INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

March 2021

Something Good Is Coming

Comic Corner
Building our path into understanding behavior, and then (hopefully) change it!

Science Corner
COVID-19 Vaccination Roll-Out: The World's Effort To Weaken The King With The Jabs

Sports & Lifestyle
COVID, I'm Back!

APRIL 2021

NATIONAL INSTITUTE OF HEALTH RESEARCH AND DEVELOPMENT
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2021

INA-RESPOND newsletter

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FEATURES

INA-RESPOND

Newsletter

TRIPOD & PROACTIVE Study Updates

By: Eka Windari R., Lois E. Bang, Melinda Setiyaningrum, Venty Muliana Sari

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Per 08 March 2021, the TRIPOD study's total ongoing participants are 3 out of 490 enrolled participants. From those three ongoing participants, they are waiting for a 6-month post-treatment visit. Two hundred and fifty-one participants have completed the study, while 236 participants are terminated early (including death). Therefore, there are still 0.61 % participants from the total enrolled participants in the follow-up status. From the uploaded CRFs, all participants from sites 520, 570, and 590 have completed the study. However, 3 participants from site 580 (RSUP dr. Sardjito Jogjakarta) still need to be followed up.

The database Quality assurance (except for TB Treatment pages) was conducted for sites 520, 570, and 590 from 24 November – 22 December 2020.

The Site Close-out Visit (SCV) was conducted for site 520 on 30 November – 1 December 2020, site 570 on 15-16 December 2020, and site 590 on 19-20 January 2021.

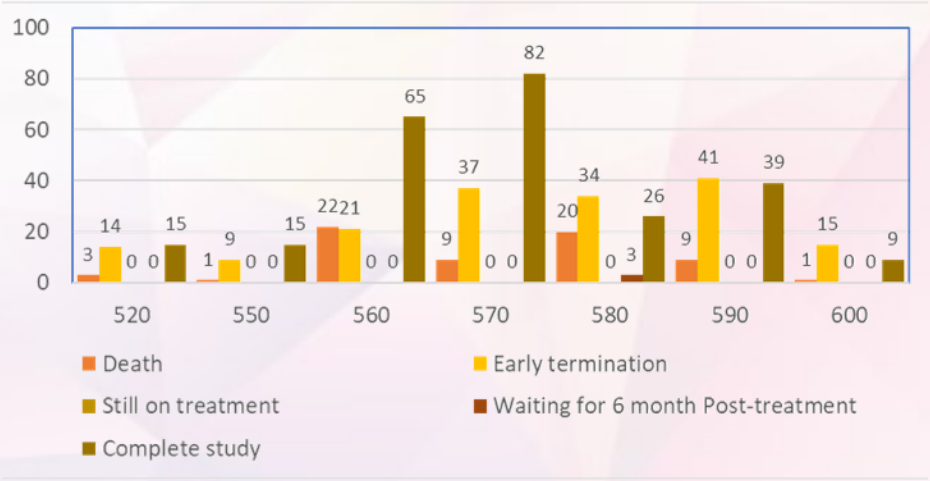

Figure 1. Participant status per site based on uploaded CRF per 08 March 2021

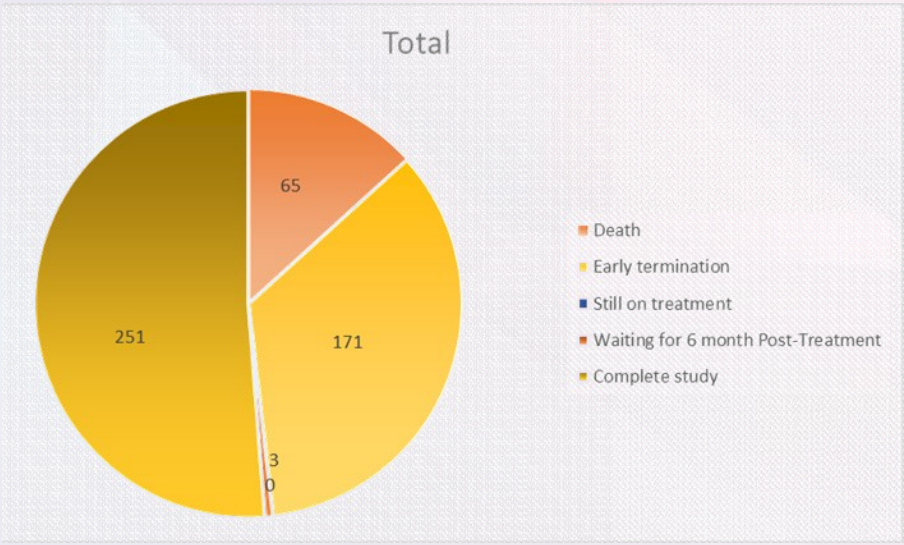

Figure 2. Total participant status based on uploaded CRF per 08 March 2021

AWAITING CULTURE AND DST RESULT

The result for baseline culture and DST results from all sites are complete.

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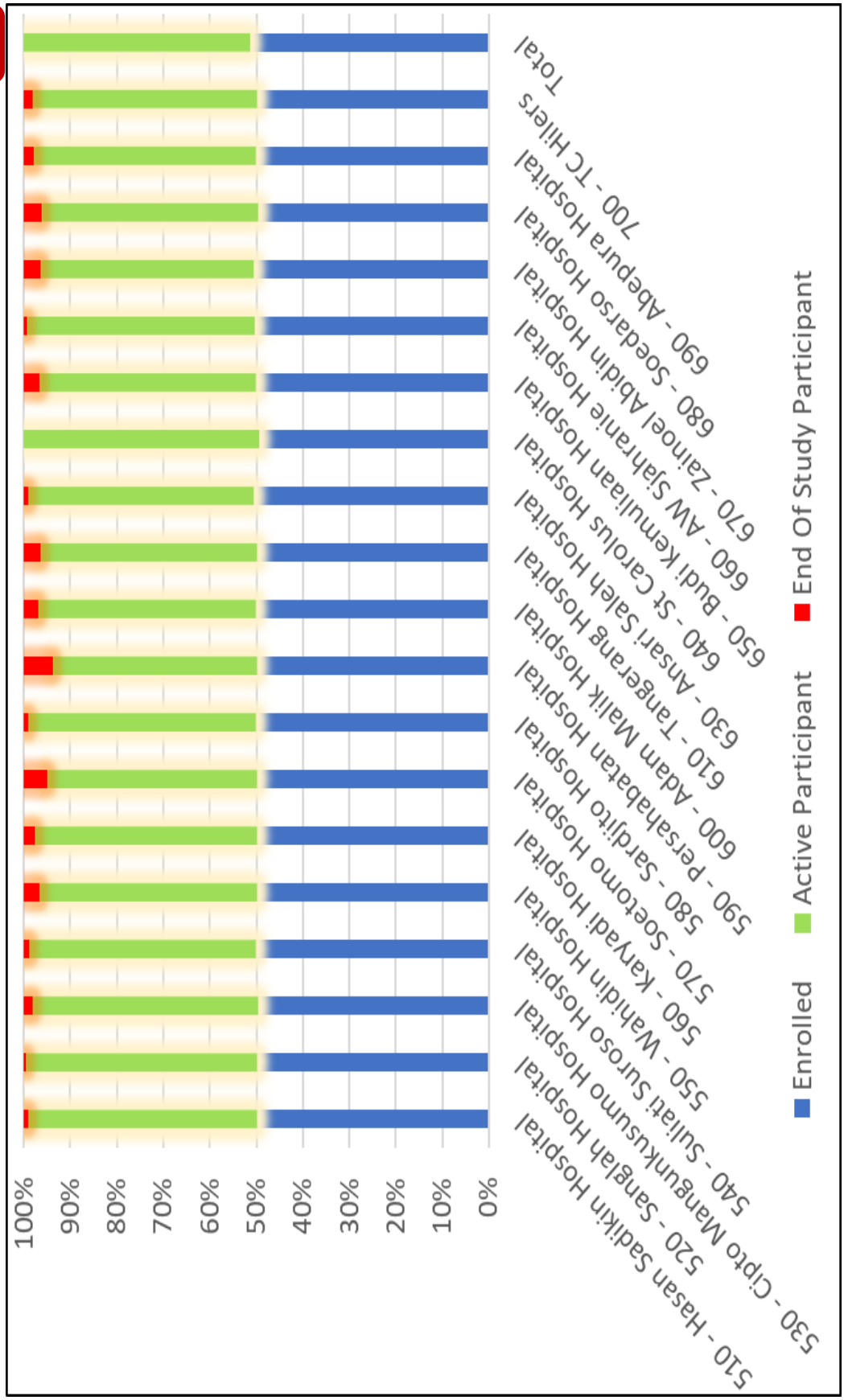
There are three subjects from two sites that have completed the last Follow Up Month 36; one subject at Site 610 (Tangerang hospital) and two subjects at Site 600 (Adam Malik Hospital, Medan) based on the latest data per 26 February 2021.

