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High-Quality Research, True Academics, Real Experts

FROM THE EDITOR'S DESK

It is with great pleasure to greet you with this newsletter again. There are some very interesting news and happenings in macrocosm of clinical research. Locally, we have the CRU annual report of the research activities in HPUPM for the first time since its inception. Also, check out the researches that have won grants and innovative surgical technique that has won recognition.

World Health Organization (WHO) has chosen the term **post COVID-19 condition** quite early this year to address the altered health of individuals after COVID-19. In addition to that are suggested approaches (Global Clinical Platform) and case record form in future research about this health condition. This issue of the newsletter sees it is fit to bring readers attention to this by forwarding the key points on this initiatives recently published in an article in the WHO Bulletin. Hopefully, a better coordinated international effort in the research in post COVID-19 condition could be materialised.

Living with COVID-19 endemic is shrouded in many uncertainties and pseudoscience indicators when it should dawn on us, and messed up by the recent arrival of SARS-CoV-2 Omicron variant. In the 8th response, the **Pandemic Scientific Response team** has provided the latest information on Omicron, explanation on proper use of the RTK-Ag and antibody testing and the possible safe living routines with SARS-CoV-2 and COVID-19 in the presence of better vaccines as the preventive measure, and anti-viral treatments as an effective therapy.

HPUPM has the motto of Providing Extraordinary Care Together. Being an academic medical centre or more commonly known as a university teaching hospital, its indispensable roles of providing effective therapy to people with illness, best teaching and training students will be relying on a strong know-how and know-what foundations. These come from ability to appreciate high-quality clinical evidence, to produce and to translate those evidence to clinical and teaching practices in the hospital. The central to this all is none others but having high-quality researchers and scholars among the staffs who not only are the users but also producers of high-quality evidence. This leads to becoming true academics and real experts who are sensitive and courageous to the needs of the people. Take your time to scrutinise the faculty's research strategic planning for years 2021-2025 and to reflect on **High-quality Research, True Academics, Real Experts** movement concept sharing. Do this individually and as a group in your department, repeatedly, to encourage and motivate each other as well as to hold each other including the CRU and administrators in both hospital and faculty responsible until we achieve these in ourselves, together. An exciting research culture exists when it is done collectively, present with integrity and productive. I will leave the opposites of high-quality research, true academics and real experts to you for they have been around for too long in many.

The landmark systematic review by Chu DK, Akl EA, Duda S. et al. on the **Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis.** *Lancet.* 2020; **395**: 1973-1987 has shaped many SOPs in Malaysia and other countries in the early days of the COVID-19 pandemic and even today. Equally, it has sparked many debates on its necessity and quality of clinical research that produced it. In this issue, the points of argument and counter arguments have been collected and published as polemics in the Lancet volume 398, issue 10301 (August 21, 2021). These are indeed very educational and they drive home the message that medical evidence is to be judged with care, it is on a continuum rather than categorical.

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BREAKING NEWS

Post COVID-19 Condition

Janet V Diaz, Margaret Herridge, Silvia Bertagnolio, et al. Towards a universal understanding of post COVID-19 condition. Bull World Health Organ 2021;99:901–903.
doi: http://dx.doi.org/10.2471/BLT.21.286249

*"In September 2020, the World Health Organization (WHO) convened a consultation with Member States on the International Classification of Diseases ICD-10 and ICD-11 codes (Fig. 1) and proposed the use of the term **post COVID-19 condition** to diagnose and code patients with this condition. This terminology does not attribute causality and does not refer to any duration, unlike other terms such as chronic COVID-19 syndrome; late sequelae of COVID-19; long COVID; long haul COVID; long-term COVID-19; post COVID syndrome; post-acute COVID-19; post-acute sequelae of SARS-CoV-2 infection and others."*

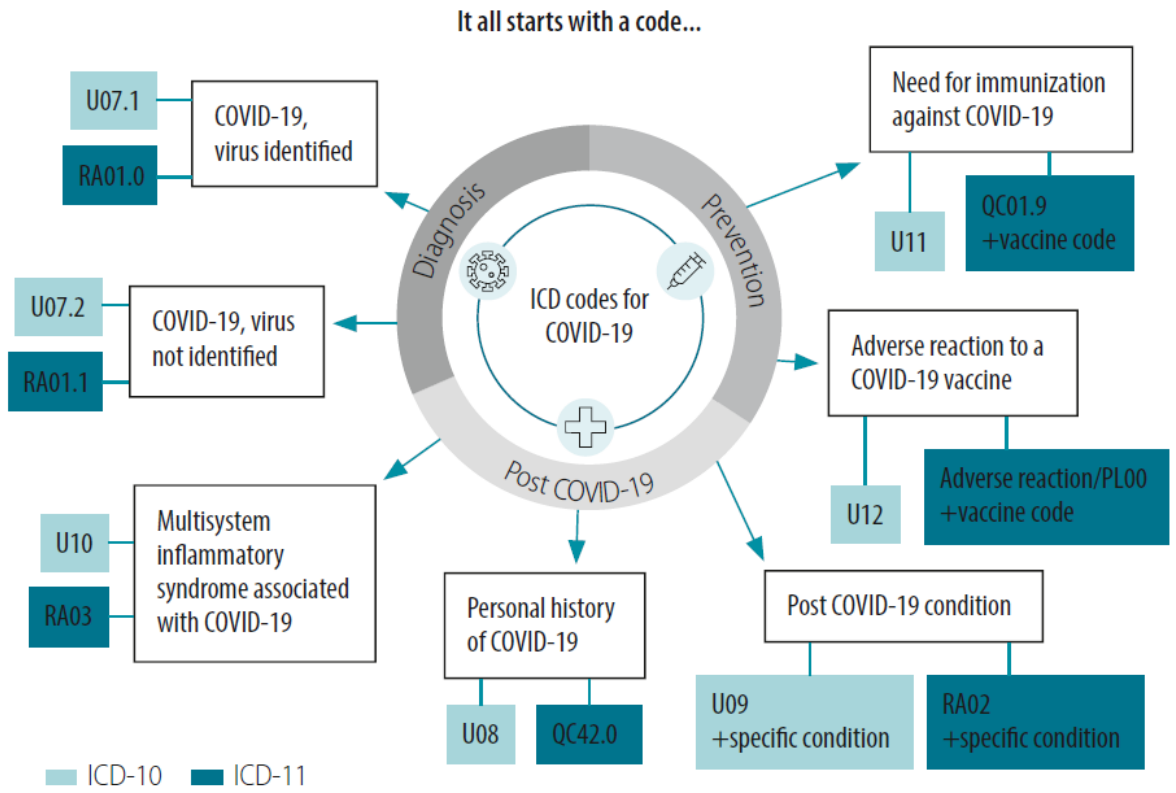
"The foundational work was initiated, but the development of a case definition is an ongoing process. WHO will request further inputs using a methodologically rigorous approach through a Delphi process. More evidence is needed to determine the relationship between the time course from exposure to infection and the duration and severity of the acute episode of COVID-19 on the one hand, and the recovery from or persistence of the post COVID-19 condition on the other."

"Fewer than 1% (45/5000) of ongoing COVID-19 research studies are focused on studying post COVID-19 condition – or its associated terminologies.14 Most studies are based on patients from hospital series. For this reason, new research from primary care and community-based settings is essential to incorporate the experience of those patients who were less likely to be hospitalized, including younger patients, and those who had either a mild infection with fewer symptoms or were undiagnosed."

