INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

March 2022

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Co-Pathogenesis of TB and COVID-19

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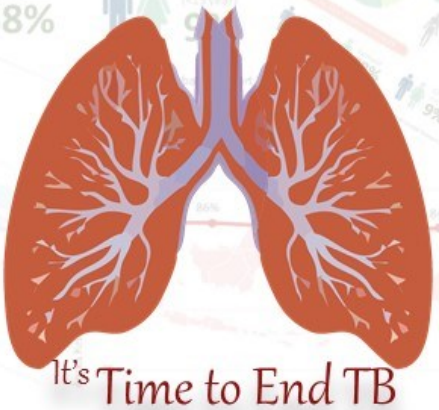
Comic Corner

ZOTERO: For People Who Love Freebies

WORLD TB TUBERCULOSIS DAY



BADAN KEBIJAKAN PEMBANGUNAN KESEHATAN
MINISTRY OF HEALTH REPUBLIC OF INDONESIA
2022

MASTHEAD

INA-RESPOND newsletter

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FEATURES

INA-RESPOND Newsletter

TRIPOD, PROACTIVE, & ORCHID Study Updates

By: Eka Windari R., I Wayan Adi Pranata, Lois E. Bang, Melinda Setiyaningrum, Nur Latifa Hanum, Retna Mustika Indah, Riza Danu Dewantara

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Two manuscripts from baseline data, "*The Characteristic of Drug Sensitive and Drug Resistance Tuberculosis in Indonesia*" and "*Performance of Xpert TB/Rif and Sputum Microscopy Compared to Sputum Culture for Diagnosis of Tuberculosis in Seven Indonesian Hospitals*" have been submitted to American Journal of Tropical Medicine and Hygiene and BMC Infectious Diseases Journal.

Other ongoing activities regarding TRIPOD are summarized below:

1. Central Lab Padjajaran University, Bandung has provided the DST results for 32 discordant participants. Some discordant between the DST results from TRIPOD and Central Lab Padjajaran University, Bandung are still found. Thus, the best way to overcomes the discordant is being discussed.
2. Collaboration within the RePORT network on Epidemiology of TB Progression and Outcomes Study, using the TRIPOD data is still on going.

The INA-RESPOND Secretariat is planning to hold a meeting with TRIPOD study team in May 2022, after the Eid Al'Ftr holiday to discuss specimen repository used and to talk about other possible manuscripts from the TRIPOD data.

Indonesia will conduct TB Prevalence Survey This Year followed by Whole Genome Sequencing.

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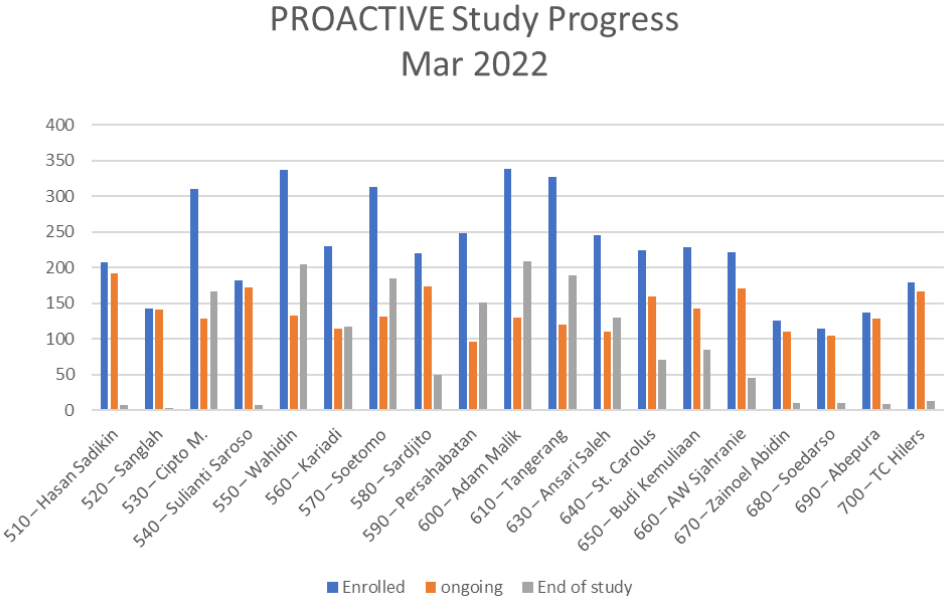
As of March 8, 2022, from 4,336 subjects enrolled, 39.2 % of the subjects have ended their study, and 65.3% of the subjects are still ongoing. The picture on the right shows the study progress from each Site.



As for the end-of-study subjects, 1,346 subjects had already completed the study until follow up visit month 36, 218 subjects died, 105 subjects were lost to follow up, 30 subjects withdrew their consent, 29 subjects moved to a city without a PROACTIVE Site, five subjects were HIV negative, and one subject was suspended (imprisoned).

The site monitoring activity was conducted in site 630, RSUD Dr. M. Ansari Saleh, Banjarmasin on 14-16 Maret 2022. In early April 2022, there will be monitoring activities for two-site, site 600, RSUD Adam Malik Medan and Site 680, RSUD Soedarso Pontianak.

No	Site	*End of Study Duration/ Complete*	Withdrew Consent	Participants with HIV negative	Moved	Death	Investigator Discretion	Lost to Follow Up	Other	Total
1.	510 – RSUP Dr. Hasan Sadikin	18	1	0	2	4	0	0	0	25
2.	520 - RSUP Sanglah	1	0	0	0	2	0	0	0	3
3.	530 – RSUPN Dr. Cipto Mangunkusumo	148	0	0	0	15	0	4	0	167
4.	540 – RSPI Dr. Sulianti Saroso	0	0	0	2	6	0	0	0	8
5.	550 – RSUP Dr. Wahidin Sudirohusodo	143	0	0	5	21	0	36	0	205
6.	560 – RSUP Dr. Kariadi	90	1	3	0	12	0	4	0	110
7.	570 – RSUD Dr. Soetomo	143	13	0	3	21	0	5	0	185
8.	580 – RSUP Dr. Sardjito	55	0	0	3	4	0	11	0	73
9.	590 – RSUP Persahabatan	109	0	1	0	35	0	7	0	152
10.	600 – RSUP Dr. H. Adam Malik	160	3	0	2	20	0	24	0	209
11.	610 – RSU Kabupaten Tangerang	151	6	0	3	19	0	9	1	189
12.	630 – RSUD Dr. M. Ansari Saleh	113	1	0	1	7	0	5	0	127
13.	640 – RS St. Carolus	84	0	0	0	1	0	0	0	85
14.	650 – RSU Budi Kemuliaan Batam	94	3	0	5	8	0	0	0	110
15.	660 – RSU A. Wahab Sjahranie	37	0	0	2	4	0	0	0	43
16.	670 – RSUD Zainoel Abidin	0	0	0	0	11	0	0	0	11
17.	680 – RSUD Soedarso	0	0	0	0	10	0	0	0	10
18.	690 – RSUD Abepura	0	1	1	1	6	0	0	0	9
19.	700 – RSUD TC Hillers	0	1	0	0	12	0	0	0	13
Total		1346	30	5	29	218	0	105	1	1734