According to the data on 27 February 2021, from 4,336 subjects enrolled, 209 subjects are End of Study due to some reasons: 161 subjects' death, 22 subjects move away to the city which site PROACTIVE is not available, 21 subjects withdrew, and five subjects with negative HIV test result. To date, there are 4,134 active subjects in this study. Below is the Chart of Enrolled and Active Participants by Sites:



INA-RESPOND Newsletter

MONTHLY WEBINAR SERIES
ONE YEAR LIVING WITH SARS-COV-2: PROGRESS ON PREVENTION AND TREATMENT

By: Yan Mardian, Adhella Menur, Herman Kosasih, and the Webinar Committee

I. BACKGROUND

COVID-19 pandemic caused by the new beta-coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has been around for one year. It has proven to be one of the greatest challenges modern medicine has ever faced. The COVID-19 symptoms started in December 2019 with four atypical pneumonia cases in Wuhan, China, connected to a local seafood market, the Huanan Seafood Market. The disease heavily affects the world, with a total number of cases and deaths reaching 100 million and 2 million, respectively, as of the end of January 2021. Previous knowledge of its coronavirus outbreak predecessors (SARS-CoV and MERS-CoV) is not enough for the authorities, clinicians, and researchers to handle this new virus. Therefore, it is crucial to understand the virus's unique characteristics and impact on the human body. This is very important for choosing the ideal treatment, vaccine, and control measure, and they may help prevent future pandemics.

SARS-CoV-2 is a new virus, and we are still learning how it behaves. The virus originally came from a wild animal, most likely, a bat. It then jumped into humans via an animal host, probably pangolin. Later, we found that humans could infect other animals like mink, and then the virus spilled back to humans with some genetic changes. The main transmission mode is via respiratory droplets; however, transmission via air and contact (fomite transmission) is still debatable. The pathogenesis of SARS-CoV-2 is not clearly understood yet. The virus is mainly using angiotensin-converting enzyme 2 (ACE2) receptor to invade the human cells. However, a recent discovery has found that entry co-factors on the surface of host cells, such as serine protease TMPRSS2, protease furin, and a protein called the neuropilin-1 (NRP1), can increase SARS-CoV-2 infectivity and may become potential targets for future therapeutics. The mystery continues as to how SARS-CoV-2 interacts with different organs, how it causes various clinical features and severity, and how long the survivor will retain their acquired immune-memory response to the virus. The involvement of overactive immune response -the so-called cytokine storm- and hypercoagulability is found in severe cases, but the exact mechanism is still unknown.

The trials to find an effective yet feasible treatment such as re-purposed drugs to block the virus, anti-inflammatory agents, passive immune-therapy agents, and other treatments (e.g., immune-modulators, anticoagulants, vitamin and mineral supplements, and respiratory support devices) are needed. However, there has not been a cure for COVID-19 yet. One re-purposed antiviral Remdesivir, which the FDA has approved, only suggests a modest to no benefit for patients. The passive immune-therapy attempts have successfully fought against similar COVID-19 viruses such as SARS-CoV and MERS-CoV to reduce the viral load and disease mortality. Currently the main passive immune-therapy methods that have been used are convalescence plasma transfusion from COVID-19 survivor, hyperimmune intravenous immunoglobulin, and monoclonal antibody candidates. The benefit from passive immune-therapy is still under investigation. However, it seems that it is performed best in early COVID-19 disease progression.

The worldwide endeavor to create a safe and effective COVID-19 vaccine in less than one year is very historical in humankind's lifetime. A handful of vaccines now have been authorized for use worldwide; many more remain in development. More than 82.5 million doses in 59 countries have been administered, and scientists must prepare to face the outcome. The Antibody dependent-enhancement (ADE) issue and anecdotal shreds of evidence of some viral genomic mutations might influence those vaccine candidates' efficacy and safety. Three new worrying variants have been identified from United Kingdom (B.1.1.7), South Africa (B.1351), and Brazil (P.1) with multiple spike mutations.

They appear to be more infectious and might have the immune-escape ability. Although the variants are observed not to affect disease severity, the high transmission will threaten medical care capability and give the virus higher chances to develop further mutations. Over 380,000 virus genomes were sequenced in just one year to help scientists get real-time data about the evolution and work together to solve the problem.

While the are no powerful drugs and approved vaccines to combat this disease, some public health protocols such as wearing a mask and physical distancing still seem to become the best approaches against the pandemic. Experience sharing from other countries that have successfully controlled this pandemic is also very important for public health learning. Genomic surveillance needs to be optimized as a tool that helps drive public-health decisions quickly. Surveillance needs to be widespread, standardized and embedded in national pandemic-prevention programs.

While these on-going uncertainties in every aspect of COVID-19 are unavoidable, however, the explosive information about this virus must be filtered according to evidence-based medicine principles to avoid pseudoscience and fraud. In answering those challenges, the Indonesia Research Partnership on Infectious Diseases (INA-RESPOND) is planning to conduct a monthly webinar about COVID-19. INA-RESPOND is a multi-center clinical research network for infectious disease managed by National Institute of Health Research and Development (Indonesia) in collaboration with the National Institute of Allergy and Infectious Diseases (United States) at designated Indonesian medical faculties and their teaching hospitals. As a network research organization focused on infectious disease, we also have a responsibility to provide comprehensive updates and recent evidence of COVID-19 to clinicians, researchers, and public health authorities to help tackle this disease.