"New investigations must include a focus on children, women, older adults, diverse ethnic origins and socioeconomically disadvantaged groups and marginalized populations including incarcerated individuals, migrants, refugees and all those suffering stigma and discrimination."

"Finally, this work must be multicentre and multidisciplinary, and involve international cooperation. Collecting standardized and harmonized data on post COVID-19 condition will be paramount, as available published studies are small, heterogeneous in nature, too short in their follow-up, and with narrow focus on a few organ systems assessed. To support systematic collection of comparable data across the world, WHO has developed a Global Clinical Platform and standardized case report forms for acute COVID-19 and post COVID-19 condition that are available for all Member States and interested parties."

Fig. 1. **Emergency use ICD codes for COVID-19 disease outbreak**



COVID-19: Coronavirus disease 2019; ICD: International Classification of Diseases.
Source: World Health Organization.[10]

Reproduced from Bull World Health Organ 2021;99:901–903, Janet V Diaz, Margaret Herridge, Silvia Bertagnolio, et al. Towards a universal understanding of post COVID-19 condition, page 902, Copyright (2021).

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Living with COVID-19 endemic (of SARS-CoV-2 Omicron): self-test with RTK-Ag, antibody testing and antivirals against SARS-CoV-2

First published on 23rd December 2021 by Boon-How Chew, Beng-Kah Song, Hui-Yee Chee and Yit-Siew Chin for the Pandemic Scientific Response team

Caution: Summary is a preliminary report of work by Pandemic Scientific Response team. It will be continuously updated in accordance to the unfolding of events and emerging of scientific evidence.

In Brief

- Living with SARS-CoV-2 in the endemic COVID-19 will depend on the circulating variant's pathogenicity to humans (gentle or ferocious), this would decide the nature of the booster vaccine, and the level of appropriate SOPs in daily life.
- Armamentarium of the world living in the endemic COVID-19 would include accurate and rapid diagnostic testing for SARS-CoV-2, viral genomic surveillance, availability of and accessible to better vaccines, healthy lifestyle as the mean to good immune system, effective and safe oral antiviral drugs against SARS-CoV-2.
- Any dispute or doubt about COVID-19 vaccine effectiveness is unintelligible and irrational. Long-term safety and efficacy are yet ascertained.
- The vaccines are effective in preventing SARS-CoV-2 infection, transmission to others, preventing severe COVID-19, lesser hospitalisation, faster recovery and lower deaths even in the face of the SARS-CoV-2 Delta and Omicron variants (but reduced efficacy from laboratory findings).
- Breakthrough infections are more likely in older people with other comorbidity, immunocompromised people, related to vaccine type and concentrate, time after vaccination and community incidence rates.
- RTK-Ag tests performance has to be interpreted based on the study population from where the results came about. They were most accurate when used in the first week after onset of symptoms.
- Based on a recent review, in people with confirmed COVID-19, antigen tests correctly identified the infection in an average of **72% of people with symptoms**, compared to **58% of people without symptoms**; in people who did not have COVID-19, antigen tests correctly ruled out infection in **99.5% of people with symptoms** and **98.9% of people without symptoms**.
- COVID-19 antibody tests measure antibodies to SARS-CoV-2 which are produced 1-3 weeks after infection or vaccination.
- Not all antibodies neutralize the virus, the laboratory analysers are machine- and laboratory-dependant, concurrent memory B cells, CD8+ T cells and CD4+ T cells against SARS-CoV-2 are believed to be protective and can persist for more than 6 to 8 months.
- Antibody tests are not recommended for checking whether one has been truly vaccinated, or the immunity is working well, or whether it is time for a booster jab.
- Two most promising oral antivirals to date are the **molnupiravir** and **ritonavir**.
- Molnupiravir has an efficacy of **3.0%** absolute risk reduction or a **30%** relative risk reduction in reducing hospitalization and death in at risk adults with mild-to-moderate COVID-19 compared with a placebo.
- Ritonavir (PAXLOVID™) reduced risk of hospitalization or death by **89%** in Phase 2/3 EPIC-HR STUDY in an interim analysis.

Living with COVID-19 endemic (of SARS-CoV-2 Omicron): self-test with RTK-Ag, antibody testing and antivirals against SARS-CoV-2

First published on 23rd December 2021 by Boon-How Chew, Beng-Kah Song, Hui-Yee Chee and Yit-Siew Chin for the Pandemic Scientific Response team

SARS-CoV-2 has caused much changes to the world socio-economic routines and many lives lost, more than 5 million recorded from more than 260 million cases till now [1]. From the past years of worldwide effort of combating the COVID-19 pandemic, the SARS-CoV-2 behaviours known to us has thus far produced some insightful viewpoints [2,3]. COVID-19 could be compared to influenza on possible scenarios of humans living with SARS-CoV-2 suggesting the life with repeat booster vaccination, repeated self-testing and a need for effective antivirals as the treatment for COVID-19 [3].

COVID-19 RTK-antigen and antibody tests are expected to be a new norm of life or even routine tests before travelling. These tests have their clinical indications and performance to be understood less they are misunderstood, misused or abused. Since the commencement of vaccination program in February 2021, the public's clamour for antibody testing is not waned, especially when the need for booster shot was recently raised, for "checking" whether one had been genuinely vaccinated, or whether one's antibody level is "high enough" to provide protection. While the antigen testing has gained a foothold in almost daily life of many school children, travellers and even larger meeting attendees as a compulsory screening testing.

Recent evidence has proven the effectiveness of the vaccines in preventing COVID-19 and to a larger extends in preventing severe COVID-19 and deaths even in the face of new SARS-CoV-2 variants namely the Delta and Omicron. Early reports showed that the vaccine efficacy against the Omicron is 40x lesser after the 2 doses and **75%** against symptomatic COVID-19 after the booster of the 3rd dose when compared to that against the Delta [4,5]. People who are vaccinated are less likely to develop symptoms, more likely to recover from their illness, and much less likely to require hospitalization compared with unvaccinated people [6-8]. The similar with Omicron is yet to be clear [9,10]. With more than 50 mutations [9] multiplies **70 times faster** in human bronchus [10], Omicron is very infectious with > **5 times** more than the Delta which was **2 times** more transmissible than the original Wuhan strain, and the viral loads **> 1000 times** higher than those in people infected with the original viral strain [11,12]. The reports so far have indicated that there were mostly mild diseases in the vaccinated but no milder than the Delta in the unvaccinated [12]. The protection afforded by past infection against reinfection with Omicron may be lower than 20% [12], lower than 40 times with Pfzer/Moderna vaccination, almost none with Sinovac vaccinations [13,14]. Omicron COVID-19 symptoms were mild flu-like include mainly myalgia (muscle ache), headache (could be very severe), sore throats, nausea, and slight temperatures.