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Based on uploaded CRFs as of 2 March 2022, 178 participants were enrolled in the ORCHID-COVID-19 study, with 115 from site 610 (RSU Kabupaten Tangerang, Tangerang) and 63 from site 521 (RS Universitas Udayana, Denpasar). This study had 161 (90%) participants who completed the visits, and 5 participants died during the study. In terms of deaths, 2 subjects from site 610 died as a result of COVID-19 and heart failure, while 3 subjects from site 521 died from thromboembolism, non-ST-segment Elevation

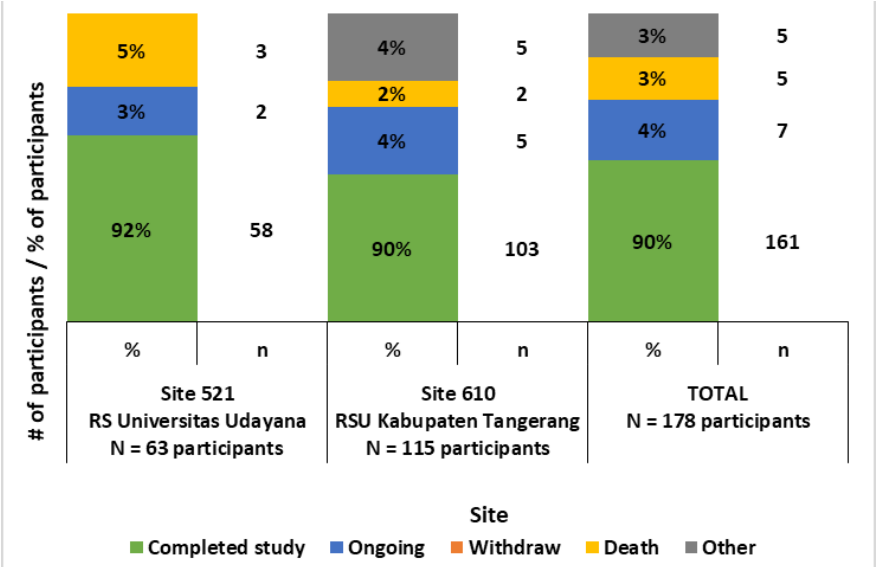

Figure 1. Participant status per site based on uploaded CRF as of 2 Mar 2022

Myocardial Infarction, and thromboembolism. On the other hand, 7 subjects are still participating in the study, 2 subjects from site 521 and 5 subjects from site 610. While 5 participants decided to not continue participating in the study (categorized as other) (figure 1).

Up to 2 March 2022, 149 participants (84%) were identified as positive COVID-19, and 29 participants (16%) were identified as negative COVID-19. In site 610, the number of participants identified as positive COVID-19 was 105 (91%) and 10 (9%) participants as negative COVID-19. While in site 521, there were 44 (70%) participants identified as positive COVID-19, and 19 (30%) participants identified as negative COVID-19 (figure 2).

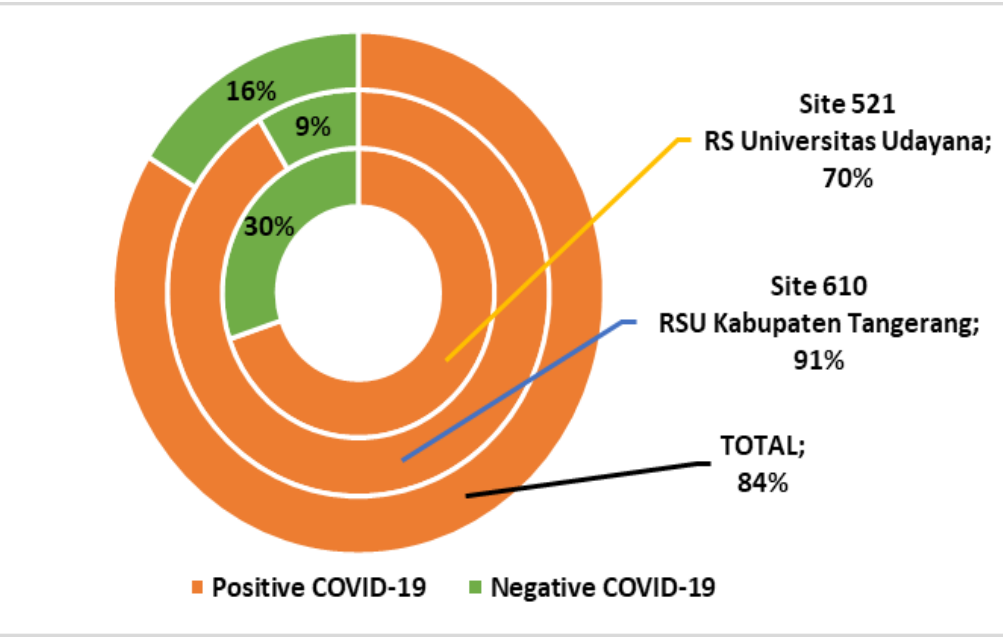

Figure 2. COVID-19 identification at enrolment based on uploaded CRF per 2 Mar 2022