II. OBJECTIVE

The purpose of the INA-RESPOND COVID-19 Webinar is to:

1. Provide current updates on COVID-19 epidemiology, virology, pathogenesis, treatment, and vaccine development
2. Discuss strategies and experiences from other countries that regarded successfully controlling the COVID-19 pandemic.

III. AGENDA

The INA-RESPOND COVID-19 Webinar will be held once a month for four months, starting from April to July 2021.

IV. AUDIENCE

- National Institute of Health Research and Development (NIHRD), Ministry of Health, Indonesia
- INA RESPOND Study Site Team
- INA-RESPOND Secretariat
- Clinicians
- Researchers
- General participants

V. REGISTRATION

The First Webinar series will be held on Saturday, April 10, 2021 at 07.00-11.00 WIB. This webinar is supported by INA-RESPOND and partners and is free of charge for all participants. Participants will receive *IDI SKP* and an electronic certificate. For further information, please contact Ms. Yayu at 021-420 8693 ext.112

INA-RESPOND Newsletter

COVID-19 VACCINATION ROLL-OUT: THE WORLD'S EFFORT TO WEAKEN THE KING WITH THE JABS

By: Adhella Menur

March 2020, a year ago, the world health organization (WHO) declared the COVID-19 as a pandemic, with SARS-CoV-2 as the most treasured virus to be studied. The novel beta-coronavirus with its crown is becoming the ruthless king in the world. Until the end of March 2021, the virus already infected 124 million people, with death cases reached 2.7 million. The public health authorities and almost all scientists worldwide worked together to learn the full characteristics and find the effective weapon to defeat it. Those struggles also became the most comprehensive and the fastest breakthroughs in the history of science. Within a week of Wuhan unexplained pneumonia cases formally reported, China scientists used metagenomic sequencing to identify the causative pathogen. Six genomes were shared publicly before mid-January 2020, allowing the rapid research of diagnostic assays and vaccine development strategies. Carvalho et al., in their article about 12 months of COVID-19 immunological insights, underscore the birth of the 'team science' approach, which are the collaboration of immunologists, virologists, physicians, nurses, epidemiologists, biostatisticians, and computer scientists for the rapid discovery of key aspects of the SARS-CoV-2 immune response.[1,2,3]

COVID-19 vaccine race becomes the sexiest field as finding the safe and effective vaccine to stop the pandemic is an amenable idea. Traditionally, we need more than ten years to develop a vaccine for a disease. Favorably, the scientists can hasten the timeline using the knowledge about SARS-CoV-2 predecessors (SARS-CoV-1 and MERS-CoV) with the latest technologies. About 11 months after the publication of SARS-CoV-2 genomic sequencing, United Kingdom confidently administered the Pfizer-BioNTech vaccine to their people under emergency use authorization after optimist interim results. Until Mar 22, 2021, there are 99 vaccine candidates in 274 trials, with 13 vaccines have already approved by at least one country. It might be a little confusing to several people questioning why we must support every vaccine candidate. The answer is quite simple: we want to ensure that the public health authorities will distribute the effective vaccine equally, and everyone can get the shots. Nowadays, more than 468 million doses from various platforms have been administered across 135 countries. However, global immunity still faraway to achieve with the current vaccination pace (up to 3.1% of the global population already vaccinated at the end of March 2021). As new vaccines by many manufacturers are coming to the real world, we hope it will accelerate the pace.[4,5]

The vaccine roll-out euphoria is not long last as we should face the real-world data experience. It should keep in mind that the definition of efficacy is an intervention's performance under an ideal and controlled setting (e.g., randomized controlled trial). The real challenge is to assess the effectiveness of the vaccine in the real-world. The public health authorities and scientists should continue the vaccine research: assess how much the vaccine impact public health parameters, the vaccine-immunogenicity (evaluate the protective quality and quantity of the neutralizing

Vaccine	Platform	Progress	Update
Anhui Zhifei Longcom: RBD-Dimer/ ZF2001	Protein Subunit	• Approved in China and Uzbekistan • Five trials in 5 countries	• Ongoing phase 3 in China, Ecuador, Indonesia, Pakistan, and Uzbekistan with a total enrolment of 29,000 • Efficacy not reported yet, no information related to new variants
Bharat Biotech: Covaxin/ BBV152	Whole inactivated viral	• Approved in India, Iran, Mauritius, Nepal, and Zimbabwe • Five trials in 1 country	• Ongoing phase 3 in India with a total enrolment of 25,800 • Latest efficacy report 80.6%, no information related to new variants
CanSino: Ad5-nCoV/ Convidecia	Non-replicating viral vector	• Approved in China, Hungary, Mexico, and Pakistan • Six trials in 6 countries	• Ongoing phase 3 in Argentina, Chile, Mexico, Pakistan, and Russia with a total enrolment of 40,500 • Latest efficacy report 65.28%, no information related to new variants

Table 1. Update on 13 vaccines which have already approved by at least one country[4,6]

FBRI/ EpiVacCorona	Protein Subunit	• Approved in Russia • 3 trials in 1 country	• Ongoing phase 3 in Russia with a total enrolment of 3,000 • Efficacy not reported yet, no information related to new variants • The company claimed that the immune response from EpiVacCorona lasted for approximately a year (unpublished data)
Gamaleya: Sputnik V/ Gam-COVID-Vac	Non-replicating viral vector	• Approved in 55 countries • 19 trials in 6 countries	• Ongoing phase 3 in Belarus, India, Russia, United Arab Emirates, and Venezuela with a total enrolment of 50,700 • Latest efficacy report 91,6%, no information related to new variants • Trial expansion on a single-dose version (Sputnik Light) and collaborate with Oxford- AstraZeneca (vaccines combination to increase the efficacy)
Janssen (Johnson& Johnson)/ Ad26.COV2.S/ Ad26COVS1/ JNJ-78436735	Non-replicating viral vector	• WHO emergency use listing • Approved in 35 countries • Seven trials in 17 countries	• Ongoing phase 3 in Argentina, Belgium, Brazil, Chile, Colombia, France, Germany, Mexico, Philippines, Per, South Africa, Spain, Ukraine, UK, and the USA with a total enrolment of 90,000 • Latest efficacy report 72% in the US, 64% in South Africa, and 61% in Latin America • Trial expansion for children, pregnant woman, and trial of two doses to increase the efficacy
Moderna/ mRNA-1273	mRNA	• Approved in 41 countries • Ten trials in 2 countries	• Ongoing phase 3 in Canada and USA with a total enrolment of 33,750 • The latest efficacy report 94,1%, reduced B.1.351 variant à ongoing study to develop B.1.351-specific booster • Trial expansion for babies, young children, and adolescents
Oxford/ AstraZeneca/ AZD122	Non-replicating viral vector	• WHO emergency use listing • Africa Regulatory Taskforce endorsed • Approved in 81 countries • 22 trials in 13 countries	• Ongoing phase 3 in Argentina, Brazil, Chile, Colombia, India, Peru, Russia, UK, and the USA with a total enrolment of 64,450 • Latest efficacy 69-74%, reduced in B.1.1.7 and B.1.351 variants à working on a new version of the vaccine tailored to B.1.351 variant • Trial expansion on children and collaboration with Sputnik V (vaccines combination to increase the efficacy)
Pfizer-BioNTech/ BNT162b2/ Tozinameran/ Comirnaty	mRNA	• WHO emergency use listing • Approved in 79 countries • 12 trials in 9 countries	• Ongoing phase 3 in Argentina, Brazil, Germany, South Africa, Turkey, and the USA with a total enrolment of 49,278 • Latest efficacy report 95%, reduced in B.1.1.7 and B.1.351 variants à ongoing study to develop B.1.351-specific booster • Trial expansion for age 12-15 y.o, HIV, HBV, and HCV individual (trial plan for age 5-18 y.o and pregnant woman)
Serum Institute of India-Covishield	Non-replicating viral vector	• WHO emergency use listing • Approved in 30 countries • Two trials in 1 country	• Ongoing phase 3 in India with a total enrolment of 1,600 • It is the same formulation as the Oxford/ AstraZeneca vaccine