> *A point-prevalence survey of almost 100 000 people conducted in England in June-July 2021 during the height of that country's spring Delta variant surge found that fully vaccinated people (n = 55 962) were two-thirds less likely to harbor SARS-CoV-2 compared with unvaccinated people (n = 15 135), with absolute rates of 0.40% vs 1.21%, respectively* [15]*. Likewise, in a randomized trial of the mRNA-1273 vaccine (Moderna) vs placebo, vaccinated participants (n = 14 287) were two-thirds less likely to be asymptomatic carriers than unvaccinated participants (n = 14 164), with absolute rates of 1.5% vs 3.5%, respectively (estimated vaccine effectiveness against asymptomatic infection, 63.0% [95% CI, 56.6%-68.5%])[6].*

Another study [16] among 1197 patients hospitalized with symptomatic COVID-19 observed that those vaccinated were less likely to require intensive care (25% vs 40%), less likely to require invasive mechanical ventilation (7.7% vs 23%), and less likely to die (6.3% vs 8.6%). These differences persisted after risk adjustment: the odds of invasive mechanical ventilation or death by day 28 among vaccinated patients was significantly lower than among unvaccinated patients (12.0% vs 24.7%; aOR, 0.33 [95% CI, 0.19-0.58]).

However, new evidence shows that fully vaccinated people can still infected with SARS-CoV-2 and down with COVID-19 but they are less likely to become infected and contagious for shorter periods than the unvaccinated people. Studies of viral dynamics suggest viral loads in vaccinated people with breakthrough infections may be as high in unvaccinated people, but the viral loads in the vaccinated decline more rapidly and less likely to be culture-positive compared to that in the unvaccinated people [17, 18].

In a study of 7771 household contacts of 4921 index cases in the Netherlands, the rate of transmission from fully vaccinated household members was 13% vs 22% from unvaccinated household members (estimated vaccine effectiveness against transmission, 63% [95% CI, 46%-75%]) [17]. Similarly, in an English study of 151 821 contacts of 99 567 index patients, the rate of transmission from people fully vaccinated with BNT162b2 (Pfizer-BioNTech) was 23% vs 49% for transmission from unvaccinated people (adjusted odds ratio [aOR], 0.35 [95% CI, 0.26-0.48] for transmission of Delta to unvaccinated contacts; aOR, 0.10 [95% CI, 0.08-0.13] for transmission of Delta to fully vaccinated contacts) [18].

Breakthrough infections are due to differences in the person's immune status, age, vaccine type/preparation, time since vaccination, and infection with the Alpha vs Delta variants. Breakthrough infections are more likely in the older people with other comorbidity, immunocompromised people, related to vaccine type and concentrate, time after vaccination and community incidence rates [6]. Yet, it is unknown why both humoral and cellular immunity wane over time and do not seem to protect against breakthrough infections when the same viruses are circulating.

*Among immunocompetent hospitalized patients for COVID-19, **11.2%** were vaccinated vs **53.5%** among controls (aOR for vaccination, 0.10 [95% CI. 0.09-0.13]). Whereas among the immunocompromised patients hospitalized with COVID-19, **40.1%** were vaccinated vs **58.8%** of immunocompromised controls (aOR for vaccination, 0.49 [95% CI, 0.35-0.69]). Protection against hospitalization was similar for the Alpha and Delta variants (aOR, **0.10** [95% CI, 0.06-0.16] for Alpha; aOR, **0.14** [95% CI, 0.10-0.21] for Delta). This similar observation was noted across different age groups.*

The Moderna vaccine (aOR, 0.11 [95% CI, 0.08-0.14]) was better than the BioNTech-Pfizer vaccine (aOR, 0.19 [95% CI, 0.16-0.23]) ($P < 0.001$) in overall protection again COVID-19, but they showed marked differences when taking into consideration time since vaccination. The protective association against hospitalization for the BioNTech-Pfizer vaccine more than 120 days following vaccination declined somewhat (aOR, 0.36 [95% CI, 0.27-0.49]; the median was 143 days from vaccine dose 2 to illness onset), whereas the effectiveness of the Moderna vaccine more than 120 days postvaccination was largely preserved (aOR, 0.15 [95% CI, 0.09-0.23]; the median was 141 days from vaccine dose 2 to illness onset) ($P < 0.001$).

COVID-19 antigen testing

In a recent Cochrane review [19] that included 64 studies with a total of 24087 nose or throat samples, and 7415 confirmed COVID-19 samples, investigated 16 different antigen tests and 5 different molecular tests, and studies were mainly in Europe and North America. Some of these assays were shown to meet appropriate criteria, such as the WHO's priority target product profiles for COVID-19 diagnostics as 'acceptable' when the **sensitivity is ≥ 80%** and **specificity ≥ 97%**.

The tests performance were reported that in people with confirmed COVID-19, antigen tests correctly identified COVID-19 infection in an average of **72% of people with symptoms**, compared to **58% of people without symptoms**. Tests were most accurate when used in the first week after symptoms first developed (an average of 78% of confirmed cases had positive antigen tests). This is because people have the most virus in the first few days after infection. In people who did not have COVID-19, antigen tests correctly ruled out infection in **99.5% of people with symptoms** and **98.9% of people without symptoms**. For molecular tests, although overall results for diagnosing and ruling out COVID-19 were good (95.1% of infections correctly diagnosed and 99% correctly ruled out), 69% of the studies used the tests in laboratories instead of at the point-of-care.

Understanding and Interpreting the Test Performance

Before reading the test performance results, do make sure you understand about the study designs. The meaningful results rely on whether the diagnostic test study was carried out

- using a test kit that was of high quality in its creation such as based on sound scientific basis (eg. best antigen and reagent) and good materials,
- in study samples who were experiencing the disease, in situations where the test was required or indicated (the study samples should not be all or mostly in the highly likely or unlikely to have the disease category),
- the test must be compared to a referent test of proven accuracy,
- the researcher or assessor who performance the test should be blinded from the referent test result, and vice versa, and
- all the test performance indicators are analysed and generated from the same study samples and not separate study samples for different indicators.

The **sensitivity** of a test indicates the proportion of the people with the disease who have a positive test for the disease. A sensitive test will rarely miss the people with the disease. This causes a highly sensitive test to have many **false-positive** test results. Since a highly sensitive test tends to give positive results, it gives very few negative results and naturally also very few false-negative results. Therefore, a highly sensitive test should be highly regarded when its test result is negative; it is useful to 'rule out' diseases. Therefore, a highly sensitive test has high **negative predictive value**, given the same setting. Without concurrent proven good specificity level, a test with high sensitivity is a 'strong' but poor in differential quality.

The **specificity** of a test signifies the proportion of people without the disease who have a negative test for the disease. A specific test will rarely misclassify the people without the disease as diseased. This causes a highly specific test to have many **false-negative** test results. In other words, a highly specific test has very few false-positive results. Thus, a highly specific test should be highly regarded when its test result is positive; it is useful to 'rule in' the disease. Therefore, a test with a higher specificity is also a test with higher **positive predictive value**, given the same setting. Without concurrent proven good sensitivity level, a test with high specificity is a 'weak' and poor quality test.

Conventionally, high **sensitivity** tests are desirable for dangerous but non-fatal and treatable conditions; and high **specificity** tests are used to confirm conditions that are serious, without efficacious treatment and traumatic physically, psychologically, socially and financially from the diagnosis or treatment.

In the context of COVID-19 pandemic and endemic, test kits that are high in sensitivity is preferred among the vaccinated for social activity related decisions. Whereas test kits that are high in specificity is preferred among the unvaccinated as they are more likely to contract the infection where 'ruling-in' quality is more important than unnecessarily 'strong' sensitive test.

Extracted and adapted from Chapter B: Classification of clinical research, Section: Diagnostic research, page 39. Chew Boon How. Understanding and Conducting Clinical Research- A Clinical Epidemiology Approach by a Clinician for Clinicians. 3rd Print, 2021. ISBN 978-967-960-449-8. UPM Serdang. Malaysia.