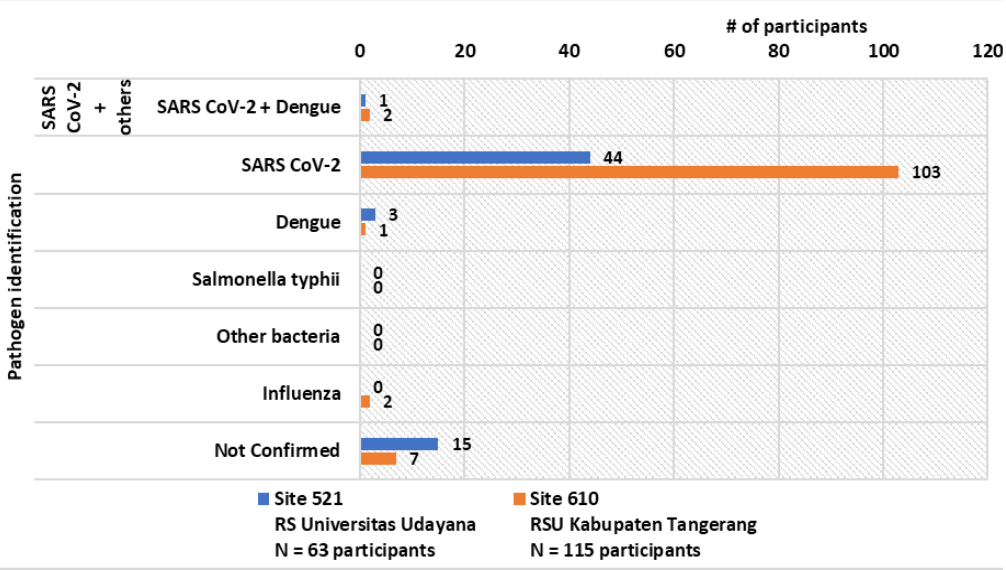

Figure 3. Pathogen identification based on uploaded CRF per 2 Mar 2022

In site 521, SARS-CoV-2 was identified in 44 (70%) participants based on the pathogen identification data. SARS-CoV-2 and Dengue (confirmed by PCR SARS-CoV-2 and RDT Dengue IgM) co-infection were identified in 1 (2%) participant. Dengue (confirmed by RDT Dengue NS-1) was also identified in 3 (5%) participants. While in site 610, SARS-CoV-2 was identified in 103 (90%) participants. SARS-CoV-2 and dengue (confirmed by PCR SARS-CoV-2, RDT Dengue NS-1, and RDT Dengue IgM IgG) co-infection were identified in 2 (2%) participants. Influenza (confirmed by PCR) was identified in 2 (2%) participants. Dengue (confirmed by RDT Dengue NS-1 and RDT Dengue IgM IgG) was also identified in 1 (1%) participant. The pathogen was unidentifiable among 22 (12%) participants; 15 were from Site 521 and 7 were from site 610 (figure 3).

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UPDATE ON INDONESIA'S COVID-19 SITUATION

By: Erlina Burhan

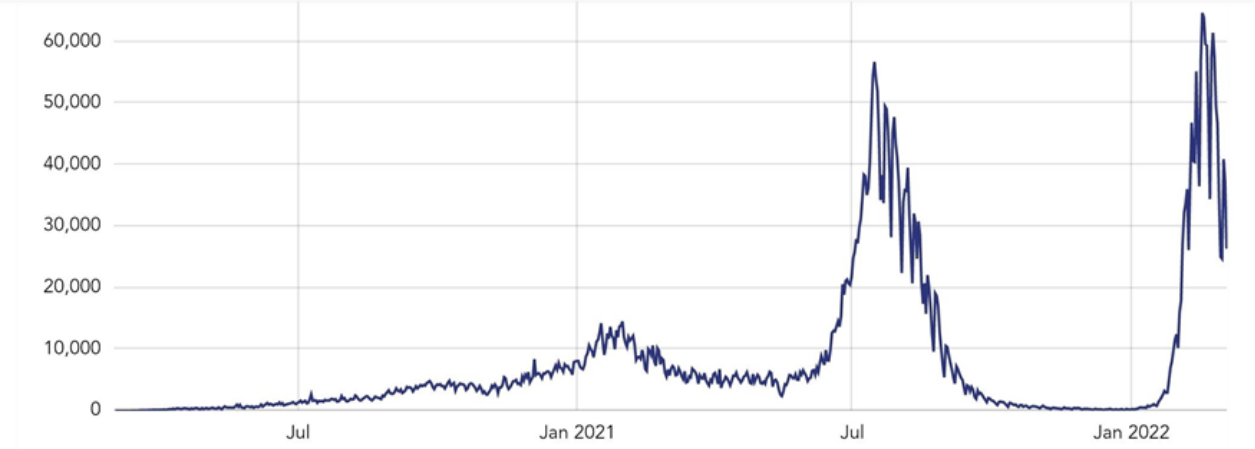

Figure 1. The COVID-19 infection trend in Indonesia since the beginning of 2020. We can observe 2 significant peaks. The first peak occurred after July 2021, the wave of delta variant infection. The second peak is after January 2022, the surge of the Omicron variant. It can be observed that the gradient is steeper and the peak is higher during the Omicron wave (graph obtained from https://covid19.go.id/peta-sebaran).

SCIENCE CORNER

Indonesia is currently suffering from the third wave of COVID-19 infection, predominantly due to the Omicron strain. First detected in Indonesia at the end of November 2021, it has rapidly spread, creating a more enormous wave than the Delta variant surge in mid-2021, peaking at 64,718 new cases per day on 16 February 2022. Despite this new record, the bed occupancy rate of hospitals remained low at 38% during the peak, the rate of hospitalization and severe disease and the mortality rate is comparably less than the delta surge in mid-2021.1 The total number of deaths caused by Omicron is only 15% of the number of deaths caused by the delta variant surge in mid-2021.2 The healthcare system collapse was not observed in this Omicron surge. However, the nation remains vigilant and sees the need to prepare for the worst.

Up to 19 February 2022, the total number of deaths in Indonesia caused by Omicron is 2,484, 46% were in patients with comorbidities, 53% in the elderly population, and 73% in the population who had not completed the two-dose COVID-19 vaccinations.3 Booster vaccinations have been deployed, free and accessible for every Indonesian aged over six years old. A total of 6.3 million boosters have been injected into the population.

Since the peak at 64,718 cases per day in Indonesia, the trend has decreased. However, we also observed a decreased amount of testing in the population. Indonesia's minister of health, Budi Guna Sadikin, announced a possibility of COVID-19 becoming an "endemic" in Indonesia, but reaching an endemic state has several challenges. Indonesia should have at least 70% of the population vaccinated with two doses, and Indonesia should not have new surges of COVID-19 infection. Currently, ~50% of the Indonesian population has received the two-dose vaccination, so there is still a significant gap.4 Vaccination remains an essential tool to control the spread of Omicron in Indonesia. In non-vaccinated individuals who had no comorbidities, the mortality rate is 7.5%. This is far higher than the mortality rate of fully vaccinated individuals, at 0.5%.1 Hence, despite the decreased severity compared to the Delta variant, we should remain vigilant, especially towards the population with comorbidities, the elderly, and the unvaccinated. As long as Omicron still circulates, the susceptible population remains at significant risk for severe COVID-19 disease and considerable morbidity and mortality. It is important to note that due to Omicron's increased transmissibility, it is possible for the asymptomatic young population to infect the susceptible population.