Sinovac: Coronavac	Whole inactivated viral	• Approved in 30 countries • 13 trials in 6 countries	• Ongoing phase 3 in Brazil, Chile, China, Indonesia, Philippines, and Turkey with a total enrolment of 31,372 • The latest efficacy report 50.38% in Brazil, 65% in Indonesia, and 83.5% in Turkey. The company claimed that it offers a broad spectrum of protection for SARS-CoV-2 variants (unpublished data)
Sinopharm (Beijing)/ BBIBP-CorV	Whole inactivated viral	• Approved in 27 countries • Six trials in 7 countries	• Ongoing phase 3 Argentina, Bahrain, Egypt, Jordan, Peru, and United Arab Emirates with a total enrolment of 69,000 • Latest efficacy report 70.34%, the company claimed that the antibody response was only modestly weaker against B.1.351 (unpublished data)
Sinopharm (Wuhan)/ Inactivated (Vero Cells)	Whole inactivated viral	• Approved in China and the United Arab Emirates • Six trials in 7 coun-	• Ongoing phase 3 Bahrain, Egypt, Jordan, Morocco, Peru, and United Arab Emirates with a total enrolment of 66,600 • Latest efficacy report 72.51%, no information related to new variants

antibodies, T-cell activity, and how long the durability of the vaccine-immune response), long-run safety evaluation, and monitor the impact of new variants in vaccine efficacy.

For COVID-19, which presents with a range of the clinical spectrum, endpoints' measures can include reductions in asymptomatic infections, symptomatic infection, hospitalizations, and deaths. For each of these endpoints, efficacy is determined by comparing a group of people who received the vaccine with a group who receive a placebo. However, estimating the real-world effectiveness of vaccinations is complicated. The first real-world data of vaccine impact is coming from Israel after mass vaccination with Pfizer-Biotech. Dagan et al. leveraged Israel's largest healthcare organization's integrated data repositories from almost 1.2 million people in Israel (excluding nursing home residents and healthcare workers). The vaccine was 92% effective at protecting against symptomatic COVID-19 and preventing the severe disease from seven days after the second dose, similar to results seen in clinical trials. That was absolutely great news to boost up vaccination campaign. However, in the COVID-19 vaccination, the term sterilizing immunity is still hard to achieve. Until now, many vaccination reports tell us that the vaccination will prevent the illness but still lead to asymptomatic infection. Based on the results from non-human primate models, vaccination protected the lungs and prevented disease. However, the virus still might replicate in the upper respiratory tract, but it is usually lower and shorter. Sterilizing immunity is the type of immunity that completely prevents a disease-causing pathogen like COVID-19 from establishing an infection. Unfortunately, it remains the holy grail of COVID-19 vaccine research. Unless a vaccine offers sterilizing immunity, there is a chance to COVID-19 asymptomatic transmission.[7,8]

Assessment of vaccine immunogenicity will tell us how well a vaccine works and measure the type of immune responses that the vaccine generates and their magnitude over time. When measuring immunogenicity, scientists look at two key aspects of the immune response: antibodies and T-cell response. Functionally, antibody production from the vaccine-induced immune response can be classified as binding/non-neutralizing antibodies and neutralizing antibodies (NAbs). Binding antibodies (BAbs) can bind to the surface of invading pathogen. This binding can flag the pathogen for destruction by immune cells and stimulate the development of proteins known as compliment, which further promotes pathogen destruction. NAbs can inhibit infectivity by binding to the pathogen and blocking the molecules it needs to enter cells, thereby neutralizing it. The titers of NAbs, therefore, may provide higher protection against infection on subsequent exposure to SARS-CoV-2. IgG against receptor binding domain (RBD) in spike protein has been shown to be the primary source of neutralizing antibodies against the virus. However, it should be noted that not all antibodies that bind RBD demonstrate neutralization potential. He et al. studied the seroprevalence and kinetics of anti-SARS-CoV-2 antibodies at a population level in Wuhan and found that neutralizing antibody titers remained stable for at least nine months. However, the study results about the durability of humoral responses against SARS-CoV-2 over a long period still debatable. The evidence of neutralizing antibody titers and durability both in natural infection or post-vaccination are important to inform the development of vaccination strategies (e.g., dosage and booster schedule). For those reasons, reliable serological assays are ultimately needed.[9,10]

Scientists also give full attention to T-cell responses in SARS-CoV -2 infection and vaccination. T cell-mediated immunity is crucial for the effective clearance of SARS-CoV-2. A study reported that exposure to SARS-CoV-2 within households had induced virus-specific interferon IFN-γ producing T cells without seroconversion. Zuo et al. reported that robust functional SARS-CoV-2-specific T cell responses were retained six months following primary infection. Measurement of T-cell responses can be more