What: There are antigen and molecular-based tests for detection of current infection that are suitable for use at the point of care [19]. Both tests use the same respiratory-tract samples by swabbing, washing or aspiration as for laboratory-based RT-PCR, and newer tests accept saliva sample. Rapid antigen tests use lateral flow immunoassays in the form of disposable plastic cassettes akin to a pregnancy test. Antigen detection is captured and indicated by visible lines on the test strip (colloidal gold-based immunoassays, or CGIA), or through fluorescence, which can be detected using an immunofluorescence analyser (fluorescence immunoassays or FIA). While, the molecular-based tests detect viral ribonucleic acid (RNA). This has historically been the laboratory-based assays using RT-PCR technology. Recent technological advances have allowed molecular technologies to be suitable for use at the point-of-care. However, these are small portable machines and they take longer to produce results compared to antigen tests. The Foundation for Innovative Diagnostics (FIND) and Johns Hopkins Centre for Health Security have maintained online lists of available tests for SARS-CoV-2 (FIND 2020). Table 1 enlists the currently available self-test kits and their reported performance. Medical Device Authority (MDA) Malaysia is routinely updating the approved self-test kits on their website. However, beside administrative information about the test kits there are no clinical performance results being published even though these are believed to be submitted to MDA. It is also stated on the website that "*the use of COVID-19 self- test kit shall be limited for screening purpose only and all test results need further confirmation using RT-PCR*". This blanket statement is unjustified and every test kit should stand it its own pit of performance.

Why: Point-of-care tests could be a good replacement for RT-PCR if they are sufficiently accurate. This test can help in screening and rapid management such as for quarantine or treatment, contact tracing or for confirmatory RT-PCR testing for those with symptoms and a negative test result.

> If sufficiently accurate, **negative** rapid test results in **symptomatic** patients could allow faster return to work or school, therefore conferring important economic and educational implications; or prompts immediate consideration of other causes of the symptoms, for example bacterial pneumonia or thromboembolism. For **asymptomatic** individuals, accurate rapid tests may also be considered for screening at-risk (exposed) populations such as frontliners, in-hospital workers or in local outbreaks [19].
>
> *Rapid tests, particularly antigen tests which can be more easily delivered at scale, could also be used for mass screening purposes or used in a more targeted fashion such as single test application at airports or for border entry, to allow entry to large public gatherings, or screening students as a risk-reduction strategy. Preliminary data on the rollout of such a policy in the UK has highlighted the many challenges in such an approach, and the requirement for full and proper field trial evaluations. Frequent repeated use of antigen tests in asymptomatic individuals with no known exposure to identify COVID-19 cases has also been proposed, but field trial evaluations would be required to determine whether promising results from modelling studies can be borne out in practical settings [19].*

When: Patients may be tested for SARS-CoV-2 when they present with symptoms, have had known exposure to a confirmed case, or in a screening context asymptomatic and no known exposure to SARS-CoV-2. The standard approach to diagnosis of SARS-CoV-2 infection is through laboratory-based testing of swab samples taken from the upper respiratory (e.g. nasopharynx, oropharynx) or lower respiratory tract (e.g. bronchoalveolar lavage or sputum) with RT-PCR.

RT-PCR is considered the reference standard. However, ***RT-PCR continues to detect viral RNA days and weeks after the onset of infection****, and this will wrongly classify some people as infectious if clinical history is ignored. The use of the* ***cycle threshold*** *(**Ct** value) [also known as* ***quantification cycle*** *(**Cq**) or* ***crossing point*** *(**Cp**) values] from RT-PCR results to group individuals above or below a particular value (as a proxy for viral load) as more or less likely to be infectious is machine- and laboratory-dependant. Thus, Ct values are unlikely to be comparable across studies [19].*

Alternative reference standards that have been proposed for ***infectiousness*** *include assessing the viability of the virus using* ***viral culture****. However, viral culture is unsuitable as a reference standard because it is technically complex and often unreliable, and insensitive test because the failure to culture virus is often a result of the culture technique and not an indicator of non-infectiousness [19].*

COVID-19 antibody testing

Serology tests to measure antibodies to SARS-CoV-2 have been evaluated in people with active infection and in convalescent cases [20]. Antibodies are formed by the body's immune system in response to infections, and can be detected in whole blood, plasma or serum. Antibody tests are available for laboratory use including enzyme-linked immunosorbent assay (ELISA) methods, or more advanced chemiluminescence immunoassays (CLIA). There are also rapid lateral flow assays (LFA) for antibody testing that use a minimal amount of whole blood, plasma or serum on a testing strip as opposed to the respiratory specimens that are used for rapid antigen tests.

The "antibody testing" here refers to serology test looking for antibodies in the blood that are produced by our own immune system after being vaccinated or infected. The test must not be confused with the RT-PCR and RTK-Ag tests, which are respectively meant for assessing the viral RNA and antigen in the body. RTK-Ag serves as a screening test while RT-PCR is the gold standard to confirm the SARS-CoV-2 infection. This cannot be achieved by antibody testing. The reason is that the time needed for our body to produce antibodies after an infection is too long, ranging from 1 to 3 weeks or longer in some people.

So, since the antibody test could gauge the level of antibody after vaccination, and existence of these antibodies could implicate the body's preparedness to fight off the SARS-CoV-2 virus, why the "level of antibody" cannot be translated into the "strength of immunity"? To understand the rationale behind this, we need to know the basic immunology.

First of all, not all antibodies neutralize the virus. Only some antibodies can bind SARS-CoV-2 spike protein and prevent the virus from infecting cells, and almost all the clinical tests available on the market cannot differentiate between neutralizing antibodies from other non-neutralizing antibodies.

Second, even if there is, say, a company claims that the rapid test can be used to assess the level of neutralizing antibodies, it doesn't mean that low or high level of the neutralising antibodies translate into weak and strong immunity.

Although it is possible that higher titre (a technical term for "amount of antibody" in immunology) of antibodies does correlate with "increased protection", it merely means that a vaccinated person "might be" protected against COVID-19 [21]. In this case, the variants under study are B.1.177 and Alpha B.1.1.7, tested

using AstraZeneca vaccine. Such "no simple relationship" between the level of neutralizing antibodies and protection is made complicated by the fact that scientists still do not know the "minimum level" of the antibodies conferring protection. How high should the antibody level be to ensure an immunity protection, is dependent upon individual's immune system, which can be complicated. It is currently a question with no answer.

On the other hand, if a person has a lower level of neutralizing antibodies, it doesn't mean that the person has no protection. These circulating antibodies are only part of the COVID-19 immunological components. The more important responses upon vaccination are the production and retention of memory cells, which comprise memory T (including the killer T cells) and B cells. These memory cells serve as a strong and durable defence against SARS-CoV-2 when the real virus enters the body in the future. And this is the ultimate aim of having us vaccinated.

On top of the studies proving that the SARS-CoV-2 memory B cells, CD8+ T cells and CD4+ T cells persist for 6 to 8 months after the viral infection [22, 23], there are also recent studies supporting the notion that vaccination generates robust antigen-specific memory cells in humans. For instance, scientists from the University Of Pennsylvania Perelman School Of Medicine analysed the T-cell responses in 47 healthy individuals who were fully vaccinated by Moderna and BioNTech-Pfizer mRNA vaccines, and concluded that vaccine-induced T cells responses can be long-lasting [24].