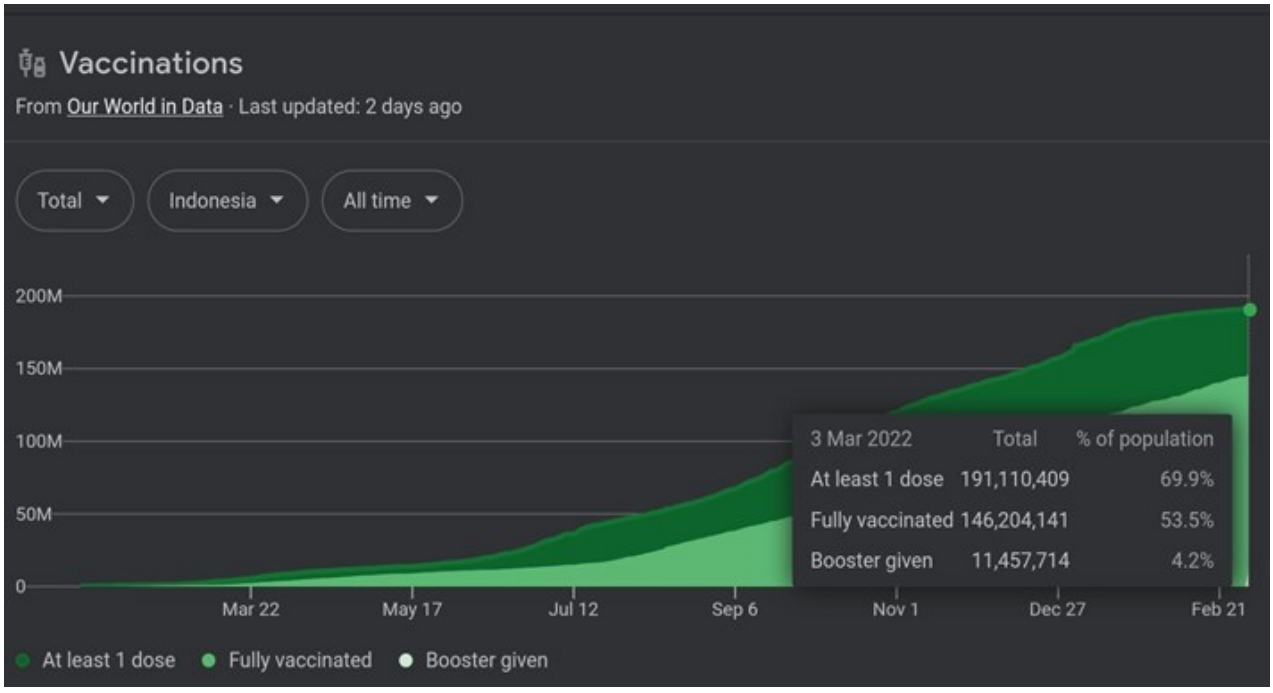

Figure 2. The graph shows the COVID-19 vaccination progress in Indonesia as of the 3rd of March 2022.

As Omicron continues to spread in Indonesia, there have been 252 confirmed cases of variant BA.2 "Son of Omicron," which is reported to have 1.5-7 times greater transmission capability compared to BA.1, the original omicron variant. The difference of severity between these two omicron variants remains unknown.5 As COVID-19 continues to circulate, there is always a possibility of the emergence of a new variant.

Stopping the spread of Omicron requires the involvement of multisectoral efforts between healthcare workers, policymakers, and the population itself. The 5M protocol should still be implemented to minimize the number of infections and decrease the COVID-19 exposure to the susceptible population. Today we observed that the population is becoming more lenient and disobedient with the COVID-19 protocols. This may be caused by an opinion formed by some parts of the population that since Omicron is not severe, it is OK to be infected by Omicron.

In addition, the two-dose vaccination coverage should be increased to achieve herd immunity, and boosters should be administered as much as possible to the citizens of Indonesia. This includes battling vaccine inequity in the nation, where a quarter of Papua is not yet vaccinated, despite over 70% of the whole of Indonesia having received the first dose.

In conclusion, the COVID-19 cases in Indonesia are decreasing, and the testing is adequate. However, there is still a lot of work that needs to be done in order to call the COVID-19 an "endemic" in our beloved nation. The health protocol should remain implemented to prevent surges of new cases, and vaccination coverage needs to be increased to achieve herd immunity. Healthcare workers and policymakers should work together to ease the implementation of the health protocol in Indonesia. Caution must be observed when dealing with the elderly, the immunocompromised, and the unvaccinated population. Stopping COVID-19 requires the effort of every individual, working together with all stakeholders. No one is safe until everyone is safe.

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Taken from online data of Indonesian hospitals, NAR dan P Care as quoted by Adam Prabata, MD)

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CO-PATHOGENESIS OF TB AND COVID-19

By: Jerrold J Ellner

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Infectious diseases that infect the same populations and the same individuals and the same organs (lung) have the potential to interact synergistically to the detriment of both. At this point in the SARS-CoV-2 pandemic, little is known about co-infection with TB. I speculate that the interactions are important, bidirectional, and have major implications for TB and for COVID-19 control

The SARS-CoV-2 pandemic has destabilized TB control programs, delaying the presentation of TB cases for diagnosis and treatment, affecting TB treatment adherence, reducing the mobility of both patients and health care professionals, decreasing health care access, and increasing poverty (1, 2). The 2021 WHO Global TB Report (3) showed an 18% decline in the number of people newly diagnosed with TB. The reduced access to care has resulted in an estimated 314,000 additional TB deaths, a 15% reduction in the provision of treatment for drug-resistant TB, and a 21% decrease in the administration of preventive therapy.

Studies have addressed the concurrence of active TB and active COVID-19. In a longitudinal analysis from the Philippines, COVID-19 patients with TB had a two-fold increased odds of death (OR 2.17, 95% CI: 1.40-3.37) (4). A meta-analysis further evaluated the outcome in COVID-19 patients with concurrent active TB (5) and found the RR for mortality was 1.93 and there was an increased risk of severe disease. There is no information to date on the more common scenario, how prior SARS-CoV-2 infection affects the presentation, severity, treatment outcomes, and chronic pulmonary consequences of TB. I predict adversely in each case.

Co-morbidities are recognized risk factors for TB (6, 7) promoting progression from latent TB infection (LTBI) to TB. The risk imposed by HIV dwarfs others because it leads to CD4 depletion and dysfunction. There is ample evidence that other viral infections predispose individuals to bacterial illness (8); for example, measles may be associated with an increased risk of TB (9, 10). Further, the "hypercytokinemic" state associated with COVID-19 also could predispose to bacterial infection (11). Data on whether COVID-19 promotes TB progression is limited to a single case report (12). Experimental data, also limited, indicate that patients with severe COVID-19 showed reduced frequency of Mtb-specific CD4+ T-cells which plausibly would potentiate progression to TB (13). I speculate that prior SARS-CoV-2 infection will be associated with a greater frequency of symptomatic TB.

The natural history of SARS-CoV-2 infection in the presence of latent TB infection (LTBI) has yet to be determined. BCG vaccination is protective against TB meningitis in children, but also against all-cause childhood mortality (14, 15). Recent studies corroborated these findings and showed a reduction in infections other than TB (16). For example, in a study conducted in Brazil prior to the COVID-19 pandemic, BCG vaccination reduced the risk of childhood death from pneumonia by 50% (17). The non-specific protection following vaccination with BCG appears to be mediated by epigenetic reprogramming of monocytes, a phenomenon called 'trained immunity" (18). I propose, as have others, that trained immunity initiated by BCG vaccination and "boosted" by recent exposure to Mtb or LTBI may have protective effects against SARS-CoV-2 infection (19-22) accounting possibly for the lower incidence and case fatality rate (CFR) of COVID-19 in TB-endemic countries. Although there are a number of potentially confounding issues (eg age of the population), the magnitude of the differences in death rates implies the existence of an additional protective mechanism. This is supported experimentally as intravenous BCG protects mice against lethal challenge with SARS-CoV-2 (23). There may be alternative mechanisms for protection by BCG apart from trained immunity, for example, induction of heterologous adaptive immunity based on the sequence similarity between HSP65 of M. bovis BCG and SARS-CoV-2 spike and nuclear proteins (24).