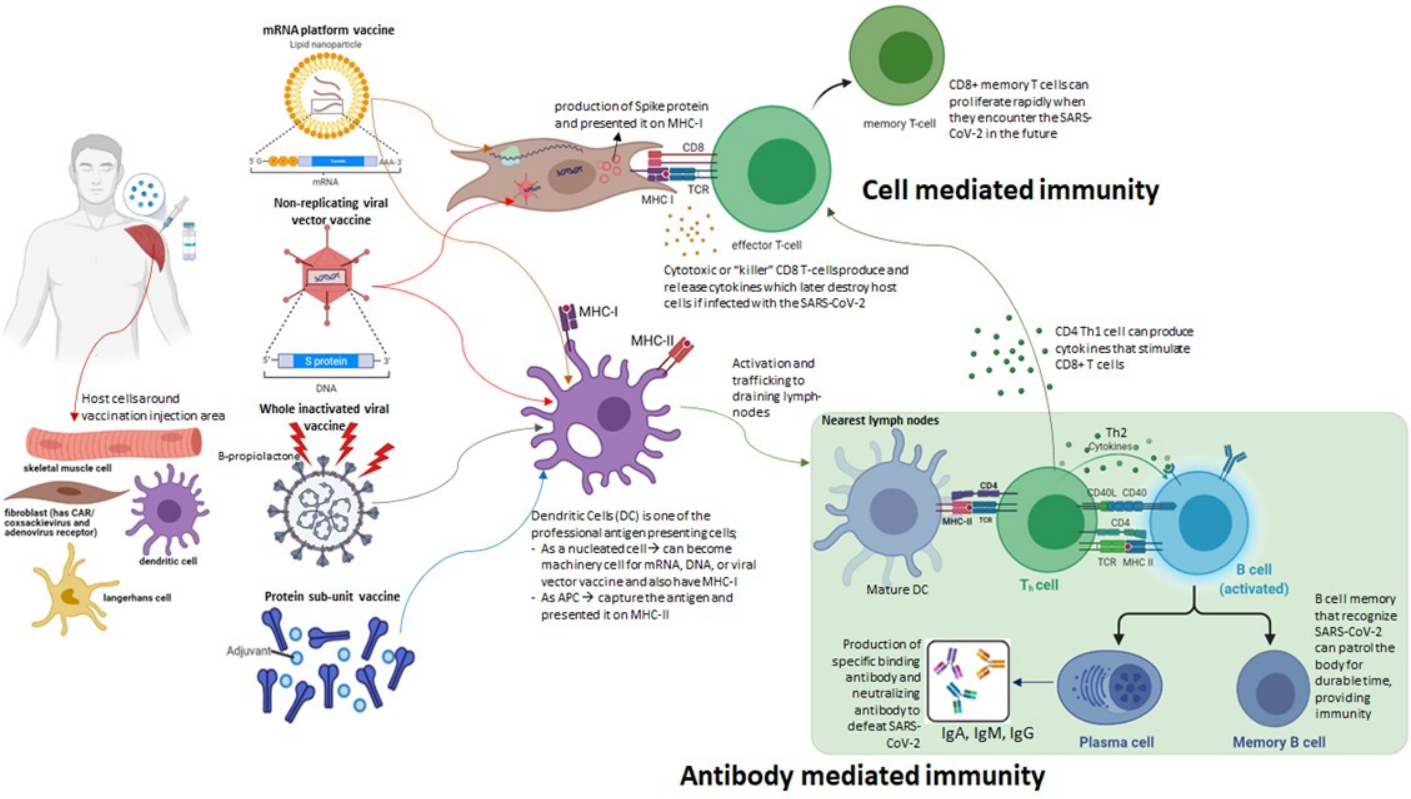


Figure 1. Immune response towards SARS-CoV-2 induced by vaccination. The big 4 leading vaccine platforms give their best shots to elicit humoral/ antibodies and T-cell immune response. However, whole inactivated viral and protein sub-unit vaccines elicit little T-cell immune response depending on the adjuvant.

complex than the measurement of antibody levels. T-cell phenotype, breadth of response, cytokine secretion, cytotoxic killing, and proliferation ability are typical parameters measured in vaccine studies. The ELISpot assay is a gold-standard method for quantifying antigen-specific cellular responses (e.g., IFN-g) after vaccination in clinical trials. Other T-cell assays are intracellular cytokine staining (ICS) and analysis by flow cytometry, analyzing cytokines using platforms that allow a multiplex analysis of soluble samples (Luminex, LegendPlexTM, and Meso Scale Discovery) or cellular samples (CHIP Cytometry and CyTOF). The novel high-throughput T-cell assay to determine immunity towards SARS-CoV-2 is based on T-cell receptor (TCR) gene sequencing using next-generation sequencing and machine learning technology.[12,13,14]

Several issues arose after the first-generation vaccine roll-out to the world. First, an increase of new confirmed cases is reported in many countries at the beginning of March 2021 after a six-week streak of falling case counts. A highly contagious variant of concerns/ VoC (B.1.1.7, B.1.351, and P.1) reduces vaccine efficacy, combined with premature loosening restriction after vaccination, is suspected. Surprisingly, the silver lining of the VoC immune-escape ability silver lining is coming in a pre-print article from Moyo-Gwete et al. They studied the antibody response to the B.1.351 from a cohort convalescent serum of hospitalized patient caused by the variant. Robust binding and neutralizing antibody titers to the variant were detected. These binding antibodies showed high cross-reactivity levels for the original variant from the first wave and the P.1 variant. It raises a hope that vaccines designed with the B.1.351 sequence may elicit more cross-reactive responses. Second, blood clot events reported in AstraZeneca vaccine recipients resulted in a temporary halt of it.

Fortunately, the AstraZeneca scientists already make it clear that those blood clot events unrelated to the vaccine. Third, the fact that we cannot avoid the disparity in vaccination between rich and emerging countries. For example, in mid-March, around 50% of Israel's population has been fully vaccinated. Meanwhile, its neighbors Lebanon, Syria, Jordan, and Egypt vaccinate not reached 1% yet of their respective populations, leaving a chance for new outbreaks. Thus, Covax (the global vaccine-sharing initiative organization) is created to prevent unequal access by negotiating vaccine deals. The biggest issue is it seems the immune response from vaccination will wane faster than expected. Scientists try hard to find a way to increase the vaccines' immunogenicity: tailoring the ideal dosage for priming and booster, booster duration, and vaccine platform mixing. Scientists think that combining two vaccines could strengthen immune responses by