Given the high standard research requirement of these assessments of memory cells, none of the currently available antibody tests on the market could relay the information of memory T or B cells. In line with the recommendation from the US CDC that "antibody testing is not currently recommended to assess for immunity to SARS-CoV-2 following COVID-19 vaccination", or to "assess the need for vaccination in an unvaccinated person" (CDC; https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html), the abovementioned research studies do not support the use of antibody tests for assessment of protection after COVID-19 vaccination. Worse still, different types of antigens are used in various antibody tests. The test used might not detect the antibodies induced by the specific vaccine type.

We do not intend to give the impression that the level of antibody does not spell out anything at all. It is just not a good idea to use it for checking whether one has been truly vaccinated, or the immunity is working well, or whether it is time for a booster jab.

Oral antivirals

Availability of effective oral antivirals against SARS-CoV-2 is perceived to be an important armamentarium of world living in the endemic COVID-19 [2]. This would come in as the widely accessible treatment for people with early or mild COVID-19. The other ends of the disease spectrum is taken care of by the vaccines and social SOP-measures as the preventive fortress, and the more invasive and restricted therapies such as monoclonal antibody infusion, intravenous steroids, supportive therapy of antimicrobials and extracorporeal or endotrachial oxygenation.

A frenzy exploration and testing of many possible and off-labels drugs of all kinds was seen in the past couple of years [25]. Two most promising oral antivirals to date are the **molnupiravir** by Merck and **ritonavir** by Pfizer.

Molnupiravir was recently reported to have an efficacy of **30%** relative risk in reducing hospitalization and death in at risk adults with mild-to-moderate COVID-19 compared with a placebo [26,27].

> The MOVe-OUT study of molnupiravir enrolled 1433 participants. The company shared data shows that the risk of hospitalization or death was 9.7% in the placebo group (68/699) and 6.8% (48/709) in the molnupiravir group; an absolute risk reduction of 3.0% (95% CI: 0.1, 5.9; nominal *p* value=0.0218) and a relative risk reduction of 30% (relative risk 0.70; 95% CI: 0.49, 0.99). Nine deaths were reported in the placebo group, and one in the molnupiravir group.
>
> *Molnupiravir (MK-4482, EIDD-2801) is an investigational, orally administered form of a potent ribonucleoside analog that inhibits the replication of SARS-CoV-2. Molnupiravir is being studied as a single medicine, without the use of concomitant medicines and without food intake restrictions or dose modifications based on renal or hepatic impairment [26].*

The FDA's antimicrobial drugs advisory committee came to a split 13–10 decision about molnupiravir [27] and some responsible clinical decision on prescribing it is cautioned. It might be used in highly selected patients who may be benefited more than its probable serious side effects:

1. Obesity and those high risk of hospitalisation and death from COVID-19 (elderly and multi-comorbid)
2. During or when there is high community infectivity rate of SARS-CoV-2
3. Not for people with diabetes mellitus, not kids, adolescents and not pregnant women as it may increase hospitalisation and inhibit bone growth, respectively
4. Those who are infected with earlier than Delta variant (uncertain on the Delta yet); also uncertain of efficacy among those vaccinated
5. To be used for a 5 day course, not less or more, or else the risk of
6. Severe probability of viral mutation to a bad variant
7. Serious probability of human DNA mutations

PAXLOVID™ (PF-07321332; ritonavir) is specifically designed SARS-CoV-2-3CL protease inhibitor to inhibit viral replication at a stage known as proteolysis, which occurs before viral RNA replication and the EPIC Development Program (see below) [28].

1. The Phase 2/3 **EPIC-HR** (Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients) randomized, double-blind study of non-hospitalized adult patients with COVID-19, who are at high risk of progressing to severe illness.
2. The Phase 2/3 **EPIC-SR** (Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients), to evaluate efficacy and safety in patients with a confirmed diagnosis of SARS-CoV-2 infection who are at standard risk (i.e., low risk of hospitalization or death).
3. The Phase 2/3 **EPIC-PEP** (Evaluation of Protease Inhibition for COVID-19 in Post-Exposure Prophylaxis) to evaluate efficacy and safety in adults exposed to SARS-CoV-2 by a household member.

The interim analysis showed that it reduced risk of hospitalization or death by **89%** in Phase 2/3 EPIC-HR STUDY. Should this treatment effect hold up in the end, PAXLOVID™ (ritonavir) would be the drug the world has been waiting for in the life of COVID-19 endemicity.

Conclusion

COVID-19 vaccine effectiveness should have no doubt from now onwards. Any dispute about it is unintelligible and irrational [2]. Similarly, the needs for and effectiveness of other protections have also been shown. These are:

1. Vaccination, complete the doses according to the type and get timely booster
2. Masking, use N95 or double masking of surgical and cloth masks, or antivirals-coated masks (coating with copper, silver, zinc, grapheme, etc.)
3. Avoid 3Cs, crowded and confined spaces, and closed conversation
4. Practise 3Ws, wear mask always as when needed, washing hands and body parts with soaps or appropriate sanitisers and on the alert about the warning symptoms
5. Improve air ventilation and indoor air quality,
6. Good mental health, good sleep, communicate nicely and frequently with all others and stay in good relationship
7. Healthy nutrition [29], consuming balance, moderate and variety of healthy foods, including 2-3 cups of coffee/day, 2-3 cups of tea/day, more vegetables, and avoid unhealthy diet such as processed meat (such as bacon, ham, sausages, meat pies, kebabs, burgers, chicken nuggets), and managing malnutrition problems (i.e. overweight and obesity, underweight, micronutrient deficiencies such as Vitamin D deficiency).
8. Exercise, both aerobic and muscle strengthening activities [30]

Some promising hopes in the near future are better vaccines (RBD-based vaccines that elicit high titres of S2X259-like neutralizing antibodies) [31] and oral antiviral drugs against SARS-CoV-2. These are to be affordable and equitable to all people to stop the pandemic of new mutated variants and as co-inhabitants of the 'new' world. Obviously, living with SARS-CoV-2 in the endemic COVID-19 will depend on the circulating variant's pathogenicity to humans ie. gentle or ferocious, this would decide the nature of the booster vaccine, and the level of appropriate SOPs in daily life. As viral fever, influenza and COVID-19 by the SARS-CoV-2's Omicron virus (hopefully so would be the future variants) are becoming more similar in clinical manifestation and symptomatology [32], the world should know better how to live with these viruses and diseases while always keeping the watchful eyes on them.

