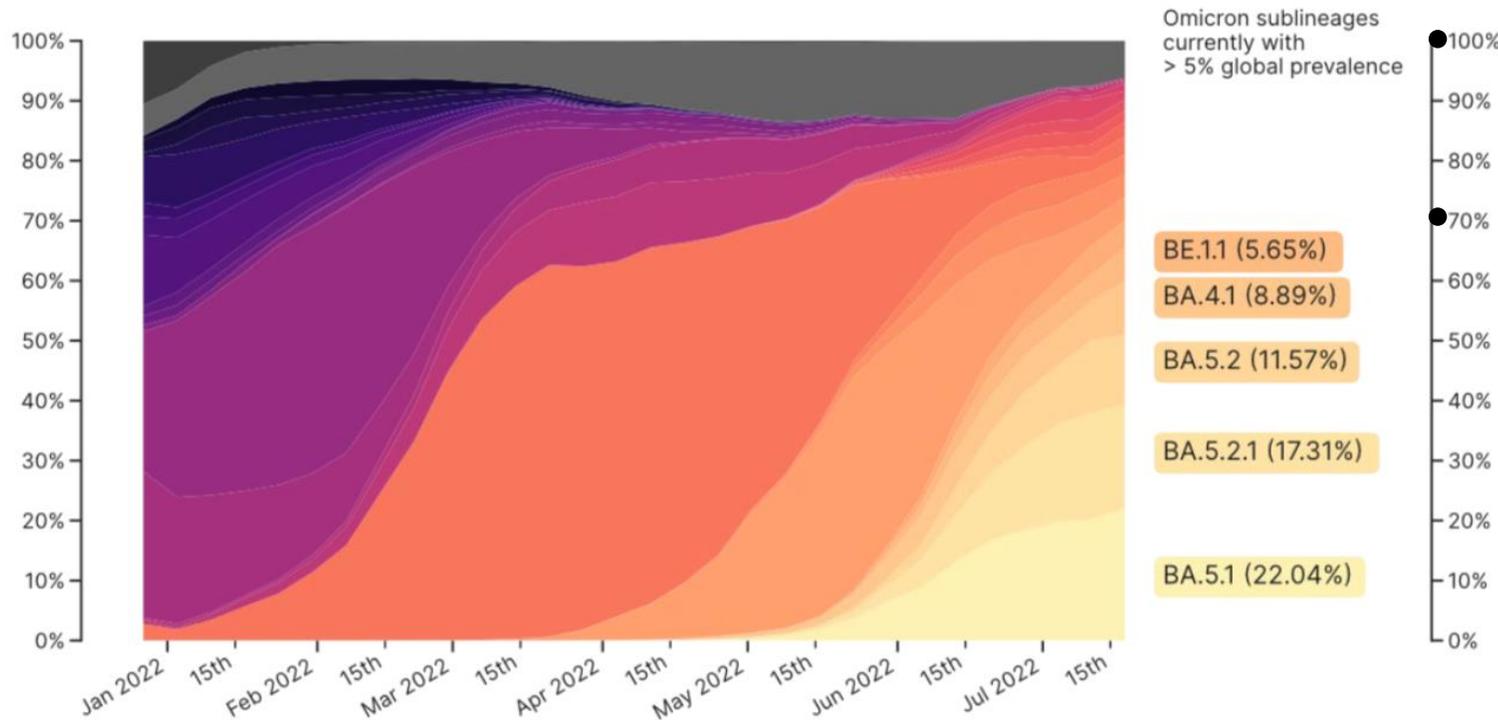
Omicron variant sublineages

26 July 2022

See <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> for variant information and definitions.