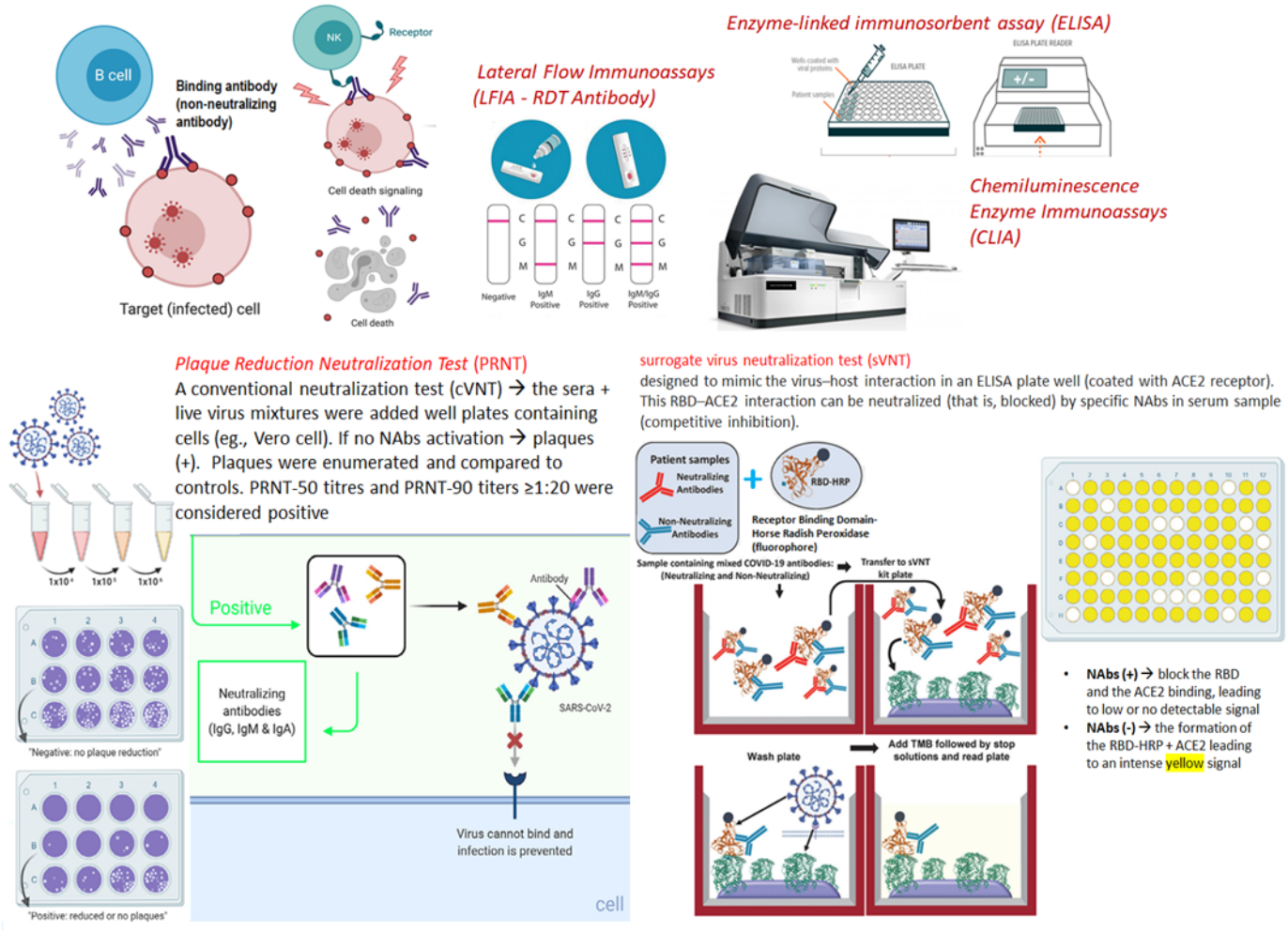


Figure 2. BAbs can be detected by qualitative method; LFIA, semi-quantitative by ELISA and CLIA with different antigen targets. NAbs assays ranging from conventional and laborious assay like PRNT as gold standard to a safe (no live virus) novel high-throughput sVNT.[11]

optimizing the best features of each. An animal study reported that a combination of an mRNA coronavirus vaccine which already good in inducing antibody response with the viral vector vaccine, roused CD8+ T cells better than either vaccine alone. Trust the proverb; when there is a will, there is a way.[15,16,17]

Will we achieve herd immunity after the vaccination roll-out? We hope we will, but it might not be in the meantime, and we cannot depend on vaccines only. Dr. Anthony Fauci estimated that we need 75% to 85% of the population to get vaccinated to achieve herd immunity, with important notes to involve the children in vaccination. In one of his interviews, he also casually answered the ultimate question on when this pandemic end; "I don't know." Scientists around the world give the nod to the probability the SARS-CoV-2 becomes endemic. It might be, we need to learn to live with the virus and get a yearly jab like the Influenza virus. If so, strict to the health protocol, strengthening healthcare, supporting researches, and genomic surveillance matters. The virus doesn't want to put-off its crown yet, but we hope we can start with weakening it with powerful jabs and eventually winning this pandemic war.[18,19] Amen!

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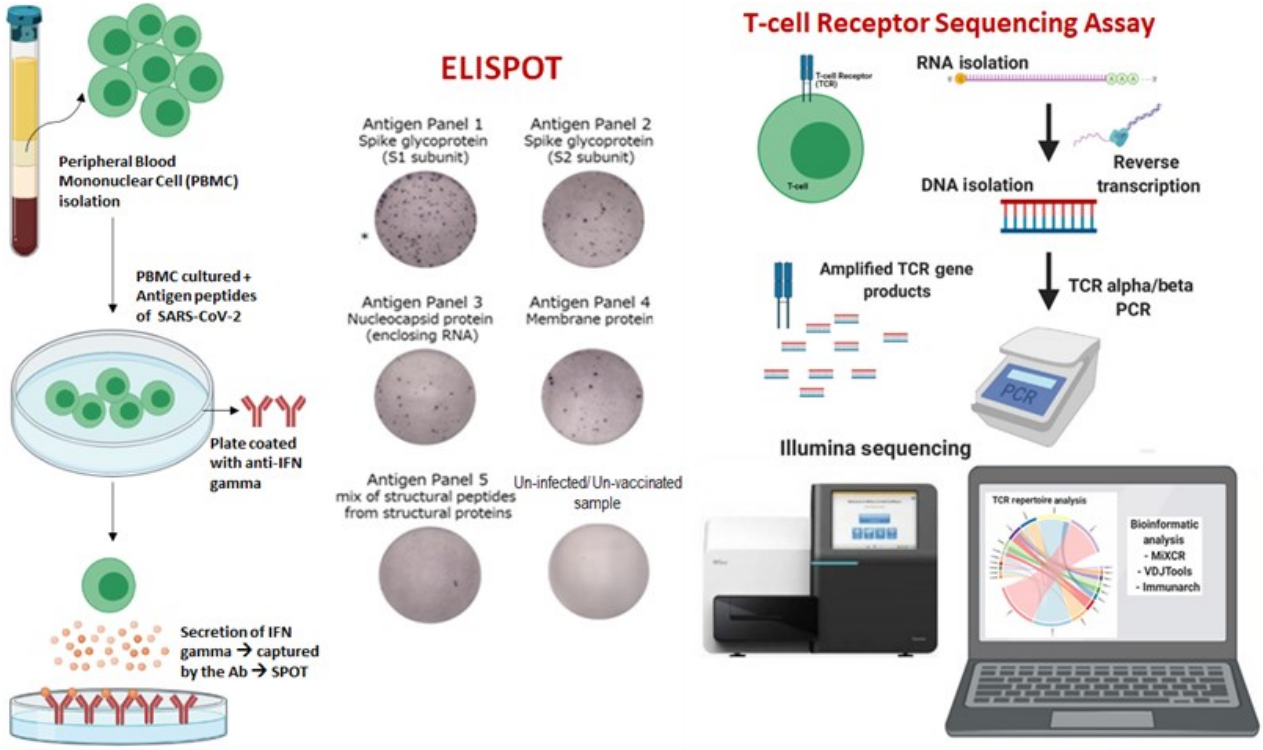

Figure 3. ELISPOT and T-cell receptor sequencing assay to assess T-cell response towards SARS-CoV-2.[14]