There is an inverse relationship between BCG vaccine policy and COVID-19 incidence and severity, possibly explained by confounding variables (25). A meta-analysis of 8 published studies, nonetheless, indicated that BCG vaccination was protective against SARS-CoV-2 infection (OR=61), but the data were insufficient as regards effects on disease severity (26). In a recent study of healthcare workers, a history of BCG vaccination was associated with a decrease in the seroprevalence of anti–SARS-CoV-2 IgG (22). A randomized placebo-controlled human challenge study, in fact, provided compelling data for heterologous protection. Participants were vaccinated with BCG or not and then challenged with attenuated yellow fever virus vaccine strain. The vaccinated group showed lower viremia compared to controls that were associated with genome-wide epigenetic reprogramming of monocytes and increased IL-1β production (27). Clinical trials of BCG re-vaccination of adults to prevent or ameliorate COVID-19 are in progress (28, 29).

Does LTBI, per se, affect the natural history of SARS-CoV-2 infection? Trained immunity has been observed in monocytes of individuals recently exposed to TB (30). Further, individuals with recent TB infection showed increased containment of BCG in an ex vivo infection model and this effect was associated with increased TNF-α, IL-1β, and IL-6, indicative of trained immunity (30). In a study conducted in India, severely ill patients with COVID-19 were less like to be interferon-gamma release assay (IGRA)+ although it was not possible to distinguish whether IGRA+ status was protective, or if severely ill patients were IGRA-anergic (31). Likewise in a study of 76 patients with COVID -19 in Turkey, a positive tuberculin skin test (TST) was associated with milder disease (32); again it is not clear whether severe COVID-19 suppressed the TST response. Another study from Turkey indicated that decreased mortality in health care workers with COVID-19 might be due to increased Mtb exposure history and BCG vaccination (33). Experimental data in animals also are supportive: In a mouse model, MTBI conferred strong protection against both aerosol challenge with MTB and heterologous challenge, which was mediated through IFN-γ dependent innate immune activation (34). I speculate that recent Mtb infection is protective against the acquisition of SARS-CoV-2 infection and/or severity of COVID-19.

Given the level of interest and funding for COVID-19, the answers to the questions I raise should be forthcoming. It is my hope that the Regional Prospective Observational Research on Tuberculosis (RePORT) – Indonesia program will contribute to our understanding in this and other areas.

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Source: https://www.who.int/campaigns/world-tb-day/2022/campaign-materials

INA-RESPOND Newsletter

OMICRON: IMPACT ON DIAGNOSTICS

By: Katy Shaw-Saliba

To identify and treat individuals infected with SARS-CoV-2, accurate diagnostics are needed. While early on in the pandemic, diagnostics were used for largely to diagnose and isolate individuals, now that treatments and vaccines are available, it is important to still use diagnostics to identify individuals who may be eligible for treatment or to identify new variants that may evade the immune response (either from infection or vaccination). For the most part, SARS-CoV-2 diagnostics were developed based upon the original Wuhan reference strain. However, the SARS-CoV-2 virus has undergone a great deal of evolution resulting in a number of different viral variants. Variants such as the alpha and delta variant have ~20-30 mutations in their genomes compared to the Wuhan reference. The omicron variant (B.1.1.529) has over 50 mutations throughout its genome (Fig 1). These mutations have the potential to render current diagnostics less sensitive or completely ineffective and therefore, manufacturers, scientists, and government organizations such as the US NIH, US FDA, and FINDx are closely monitoring the impact that different variants may have on the performance of diagnostics [2].

Diagnostic tests can tell us if someone currently has SARS-CoV-2 or was previously infected by checking for the virus or for the host response to the virus, respectively. This article will focus on the diagnostics that detect the virus: detection of the viral genome or detection of the viral proteins (antigens) in specimens taken from the nose and/or throat.

The detection of the genome is via nucleic acid amplification techniques (NAAT); usually RT-PCR. In order for NAATs to be successful, a region of the genome must first be recognized by primers and

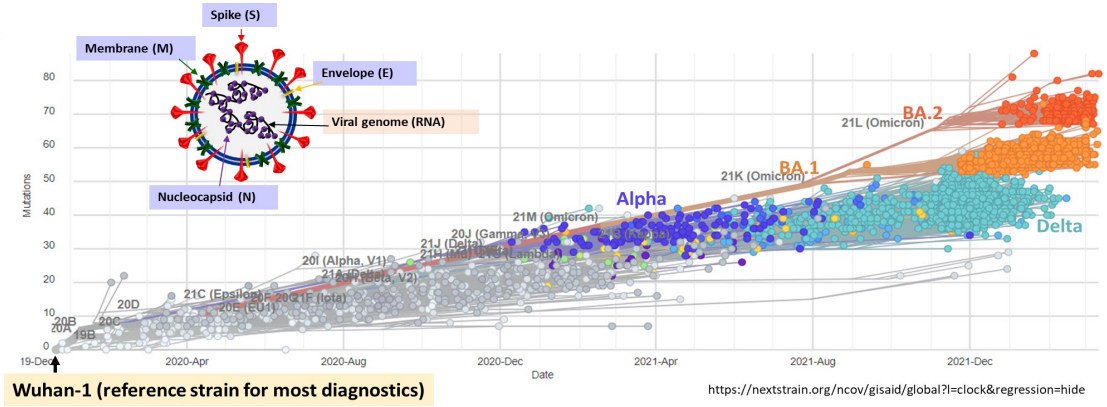
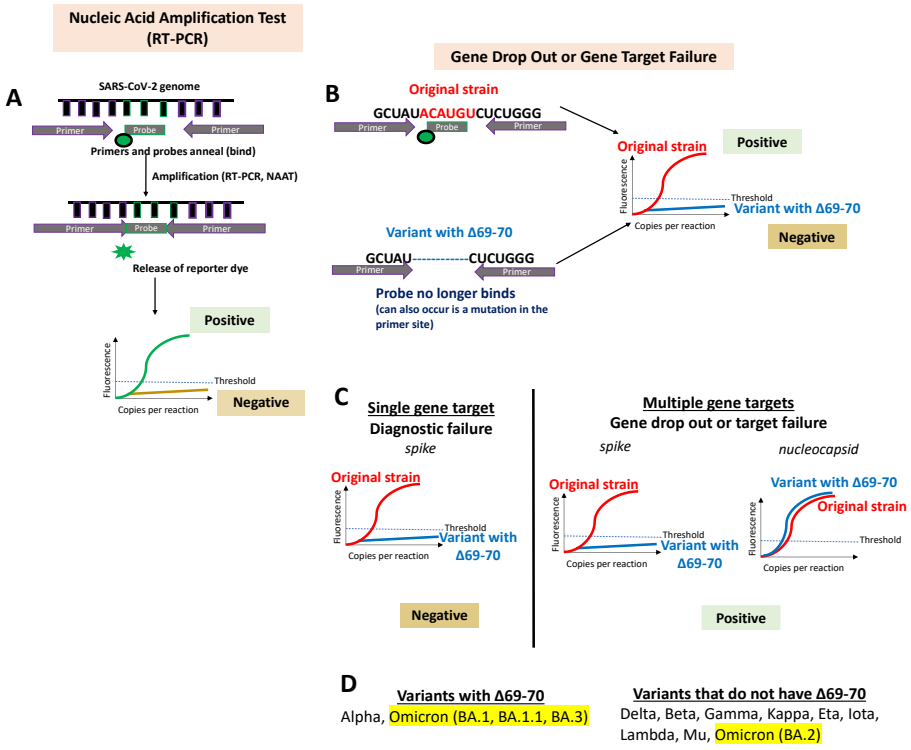


Figure 1. Schematic of the SARS-CoV-2 virus and phylogenetic tree showing the number of mutations in SARS-CoV-2 variants compared to the Wuhan reference strain over time. Phylogenetic tree from Nextstrain.org [1]

Figure 2. Impact of omicron on NAAT.