Reference

1. Ritchie H, Mathieu E, Rodés-Guirao L, et al "Coronavirus Pandemic (COVID-19)". Published online at OurWorldInData.org. Retrieved from: 'https://ourworldindata.org/coronavirus' [Online Resource]. 2020. Accessed on 08 December 2021, https://ourworldindata.org/coronavirus-data?country=~OWID_WRL#citation
2. Klompas M. Understanding Breakthrough Infections Following mRNA SARS-CoV-2 Vaccination. JAMA. 2021 Nov 23;326(20):2018-2020. doi: 10.1001/jama.2021.19063.
3. Monto AS. The Future of SARS-CoV-2 Vaccination - Lessons from Influenza. N Engl J Med. 2021 Nov 11;385(20):1825-1827. doi: 10.1056/NEJMp2113403. https://www.nejm.org/doi/full/10.1056/NEJMp2113403
4. James Gallagher. Omicron: Three vaccine doses key for protection against variant. BBC News. 10 December 2021. Accessed on 20 December 2021, https://www.bbc.com/news/health-59615005
5. The UK Health Security Agency Variant Technical Group. SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 31. 10 December 2021. Accessed on 15 December 2021, https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1040076/Technical_Briefing_31.pdf
6. El Sahly HM, Baden LR, Essink B, et al; COVE Study Group. Efficacy of the mRNA-1273 SARS-CoV-2 vaccine at completion of blinded phase. *N Engl J Med*. Published online September 22, 2021. doi:10.1056/NEJMoa2113017
7. Ke R, Martinez PP, Smith RL, et al. Longitudinal analysis of SARS-CoV-2 vaccine breakthrough infections reveal limited infectious virus shedding and restricted tissue distribution. *medRxiv*. Preprint posted online September 2, 2021. doi:10.1101/2021.08.30.21262701
8. Chia PY, Xiang Ong SW, Chiew CJ, et al. Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine-breakthrough infections: a multi-center cohort study. *medRxiv*. Preprint posted online July 31, 2021. doi:10.1101/2021.07.28.21261295
9. Charles Schmidt. Why Is Omicron So Contagious? Scientific American. December 17, 2021. Accessed on 20 December 2021, https://www.scientificamerican.com/article/why-is-omicron-so-contagious/
10. News by the Li Ka Shing Faculty of Medicine, The University of Hong Kong. HKUMed finds Omicron SARS-CoV-2 can infect faster and better than Delta in human bronchus but with less severe infection in lung. Accessed on 20 December 2021, https://www.med.hku.hk/en/news/press/20211215-omicron-sars-cov-2-infection?utm_medium=%3Cbr%3Esocial&utm_source=twitter&utm_campaign=press_rele
11. Heidi Ledford. How severe are Omicron infections? Nature. NEWS. 17 December 2021. doi: https://doi.org/10.1038/d41586-021-03794-8
12. Clara-Laeila Laudette. Omicron more likely to reinfect than Delta, no milder study. December 18, 2021. Accessed on 20 December 2021, https://www.reuters.com/business/healthcare-pharmaceuticals/omicron-five-times-more-likely-reinfect-than-delta-study-says-2021-12-17/
13. Pfizer and BioNTech Provide Update on Omicron Variant. December 08, 2021. Accessed on 20 December 2021, https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-provide-update-omicron-variant

14. Zhuang Pinghui. Omicron: 2 doses of Sinopharm vaccine offers weak protection against new strain, finds study. South China Morning Post. 17 Dec, 2021. Accessed on 20 December 2021, https://www.scmp.com/news/china/science/article/3159979/omicron-two-doses-sinopharm-vaccine-offers-weak-protection?module=perpetual_scroll_0&pgtype=article&campaign=3159799
15. Elliott P, Haw D, Wang H, et al; COVID-19 Genomics UK (COG-UK) Consortium11. Exponential growth, high prevalence of SARS-CoV-2, and vaccine effectiveness associated with the Delta variant. *Science*. 2021;eabl9551. Published online November 2, 2021. doi:10.1126/science.abl9551
16. Tenforde MW, Self WH, Adams K, et al. Association Between mRNA Vaccination and COVID-19 Hospitalization and Disease Severity. *JAMA*. Published online November 4, 2021. doi:10.1001/jama.2021.19499
17. de Gier B, Andeweg S, Backer JA, et al. Vaccine effectiveness against SARS-CoV-2 transmission to household contacts during dominance of Delta variant (B.1.617.2), August-September 2021, the Netherlands. *medRxiv*. Preprint posted online October 14, 2021. doi:10.1101/2021.10.14.21264959
18. Eyre DW, Taylor D, Purver M, et al. The impact of SARS-CoV-2 vaccination on Alpha & Delta variant transmission. *medRxiv*. Preprint posted online October 15, 2021. doi:10.1101/2021.09.28.21264260
19. Dinnes J, Deeks JJ, Berhane S, et al; Cochrane COVID-19 Diagnostic Test Accuracy Group. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database Syst Rev. 2021 Mar 24;3(3):CD013705. doi: 10.1002/14651858.CD013705.pub2.
20. Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Spijker R, Taylor-Phillips S, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database of Systematic Reviews* 2020, Issue 6. Art. No: CD013652. doi: 10.1002/14651858.CD013652.
21. Feng S, Phillips DJ, White T, et al; Oxford COVID Vaccine Trial Group. Correlates of protection against symptomatic and asymptomatic SARS-CoV-2 infection. Nat Med. 2021 Nov;27(11):2032-2040. doi: 10.1038/s41591-021-01540-1.
22. Dan JM, Mateus J, Kato Y, et al. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science. 2021 Feb 5;371(6529):eabf4063. doi: 10.1126/science.abf4063.
23. Turner JS, Kim W, Kalaidina E, et al. SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. Nature. 2021 Jul;595(7867):421-425. doi: 10.1038/s41586-021-03647-4.
24. Painter MM, Mathew D, Goel RR, et al. Rapid induction of antigen-specific CD4+ T cells is associated with coordinated humoral and cellular immunity to SARS-CoV-2 mRNA vaccination. Immunity. 2021 Sep 14;54(9):2133-2142.e3. doi: 10.1016/j.immuni.2021.08.001.
25. The WHO *Therapeutics and COVID-19: living guideline*. Accessed on 08 December 2021, *https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.3*
26. Merck News release on November 26, 2021. Accessed on 08 December 2021, https://www.merck.com/news/merck-and-ridgeback-biotherapeutics-provide-update-on-results-from-move-out-study-of-molnupiravir-an-investigational-oral-antiviral-medicine-in-at-risk-adults-with-mild-to-moderate-covid-19/
27. ScienceNews: Merck's COVID-19 pill may soon be here. How well will it work? By Tina Hesman Saey. December 2, 2021. Accessed on 08 December 2021, https://www.sciencenews.org/article/covid-pill-merck-molnupiravir-antiviral-fda
28. NEWS/ Pfizer's Novel COVID-19 Oral Antiviral Treatment Candidate Reduced Risk Of Hospitalization Or Death By 89% In Interim Analysis Of Phase 2/3 EPIC-HR Study. Friday, November 05, 2021. Accessed on 08 December 2021, https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate
29. Chin YS, Chew BH and Widyahening IS for the Pandemic Scientific Response team. Dietary Practices and Nutrition for the Prevention of COVID-19. 2021,22 July;1(3):1-5. Accessed on 08 December 2021, https://hpupm.upm.edu.my/upload/dokumen/20210722171045Dietary_Practices_and_Nutrition_for_the_Prevention_of_COVID-19_The_Brief_&_Summary.pdf
30. Lee SW, Lee J, Moon SY, et al. Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality in South Korea: a nationwide cohort study. Br J Sports Med. 2021 Jul 22:bjsports-2021-104203. doi: 10.1136/bjsports-2021-104203.
31. Tortorici MA, Czudnochowski N, Starr TN, et al. Broad sarbecovirus neutralization by a human monoclonal antibody. Nature. 2021 Sep;597(7874):103-108. doi: 10.1038/s41586-021-03817-4.
32. Omicron symptoms "totally different" from Delta COVID-19 variant: South African doctor. https://youtu.be/BtELl7-zE_w

Diagnostic Tests of SARS-CoV-2

Consisted of:

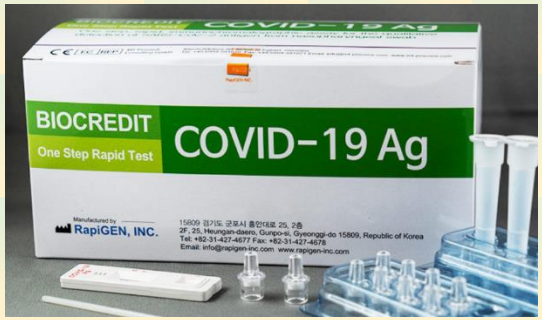
- 2 antibody detection tests
- 16 antigen detection tests
- 5 molecular tests
- 12 RT-PCR
- 2 based on taste & smell, and breaths.