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INA-RESPOND Newsletter

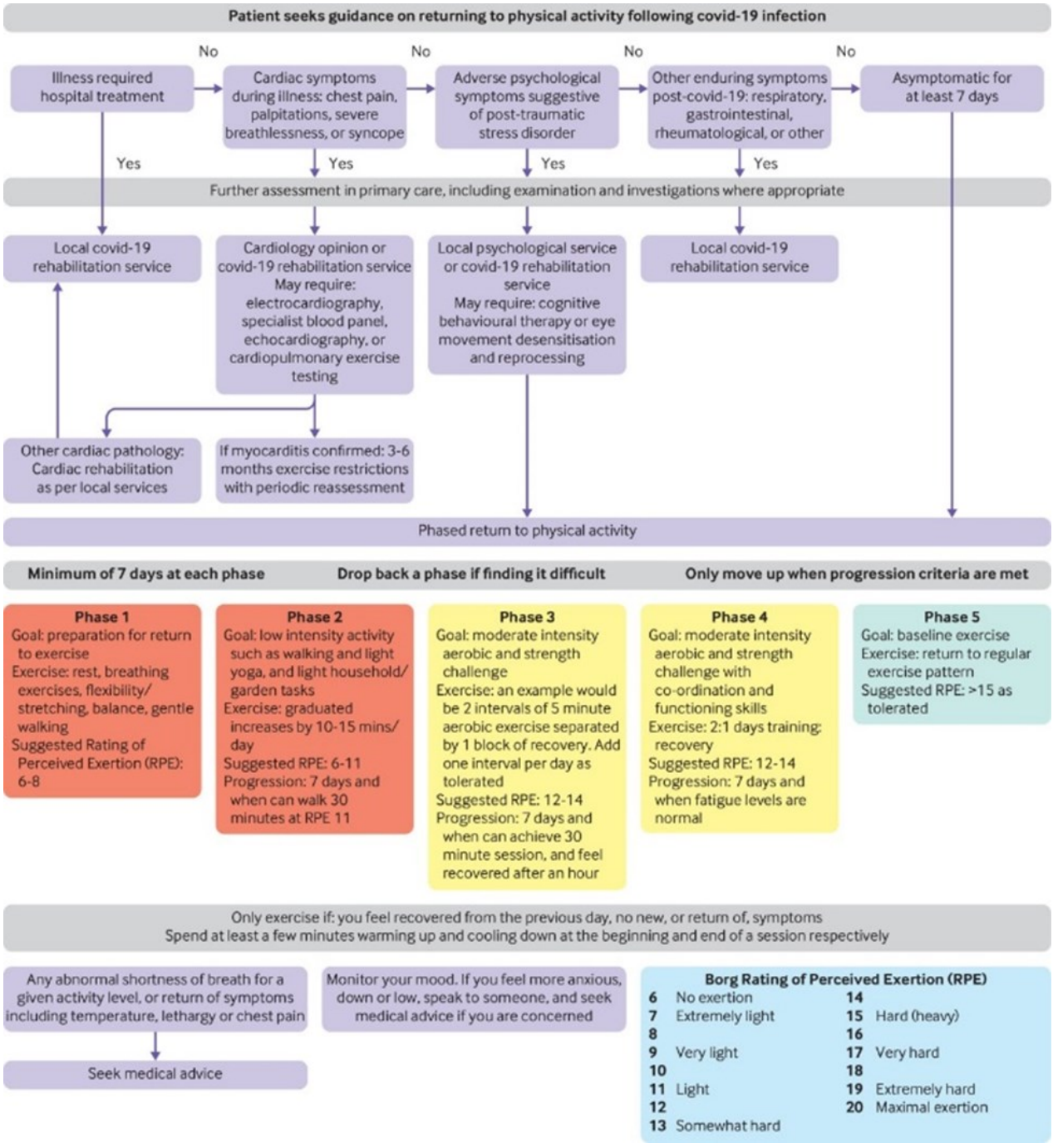
COVID... I'M BACK!

By: Caleb Leonardo Halim

It has been one full year since the COVID-19 pandemic struck our country. Our government has carried out all prevention and handling of this virus. Moreover, recently our government invite the public to take part in the COVID vaccination program. However, we never know when this pandemic will end or whether it is true that the current vaccines can reduce the spread of this virus to a very minimal level. Therefore, living "side by side" with this new state or the new normal must be adopted by everyone. This adaptation must be carried out in all areas of life, one of which is in the health aspect.

Speaking of the health aspect, public awareness to start a healthy life has increased lately, from consuming a balanced nutritional diet to regularly exercising. However, for the people who have survived COVID-19, adjustments need to be made. This adjustment includes rehabilitation after COVID infection. Because COVID-19 not only attacks the body but also attacks the mental state, the rehabilitation carried out must return a person to their previous quality of life. The health problems that most often occur after COVID infection are cardiopulmonary disorders and psychological disorders. Cardiopulmonary disorders include viral myocarditis, which increases the risk of morbidity and mortality during exercise. There are also lung disorders due to fibrosis tissue formation after COVID infection, which causes shortness of breath when doing physical activity.

A risk-stratification approach can help maximize safety and mitigate risks, and several factors need to be taken into account. First, is the person physically ready to return to activity? In the natural course of COVID-19, deterioration signifying severe infection often occurs around a week from symptom onset. Before re-initiation of exercise, daily living activities should be easily achievable, and the person can walk 500 m on the flat without feeling excessive fatigue or breathlessness. Some may not have been able to walk 500m without breathlessness before their COVID-19 illness, and they should not be precluded from starting physical activity at a level tolerable for them.



The second factor is that ongoing symptoms, regardless of system, may indicate a post-acute COVID-19 illness. People who had a more severe COVID-19 illness, such as those hospitalized, are thought to be at higher risk of cardiac complications and thromboembolic events. Third, with regards to respiratory symptoms, persistent cough and breathlessness are expected to resolve after several weeks. Still, progressive, non-resolving, or worsening symptoms may indicate pulmonary-vascular complications such as pulmonary embolism, concomitant pneumonia, or post-inflammatory bronchoconstriction, and these patients should discuss their condition with their doctor.

There is no clear, evidence-based way to guide returning to physical activity, but a prudent approach should be gradual, individualized, and based on the activity's subjective tolerance. Brief discussions regarding physical

activity in primary care can follow a modified "3As" approach: ask, assess, and advise/assist. First, ask about your current activity level and then consider your activity goal, such as increasing your fitness level / shaping your body. Last, please seek either a medical advisor or competent fitness coach who understands rehabilitation post -COVID infection to assist you if you are confused about what to do next.

HOW TO START

Phases 1-2

Begin with light-intensity activity for at least two weeks. Use the RPE scale from 6 (no exertion at all) to 20 (maximal exertion). Light intensity exercise is equivalent to an RPE of under 11 when a person feels minimal to light exertion. They should be able to hold a full conversation without difficulty at this level. Activities might include household and light garden tasks, gentle walking. You should be able to spend seven days (phase 1) on extremely light-intensity activity (RPE 6-8), including flexibility and breathing exercises, for as long as the person feels able to do them, followed by a further seven days (phase 2) incorporating light-intensity activity (RPE 6-11) such as walking with a graduated increase at 10-15 minutes per day at the same RPE when tolerated.