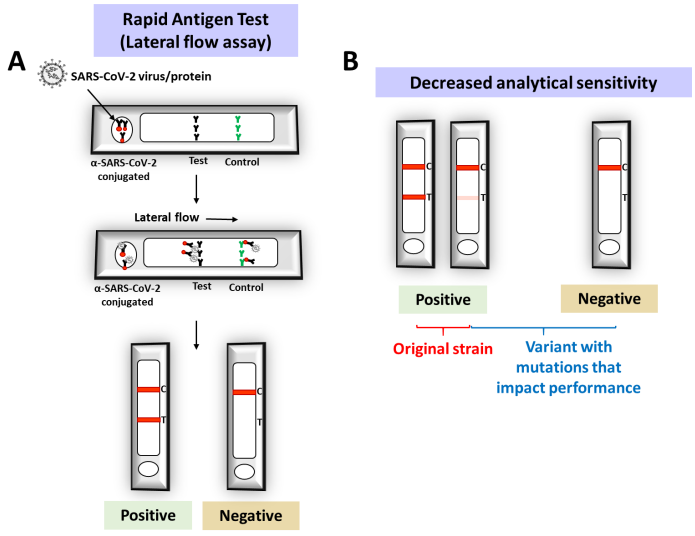


probes that contain a reporter, amplified, and detected (Fig 2A). If there are mutation(s) in regions where primers and probes bind, the binding may not occur or may occur sub-optimally resulting in no amplification. When this happens, the result will be negative despite the virus being present (false negative) (Fig 2B).

In the case of the omicron variant, there are a number of mutations in the genome that can impact NAATs. One of the mutations that impacts multiple approved NAATs is a spike (S) gene deletion (Δ69-70) (Fig 2B). For NAATs that only target the S gene, there will be a total failure (Fig 2C). However, for NAATs that target the S gene and other genes, this deletion results in what is called "S gene drop out" or "S gene target failure"(SGTF) (Fig 2C) [3]. In this case, while the S gene is not amplified, the other genes would be amplified and analytic sensitivity will be retained (Fig 2C). Because the previously globally dominant variant, delta, does not have the Δ69-70, SGTF was a useful way to monitor for the introduction and spread of omicron [4]. However, omicron now has sub-lineages (termed "BA.") (Fig 1 and 2D). BA.2 lacks the Δ69-70 which lead to the term "stealth variant" as it would not be picked up by SGTF alone and demonstrates the importance of coupling sequencing with diagnostic surveillance. In addition to the SGTF, there is also Nucleocapsid gene target failure with omicron [2].

The second type of diagnostic that can detect an acute infection are antigen assays. These assays detect the virus or viral protein (antigen) (Fig 3A). The most common are the lateral flow type, however, there are more advanced assays the have microfluidic or digital ELISA technology. We'll focus this newsletter article on the lateral flow assays as they are the most common and a number are approved for home collection. Additionally, while the overall technology may be different, the principle of detection of the virus/viral antigen via labeled antibodies is the same. Therefore, impacts due to viral variants on lateral flow assays can be applied broadly. In lateral flow antigen assays, a specimen is added to a sample pad and a liquid buffer is applied. The liquid results in capillary action, moving

Figure 3. Impact of omicron on rapid antigen tests



the sample onto a conjugate pad. The conjugate pad will contain labeled antibodies. These antibodies will bind to the viral antigen and the sample will continue up the cassette via capillary action where the viral antigen-labeled antibody will encounter lines of antibodies (specific for the virus and a control). Binding of the viral antigen-labeled antibodies resulting in the colored lines (Fig 3A).

Because antigen assays recognize a tertiary structure, they are typically thought to be less vulnerable to mutations impacting their performance compared to NAATs. Additionally, most antigen assays target the Nucleocapsid which is less prone to mutations than the Spike. In the case of omicron, however, there are mutations in the Nucleocapsid. There are three shared mutations with the lambda variant: P13L, R203K, G204R [5] which have previously been shown to not impact diagnostics (US Government RADx program). However, omicron and its sub-lineages also contains a deletion (Δ31-33). This could impact the performance of antigen assays (Fig 3B) resulting in decreased analytical sensitivity (meaning greater amounts of virus may need to be present to be detected).

The US FDA in conjunction with the RADx program is testing all available antigen assays with FDA EUA. Interestingly, initial testing was done using heat-inactivated samples in early December 2021 and no impact on performance was observed. However, when the assays were tested using live virus at the end of December 2021, a slight decrease in performance was observed for some tests [2]. This indicates that the tertiary structure may be important in the overall performance of the antigen assays; heat-inactivation may alter the viral protein target, revealing parts that may be obscured in the natural conformation. Therefore, live virus from culture or clinical samples should be used to assess performance when possible. A number of pre-prints and peer reviewed articles have come out looking at the performance of various antigen assays with the omicron variant [6-13]. In general, omicron was found to largely retain clinical performance, however, there is some impact on the analytical sensitivity with some antigen tests. For the WHO EUL tests, Panbio COVID-19 Ag Rapid Test, SD Biosensor STANDARD Q COVID-19 Ag Test [14], used in Indonesia, two studies have shown some impact on performance [12, 13], but usually only in cases where the viral load is low (corresponding to Ct values of 28 and above).

Early in the emergence of omicron, there were anecdotal reports and a few pre-prints showing that omicron may be detected in the saliva before the nasal cavity both by PCR and by antigen tests [15, 16]. While this difference may represent an importance difference in the overall biology and tissue tropism of omicron [17], it is important that the manufacturer's instructions are followed for the NAAT or antigen tests because the tests are veri-

fied and approved with specific sample types. Unless otherwise indicated, most diagnostic tests were not designed for saliva or oral/throat swabs; oral microflora may cause false positive while innate viral inhibitors in saliva can result in false negatives and therefore, diagnostics that are approved for saliva or oral/throat swabs may have additional enzymes or steps that optimize detection of the SARS-CoV-2 [18].

As the virus continues to evolve, it's important that diagnostics are monitored. Updates may be needed as most are based on the original Wuhan-1, however, for the most part omicron can still be detected with current methods with a few caveats.

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INA-RESPOND Newsletter

HIGH-INTENSITY INTERVAL TRAINING: IS IT FOR EVERYONE?