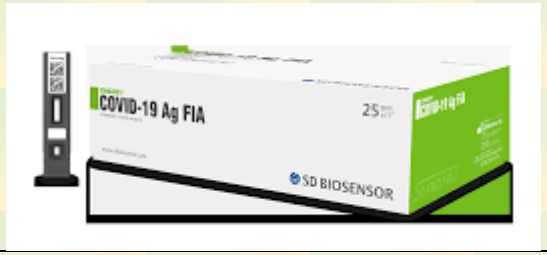
No.	Test / Brand / Picture	Mechanism	Sensitivity [a]	Specificity [b]	PPV [c]	NPV [d]	References / websites
1.	DKSH – Biolidics Rapid Test Kit for Covid-19 	IgG/IgM Antibody Detection (rapid test)	91.54% (86.87-94.65%)	97.02% (94.74 – 98.33%)			https://www.dksh.com/my-en/products/ins/biolidics-covid-19-test-kit
2.	Megna Health Rapid Covid-19 Combo test kit 	IgM/IgG Antibody Detection (rapid test)	100% (88.7 - 100%)	95.0% (87.8 - 98%)	51.3% (27.7–72.9%)	100% (99.3-100%)	https://www.fda.gov/media/140297/download

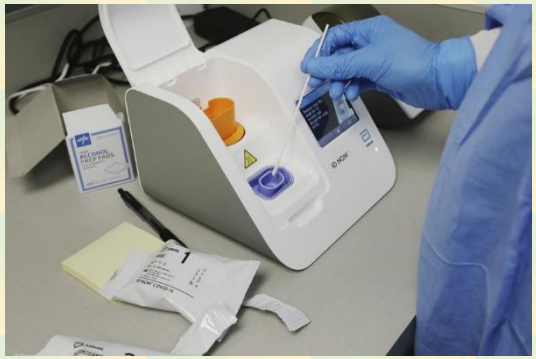
3.	AAZ - COVID-VIRO 	Antigen Detection (rapid test)	61.7 (55.9 to 67.3)	100 (98.9 to 100)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
4.	Abbott - Panbio Covid-19 Ag 	Antigen Detection (rapid test)	72.0 (60.6 to 81.1)	99.3 (99.0 to 99.6)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
5.	Becton Dickinson - BD Veritor 	Antigen Detection (rapid test)	82.3 (62.1 to 93.0)	99.5 (98.3 to 99.8)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
6.	BIONOTE – NowCheck COVID-19 Ag 	Antigen Detection (rapid test)	89.2 (81.5 to 94.5)	97.3 (94.8 to 98.8			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.

7.	Biosynex - Biosynex COVID-19 Ag BSS 	Antigen Detection (rapid test)	59.6 (53.8 to 65.2)	100 (98.9 to 100)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
8.	Coris Bioconcept - COVID-19 Ag Respi-Strip 	Antigen Detection (rapid test)	39.7 (31.3 to 48.7)	98.3 (97.4 to 98.9)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
9.	E25Bio - DART (N-based) 	Antigen Detection (rapid test)	80.0 (70.8 to 87.3)	91.1 (83.2 to 96.1)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.

10.	Fujirebio - ESPLINE SARS-CoV-2 	Antigen Detection (rapid test)	80.6 (68.6 to 89.6)	100 (96.4 to 100)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
11.	Innova Medical Group - Innova SARS-CoV-2 Ag 	Antigen Detection (rapid test)	47.9 (34.3 to 61.8)	99.8 (99.5 to 99.9)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
12.	Liming Bio-Products - StrongStep® COVID-19 Ag 	Antigen Detection (rapid test)	0 (0 to 33.6)	90.0 (55.5 to 99.7)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.

13.	Quidel Corporation - SOFIA SARS Ag 	Antigen Detection (rapid test)	93.8 (79.2 to 99.2)	96.9 (83.8 to 99.9)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
14.	RapiGEN - BIOCREDIT COVID-19 Ag 	Antigen Detection (rapid test)	63.3 (45.7 to 78.0)	99.5 (99.1 to 99.8)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
15.	Roche - SARS-CoV-2 	Antigen Detection (rapid test)	88.1 (74.4 to 96.0	19.4 (7.5 to 37.5)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
16.	Savant Biotech - Huaketai SARS-CoV-2 N Protein	Antigen Detection (rapid test)	16.7 (9.2 to 26.8)	100 (88.8 to 100)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.

17.	SD Biosensor - STANDARD F COVID-19 Ag 	Antigen Detection (rapid test)	72.6 (54.0 to 85.7)	97.5 (96.4 to 98.2)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
18.	SD Biosensor - STANDARD Q COVID-19 Ag 	Antigen Detection (rapid test)	79.3 (69.6 to 86.6)	98.5 (97.9 to 98.9)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
19.	Shenzhen Bioeasy Biotech - 2019-nCoV Ag 	Antigen Detection (rapid test)	86.2 (72.4 to 93.7)	93.8 (91.9 to 95.3)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.

20.	Abbott – ID NOW 	RT LAMP (Isothermal PCR) Molecular test (rapid test)	78.6 (73.7 to 82.8)	99.8 (99.2 to 99.9)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
21.	Cepheid – Xpert Xpress 	Automated RT-PCR Molecular test (rapid test)	99.1 (97.7 to 99.7)	97.9 (94.6 to 99.2)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
22.	DNANudge – COVID Nudge 	Automated RT-PCR Molecular test (rapid test)	94.4 (86.2 to 98.4)	100 (98.8 to 100)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.