by BII/GIS, A*STAR Singapore

Timecourse of Omicron variant sublineage distribution
2022-07-26



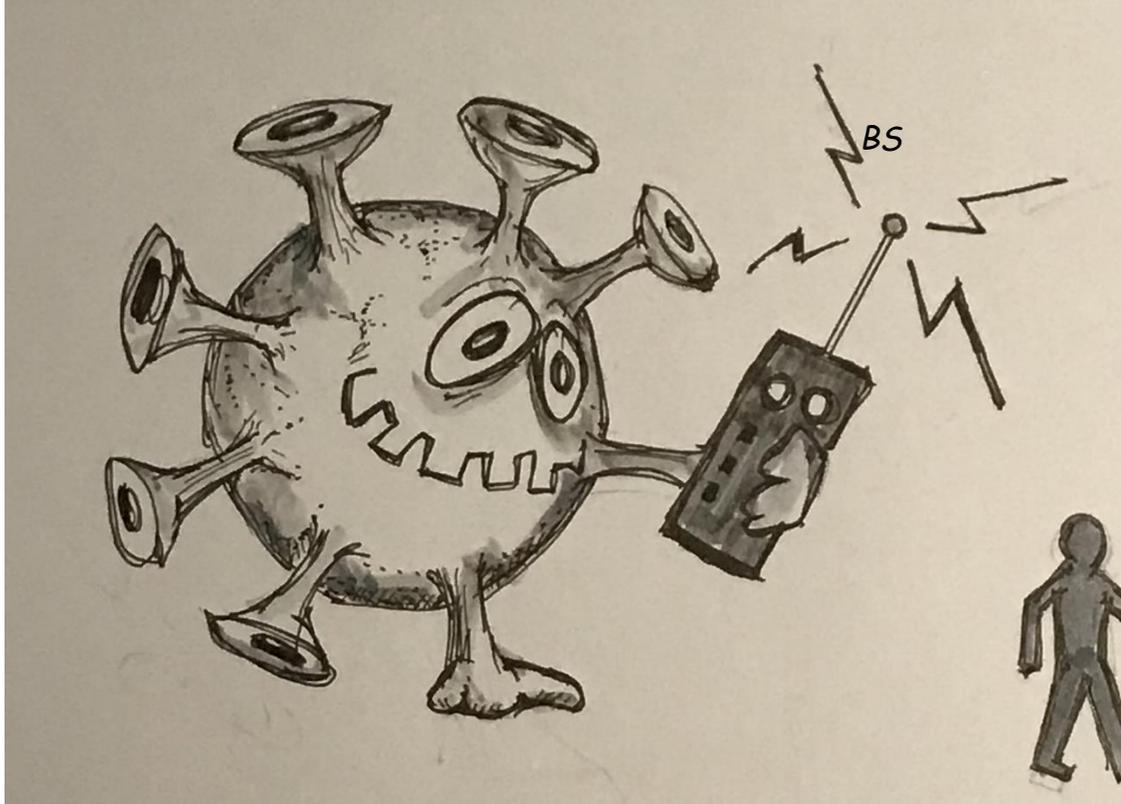
- | | | | | |
|-----------|--------|----------|-----------|--------------------------|
| BA.5.1 | BA.4 | BA.5.3.1 | BA.2.10 | BA.1.15 |
| BA.5.2.1 | BA.5.5 | BA.5.1.1 | BA.2.1 | BA.1.1.2 |
| BA.5.2 | BA.2 | BA.2.9 | BA.1.20 | BA.1.1.18 |
| BA.4.1 | BA.4.6 | BA.2.3 | BA.1.18 | BA.1.1.1 |
| BE.1.1 | BA.5.6 | BA.1 | BA.1.17.2 | Omicron sublineages < 1% |
| BA.5 | BE.1 | BA.1.1 | BA.1.17 | Other lineages |
| BA.2.12.1 | BF.5 | BA.2.23 | BA.1.15.1 | |

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.

Transmissibility
Vaccine
Immune evasion & vaccine breakthrough
"Genetic fitness"

What are we planning next?

Next gen vaccines



- **Bivalent vaccines**
Moderna, Pfizer-BioNtech, Novavax, Sanofi
- **Oral & nasal administered vaccines**
CanSino, Vaxart, Oramed
- **New vaccine formats, including pan-Corona & pan-sarbecoviruses**
Codagenix, Girtstone, Icosavax, VBI, EnGeneIC
- **Local efforts**
Arcturus, ACM Biolabs, Duke-NUS

What are we
planning next?