By: Risky Dwi Rahayu

Risky Dwi Rahayu

Introduction

People nowadays are more prone to have sedentary behavior and be physically inactive. World Health Organization (WHO) recommended adults perform 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic activity per week.1 This is a challenge for most people since technology enables people to have more screen time, either on computers for working purposes or for spending leisure time by watching television, playing video games, or scrolling the smartphones. Moreover, during the COVID-19 pandemic, people are exposed to lockdown policies. They spend more time at home, have limited access to places, and reduce their previous mobility.

Long before the pandemic, national health research in Indonesia (RisKesDas, 2018) identified that more than one-third of Indonesians aged more than ten years have less physical activity.2 The report also highlighted the proportion of overweight and obesity in adults as much as 35,4%. This is certainly a public health problem since obesity is a risk factor for non-communicable diseases. Moreover, people with obesity and physically inactive have a higher risk of mortality or receiving critical care if they are infected with COVID-19.3

Alternatives of exercise that is efficient and enjoyable at the same time might be beneficial to overcome physical activity barriers. Aside from technology-stimulated sedentary behavior and lockdown-effect on mobility, there were classical reasons to not to do physical activity. Here is listed lack of time, lack of social support, lack of energy and motivation, fear of injury, lack of skill, lack of facilities and high costs, or weather condition.4 High-Intensity Interval Training (HIIT) is currently popular as one of the fitness trends from the American College of Sports Medicine (ACSM).5 It is widely available online, pretty easy to follow, and can be performed anywhere without specialized facilities. However, following online exercise programs doesn't necessarily promote health safety. Without adequate supervision, individuals are also exposed to the risk of injury or endangered those with comorbidities. In this article, we will discuss more the safety concern of HIIT and how to assess the risk of performing HIIT.

HIIT and its benefits

HIIT is one of the interval training which incorporate short 'work' period at high intensity and rest period in an alternating pattern.6,7 Generally, the work period achieves near maximal effort at [3] 80% maximal heart rate. The rest period serves as a recovery segment and is performed at low intensity. Compared to the traditional exercise pattern (continuous training), HIIT needs shorter time, but the effort is more vigorous. However, it is challenging to meet the adult's PA recommendation by HIIT alone because the high intensity may only cover 10-12 minutes of its duration. Many HIIT programs are based on aerobic activity such as running or cycling, but there is also resistance HIIT which uses bodily movements or free weights. Any exercise modalities are acceptable while assuring the intensity is met during the session.

Several physiological responses are listed as the benefits of HIIT:6,7

1. Aerobic performance: HIIT is better than moderate-intensity continuous training (MICT) in increasing cardiorespiratory capacity through a specific mecha-

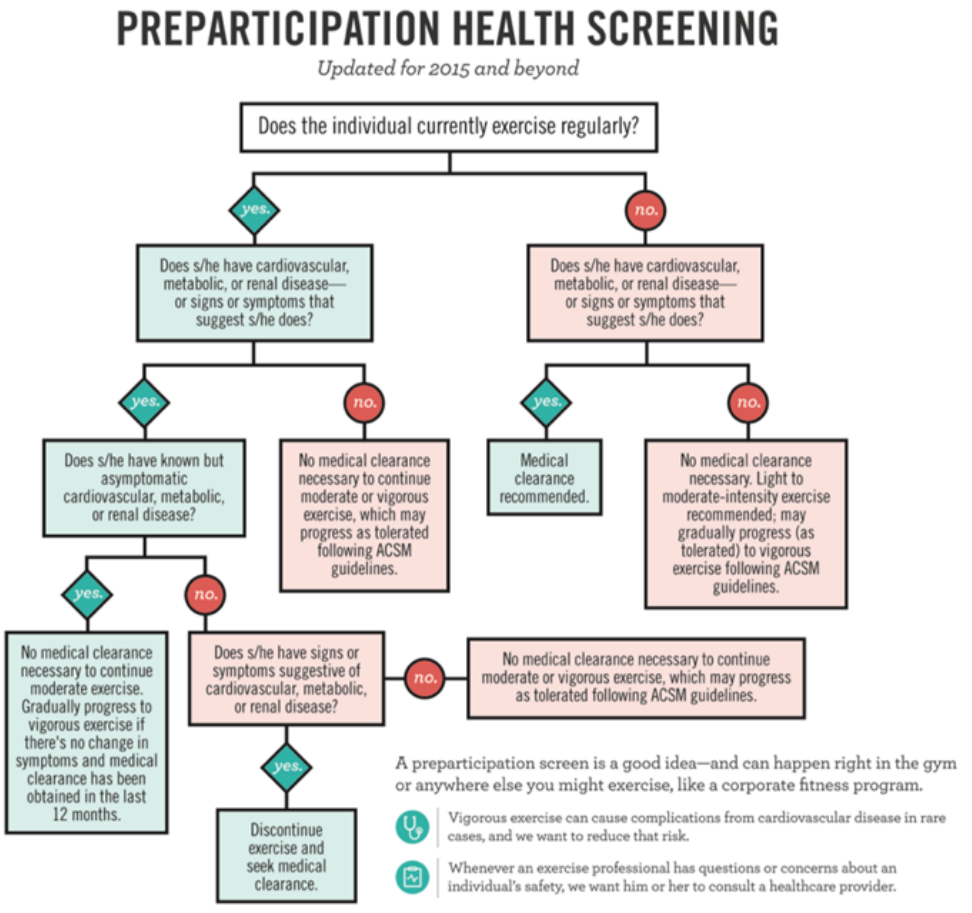
nism. Muscle mitochondrial content is increased significantly after a small volume of high-intensity exercise. After two weeks of routine HIIT, cardiorespiratory capacity could increase significantly.

2. Metabolic capacity: Replenishment of muscle glycogen after an acute HIIT is greater than other exercises. It mediated larger improvement in insulin sensitivity and glycemic control which is beneficial for type 2 diabetes mellitus patients. This effect may be seen as early as two weeks of regular training.
3. Cardiovascular health: HIIT demonstrates greater endothelial function improvement compared to continuous training. Due to the release of nitric oxide and the potential vasodilating effect, it is protective for cardiovascular function and health.

Not only does HIIT have physiological benefits it also elicits a great psychological response.7 In terms of effects, HIIT is more pleasurable not only in the rest period but also during the high-intensity work. Research indicates that during the short-intense work, the effect is not different from the MICT and is more positive than continuous vigorous-intensity exercise.7 It was found that the most pleasurable HIIT had £ 60 seconds high-intensity work period and was performed with near maximum effort (± 90 % aerobic capacity). Affective responses during exercise are better to predict adherence to the exercise program. Hence, adherence to HIIT is higher than continuous training. In terms of enjoyment, which is measured by cognitively evaluating the exercise situation, HIIT also provides high enjoyment to the participants. All psychological responses of HIIT support the fact that HIIT is well received and promising as one exercise program with long-term adherence.