Phases 3-4

Progress to more challenging movement activities depending on pre-illness capacity. These might include intervals of two 5-minute blocks of activity such as brisk walking, going up and down the stairs, jogging, swimming, or cycling separated by a rest period. The person should not feel that the exercise is "hard," and we would suggest working to an RPE of 12-14 (moderate intensity, not out of breath, and could hold a conversation). Progress by adding an interval per day as tolerated. Phase 4 would involve more complex movement that challenges coordination, strength, and balance, such as running but with changes in direction, side-steps, shuffles, and circuits of bodyweight exercises, but again without it feeling hard. After completing phase 4, people should then feel they can return to their baseline (pre-COVID) level of activity or more.

You should do at least seven days at each phase to prevent sudden increases in training load. However, people should stay at the phase they feel comfortable with for as long as necessary. They should monitor for any inability to feel recovered at 1 hour after exercise and the day after, abnormal breathlessness, abnormal heart rate, excessive fatigue or lethargy, and mental illness markers. If these occur, or the person fails to progress as expected, they should step back to an earlier phase of activity and seek medical advice. Keeping a diary of exercise progression, along with RPE, any mood changes, and, for those who are used to measuring it, objective fitness data such as heart rate can help monitor progress.

It would be best if you started moving right now. The movement will heal your body, restoring mind, and soothing your emotions. You can begin the process of recovery and healing with exercises and movements. So, come back from COVID; come back healthier, stronger, and fitter than ever before.

References:

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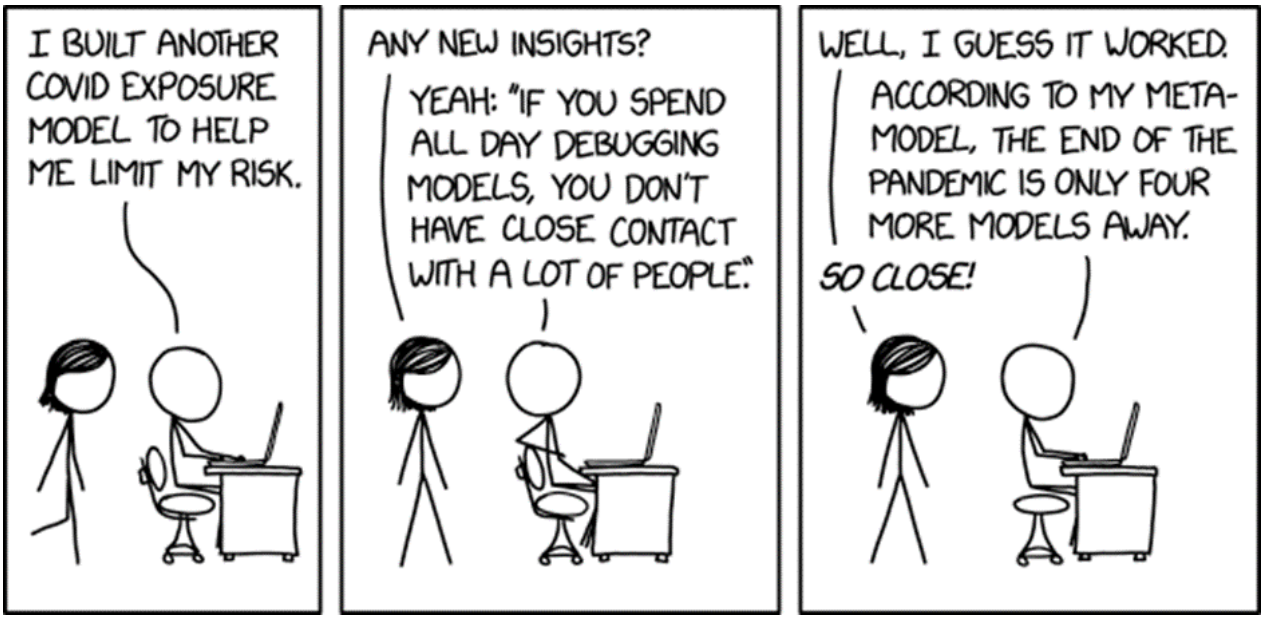
BUILDING OUR PATH INTO UNDERSTANDING BEHAVIOR, AND THEN (HOPEFULLY) CHANGE IT!

By: Aly Diana

COMIC CORNER



Behavior change seems to be more relevant than ever recently. What would we do when the main thing to prevent us from covid-19 craziness is to change our behavior, but others do not listen or do not want to follow through? Then we realized that improving the implementation of evidence-based practice and public health depends on behavior change interventions that lead to a real change, one thing that we want to do but do not know how to. At least, I don't.

Starting slow, let's start with some definitions. Behavior change interventions can be defined as coordinated sets of activities designed to change specified behavior patterns. In general, these behavior patterns are measured in terms of the prevalence or incidence of particular behaviors in specified populations. There are so many behavioral models, each designed to help us better understand what drives behavior and how decisions are made. If we do not understand behavior, how can we know what it takes to change it?

One model that I want to introduce here is the COM-B model, which proposes that there are three components to any behavior (B): Capability (C), Opportunity (O), and Motivation (M). To perform a particular behavior, one must feel they are both psychologically and physically able to do so (C), have the social and physical opportunity for the behavior (O), and want or need to carry out the behavior more than other competing behaviors (M). In other words, CAPABILITY refers to whether we have the knowledge, skills, and abilities required to engage in a particular behavior. Its two components are Psychological Capability: our knowledge/ psychological strength, skills, or stamina; and Physical Capability: our physical strength, skill, or stamina. OPPORTUNITY refers to the external factors which make the execution of a particular behavior possible. Its two components are Physical Opportunity: opportunities provided by the environment, such as time, location, and resource; and Social Opportunity: opportunities as a result of social factors, such as cultural norms and social cues. MOTI-

The COM-B Model.

VATION refers to the internal processes which influence our decision-making and behaviors. Its two components are Reflective Motivation: reflective processes, such as making plans and evaluating things that have already happened; and Automatic Motivation: automatic processes, such as our desires, impulses, and inhibitions.

As can be seen in the figure above, capability and opportunity influence motivation. Not only do all three influence behavior change, but they are also influenced by the change that occurs. For example, the capability component may be targeted to encourage someone hesitant to accept, i.e., providing education through a free webinar. If this individual initially thought that they did not have the drive to take part in a covid-19 vaccination program, then by going to this webinar, they may build the right motivation through provided knowledge (capability). This suggests that this is an interactional model and that by changing behavior, we are also impacting on determinants of behavior, which allows for long-term behavior change.

While this is a model of behavior, it also provides a basis for designing interventions aimed at behavior change. Applying this to intervention design, the task would be to consider the behavioral target and what components of the behavior system would need to be changed. However, it provides a way of identifying how far changing particular components or combinations of components could affect the required transformation for a given behavior in a given context.

And there are so many things to learn, so see you again next month. I hope you are interested in this topic as much as I do.

Some related nice Coursera courses:

https://www.coursera.org/learn/health-behavior-change

https://www.coursera.org/learn/behavior-change-in-public-health/home/welcome

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- Michie, S., van Stralen, M.M. & West, R. 2011. The behavior change wheel: A new method for characterizing and designing behavior change interventions. Implementation Sci 6, 42. https://doi.org/10.1186/1748-5908-6-42

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