Building local capacity

From R&D to filling vials

Vaccine Development

Clinical Trials

Manufacturing

Fill & Finish

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New R&D programme to deal with future public health crises unveiled; Dorscon framework to be beefed up

FRI, MAR 05, 2021 - 5:08 PM | UPDATED FRI, MAR 05, 2021 - 5:13 PM

SHARON SEE | sharons@sph.com.sg | @SharonSeeBT

SINGAPORE is developing a national programme to boost its research and development (R&D) capabilities in anticipation of future public health crises, Senior Minister of State Janil Puthucheary said on Friday.

vaccine hub
By Fraiser Kansteiner
Dec 7, 2021 12:00am

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Press Release

GERMAN

BioNTech to Establish Regional Headquarters for South East Asia and First mRNA Manufacturing Facility in Singapore

SANOFI

Press Release

Source: Sanofi (EURONEXT: SAN) (NASDAQ: SNO)

Sanofi to invest in a leading-edge production site in Singapore; continues to strengthen its vaccines manufacturing capacities

- Sanofi will invest €400 million over five years to create a unique vaccine production site in Singapore, pushing the boundaries of operations through cutting edge manufacturing and digital technologies.
- The new site will provide Sanofi with the ability to produce innovative vaccines on a massive scale for Asia, and quickly respond to future

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Thermo Fisher will add 2 new filling lines to global expansion plans with \$130M Singapore plant

By Kyle Blankenship • Oct 15, 2020 02:57am

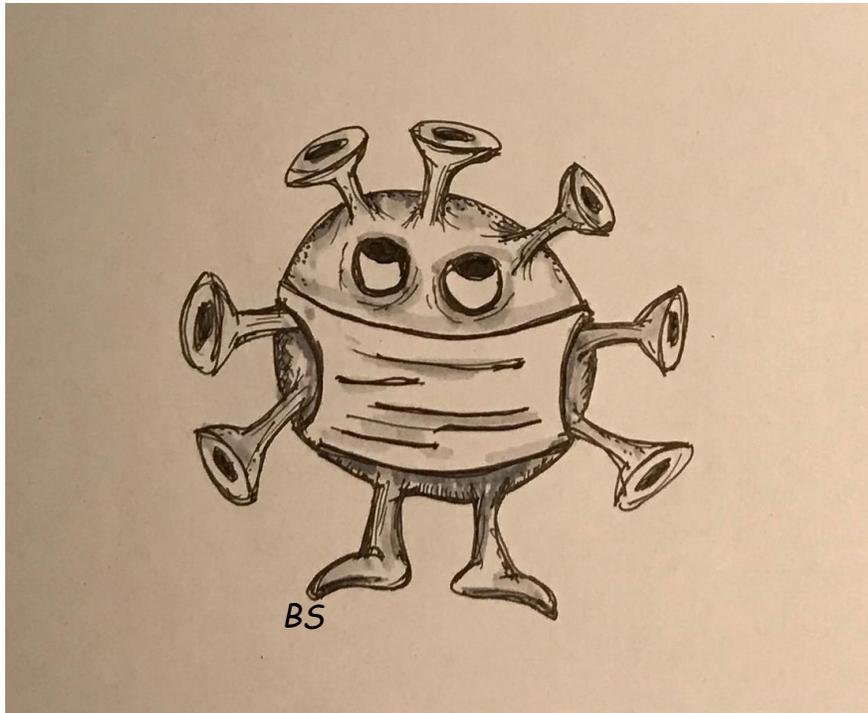
aseptic filling CDMO expansion manufacturing

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What are we planning next?

Jabbing SG

Distilling the key lessons learnt...



1. In times of uncertainty, be clear of the mission
2. Task organize for the job at hand
3. Short-cut decision making
4. Maintain flexibility & fluidity
5. Keep sight of the next lap



Core Group & Secretariat of TxVax



Thank you for your attention
and do go for your jab when it is due