Safety Concern

HIIT is probably an excellent pick if we want to improve the health and fitness of the wide population, supported by its physiological and psychological benefits. However, we should be cautious about the selection of participants since high-intensity exercise is not suitable for everyone. The best exercise for an individual is the one that is suitable to her/his health condition and level of fitness. This is important to note so they could achieve their fitness goals and gain the most for their health. In relation to that, it is important to do a risk assessment before choosing HIIT as an exercise program. Several points to be identified are current physical activity level, signs/symptoms of certain diseases, previous history of diseases or musculoskeletal injury, and planned exercise intensity.8



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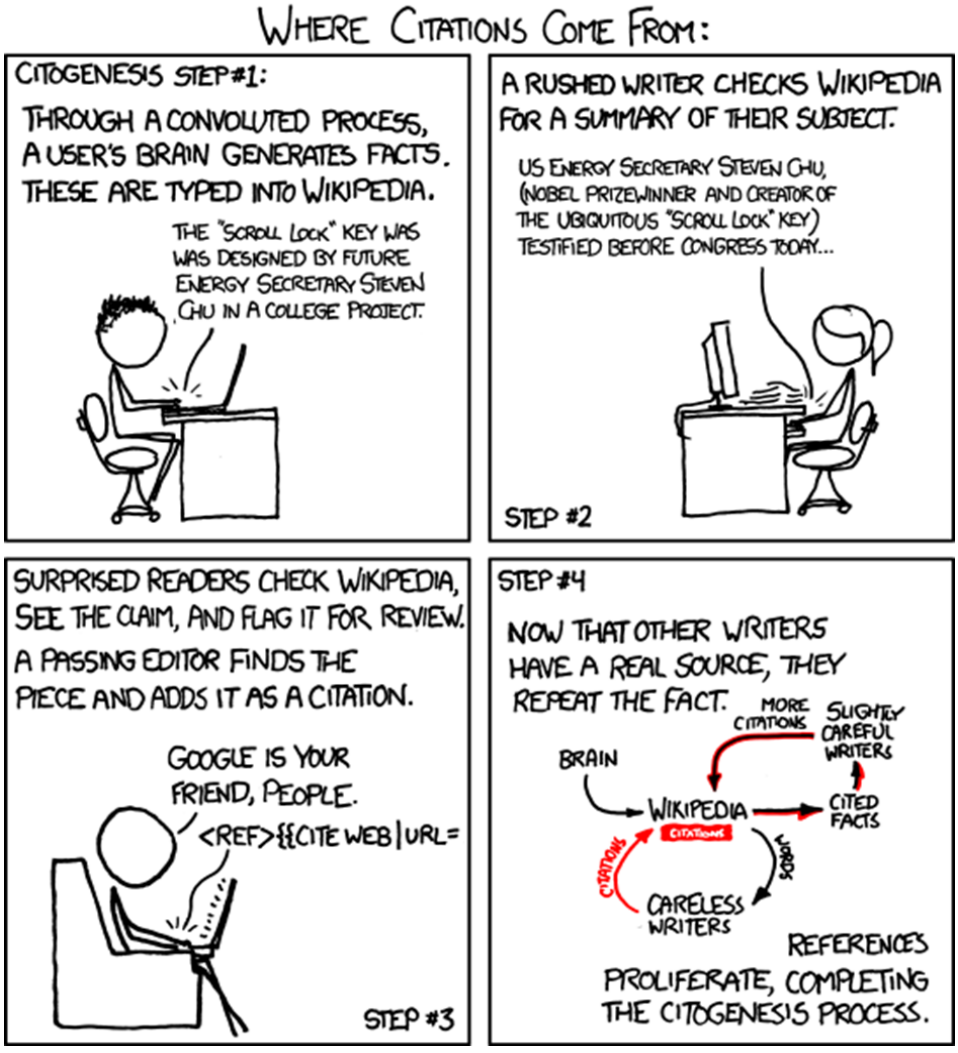
INA-RESPOND Newsletter

COMIC CORNER

ZOTERO: FOR PEOPLE WHO LOVE FREEBIES

By: Aly Diana



I used to have a paid reference manager, but then I lost my student license when I graduated. I managed to live without a reference manager for a while, but yes, life is more manageable when I have one. Later, I heard about Zotero. "Zotero is a free, easy-to-use tool to help you collect, organize, cite, and share research." Yes, that day was a good day. Disclaimer: I will not compare Zotero to any paid or free reference managers out there, I am sure you have your own favorite if you are familiar with any of them. For people who are looking to have a free reference manager or want to try one, Zotero may be the answer to your quest.

Zotero called itself "your personal research assistant" – not only a reference manager; and so far, I do agree with it. Zotero has been around since 2006, and I asked myself where I have been? Good news, for people who like their privacy, we don't even need to create a Zotero account to use it. Check https://www.zotero.org/why to learn more about why Zotero is a good choice. Among many things, Zotero enables us to 1) Create a personal database of references relevant to us, along with associated files, which will help us to manage our research easily; 2) De-duplicate references retrieved from multiple sources. Insert references into a Word document and format them automatically in a citation style of your choice; 3) Share our reference library with other researchers; 4) Showcase our work to connect and collaborate with researchers worldwide.

In terms of creating a personal database and using Zotero properly, it is recommended to install the Zotero Connector for Chrome, Firefox, or Safari and the Zotero desktop app. The Zotero Connector's save button is the most convenient and reliable way to add items with high-quality bibliographic metadata to our Zotero library. As we browse the web, the Zotero Connector will automatically find bibliographic information on web pages we visit and allow us to add it to Zotero with a single click. Clicking the save button will create an item in Zotero with the information it has identified. On many sites, Zotero will also save any PDF accessible from the page or an open-access PDF that can be found for the saved item.

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Generally, HIIT is safe for low-risk individuals. They are those who regularly exercise and do not have cardiovascular, metabolic, or renal disease. Those who don't exercise regularly and don't have cardiovascular, metabolic, or renal disease could do HIIT with gradual progress as tolerated. This group do not need medical clearance but may need a consultation with sports and exercise medicine specialist. Those who exercise regularly and have asymptomatic cardiovascular, metabolic, or renal disease fall into the moderate-risk group. They could perform HIIT if they receive medical clearance from professionals. High-risk individuals are not recommended to do HIIT unless directly supervised by medical professionals during the exercise; they are individuals who don't exercise regularly and have cardiovascular, metabolic, or renal disease or those who exercise regularly but have symptomatic cardiovascular, metabolic, or renal disease.

Other than the risk assessments aspects, exercise modalities should be carefully determined. The treadmill has a higher risk of injury so the patient should be cautious while performing HIIT. Adjusting the grade may be more acceptable than the speed.7

Conclusion

HIIT is acceptable as an exercise option for individuals who want to increase their health and fitness levels. It has many outcomes with a low volume of work and minimal time commitment. However, HIIT could come in different patterns and modalities. Moreover, there are safety concerns that should be noted especially for those who do not exercise regularly or have cardiovascular and metabolic diseases. Consultation with sports and exercise medicine specialists may help to identify the appropriate modalities and methods to perform HIIT.

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