23.	Diagnostics for the Real World – SAMBA II 	Automated RT-PCR Molecular test (rapid test)	96.0 (81.1 to 99.3)	97.0 (93.5 to 98.6)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
24.	Mesa Biotech – Accula 	RT-PCR Molecular test (rapid test)	68.0 (53.3 to 80.5)	100 (92.9 to 100)			Dinnes et al. 2021 DOI: 10.1002/14651858.CD013705.pub2.
25.	Computed Topography	Chest CT	91.9% (89.8-93.7)	25.1 (21.0-29.5)	119.4 (93.6-152.5)	30.1 (4.3-212.4)	Böger et al. 2021 https://doi.org/10.1016/J.AJIC.2020.07.011

26.	Altona Diagnostics (821003) 	RT-PCR (RUO)	RUO	RUO	RUO	RUO	van Kasteren et al. 2020 https://doi.org/10.1016/j.jcv.2020.104412
27.	R-Biopharm AG (PG6815RUO) 	RT-PCR (RUO)	RUO	RUO	RUO	RUO	van Kasteren et al. 2020 https://doi.org/10.1016/j.jcv.2020.104412
28.	BGI Real-Time Fluorescent RT-PCR Kit for 2019-nCoV 	Target ORF1ab (open reading frame 1a and b 226 of SARS-CoV-2, includes the RdRp; RNA-dependent RNA polymerase of SARS-CoV-2, part of ORF1ab) RT-PCR (one step real time test kit)	100.0% (91.1%–100.0%)	100% (69.1%–100%)	100.0%	100.0 %	van Kasteren et al. 2020 https://doi.org/10.1016/j.jcv.2020.104412 doi: 10.1002/jmv.26691

29.	CerTest Biotec VIASURE SARS-COV-2 REAL TIME PCR DETECTION KIT  	Target ORF1ab, N (nucleocapsid protein of SARS-CoV-2) RT-PCR (one step real time test kit)	97% ORF1ab: 98% (90, 100) N: 100% (93, 100), 50	97% ORF1ab: 100% (96, 100), N: 100% (96, 100),			van Kasteren et al. 2020 https://doi.org/10.1016/j.jcv.2020.104412 https://www.finddx.org/product/viasure-sars-cov-2-real-time-pcr-detection-kit/
30.	KH Medical RADI COVID-19 Detection Kit and RADI COVID-19 Triple Detection Kit  	Target RdRp (RNA-225 dependent RNA polymerase of SARS-CoV-2), S (spike protein of SARS-228 CoV-2) RT-PCR (one step real time test kit)					van Kasteren et al. 2020 https://doi.org/10.1016/j.jcv.2020.104412
31.	PrimerDesign Coronavirus COVID-19 genesig® Real-Time PCR assay 	Target RdRp RT-PCR (one step real time test kit)					van Kasteren et al. 2020 https://doi.org/10.1016/j.jcv.2020.104412

32.	Seegene Allplex 2019-nCoV assay 	Target RdRp N, E (envelope protein of SARS-CoV-2) As does the in-house "Corman" E-gene PCR, these E-gene assays are specific for bat(-related) betacoronaviruses, i.e. they detect both SARS-CoV-1 and -2 RT-PCR (one step real time test kit)	100.0% (91.1%–100.0%)	100% (69.1%–100%)	100.0%	100.0 %	van Kasteren et al. 2020 https://doi.org/10.1016/j.jcv.2020.104412 Garg et al. 2020 doi: 10.1002/jmv.26691
33.	Mylab Patho Detect RT-PCR kit 	Target E, RdRP RT-PCR (one step real time test kit)	88.8% (75.9% – 96.2%)	100% (69.1%–100%)	100.0%	66.6% (46.6 %–82.0%)	Garg et al. 2020 doi: 10.1002/jmv.26691
34.	Fosun FOSUN COVID-19 RT- PCR Kit 	Target E, N, ORF1ab RT-PCR (one step real time test kit)	95.2% (83.8%–99.4%)	100% (69.1%–100%)	100.0%	83.3% (56.3 % - 95.0%)	Garg et al. 2020 doi: 10.1002/jmv.26691

35.	Black Biotech TRUPCR SARS-CoV-2 RT- qPCR kit 	Target E, N RdRP RT-PCR (one step real time test kit)	100.0% (91.1%–100.0%)	100% (69.1%–100%)	100.0%	100.0 %	Garg et al. 2020 doi: 10.1002/jmv.26691
36.	Thermo Fisher Scientific TaqPath COVID-19 Combo Kit 	Target S, N ORF1ab RT-PCR (one step real time test kit)	100.0% (91.1%–100.0%)	100% (69.1%–100%)	100.0%	100.0 %	Garg et al. 2020 doi: 10.1002/jmv.26691
37.	Lab Genomics Lab Gun Real-Time PCR Kit 	Target E, RdRP RT-PCR (one step real time test kit)	93.02% (80.9%–8.5%)	100% (69.1%–100%)	100.0%	76.9% (52.8 %–90.8%)	Garg et al. 2020 doi: 10.1002/jmv.26691
38.	Clinical symptoms as predictor	Smell and Taste Symptom-Based Predictive Model	70%	73%			Lauren et al. 2020 doi: 10.1002/alr.22602 Note: these are less relevant with new variants Delta and Omicron

39.	Breath-based rapid 	detection and monitoring of COVID-19 from exhaled breath by using sensors composed of different gold nanoparticles linked to organic ligands, creating a diverse sensing layer that can swell or shrink upon exposure to volatile organic compounds (VOCs), causing changes in the electric resistance	83-100%	61-100%	61-100%	71-100%	https://dx.doi.org/10.1021/acsnano.0c05657

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Explanatory footnotes:

[a] **Sensitivity: "Proportion of people with a disease in whom a diagnostic test correctly indicated a positive result"**

Sensitivity

$$= \frac{\text{Number of people with a disease who tested positive}}{\text{Total number of people with a disease}} \times 100\,(\%)$$

[b] **Specificity: "Proportion of people without a disease in whom a diagnostic test correctly indicated a negative result"**

Specificity

$$= \frac{\text{Number of people without a disease who tested negative}}{\text{Total number of people with a disease}} \times 100\,(\%)$$

[c] **Positive predictive value (PPV): "Proportion of people with positive test results who are correctly diagnosed (or who are turned out to be truly infected with the disease)"**

$$\text{PPV} = \frac{\text{Number of people with the disease who have positive test results}}{\text{Number of people with positive test results}} \times 100\,(\%)$$

[d] **Negative predictive value (NPV).: "Proportion of people with negative test results who are correctly diagnosed (or who are truly not infected with the disease)"**

$$\text{NPV} = \frac{\text{Number of people without the disease who have negative test results}}{\text{Number of people with negative test results}} \times 100\,(\%)$$

(Yerushalmy 1947, Public Health Rep. 1947 Oct 3; 62(40):1432-49; Asai 2020, J Anesth. 2020 Dec 11 : 1–5; doi: 10.1007/s00540-020-02875-8)

References

Dinnes J, Deeks JJ, Berhane S, Taylor M, Adriano A, Davenport C, Dittrich S, Emperador D, Takwoingi Y, Cunningham J, Beese S, Domen J, Dretzke J, Ferrante di Ruffano L, Harris IM, Price MJ, Taylor-Phillips S, Hooft L, Leeflang MMG, McInnes MDF, Spijker R, Van den Bruel A. Rapid, point-of-care antigen and Molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013705. DOI: 10.1002/14651858.CD013705.pub2. Accessed 15 December 2021.

Beatriz Böger, Mariana M. Fachi, Raquel O. Vilhena, Alexandre F. Cobre, Fernanda S. Tonin, Roberto Pontarolo. 2021. Systematic review with meta-analysis of the accuracy of diagnostic tests for COVID-19. American Journal of Infection Control 49(1): 21-29

Puck B.van Kasteren, Basvan der Veer, Sharonvan den Brink, Lisa Wijsman, Jørgende Jonge, Annemarie van den Brandt, Richard Molenkamp, Chantal B.E.M.Reusken, AdamMeijer. 2020. Journal of Clinical Virology Volume 128, July 2020, 104412

Atul Garg, Ujjala Ghoshal, Sangram S. Patel,D. V. Singh,Akshay K. Arya,Shruthi Vasanth,Ankita Pandey,Nikki Srivastava Journal of Medical Virology https://doi.org/10.1002/jmv.26691

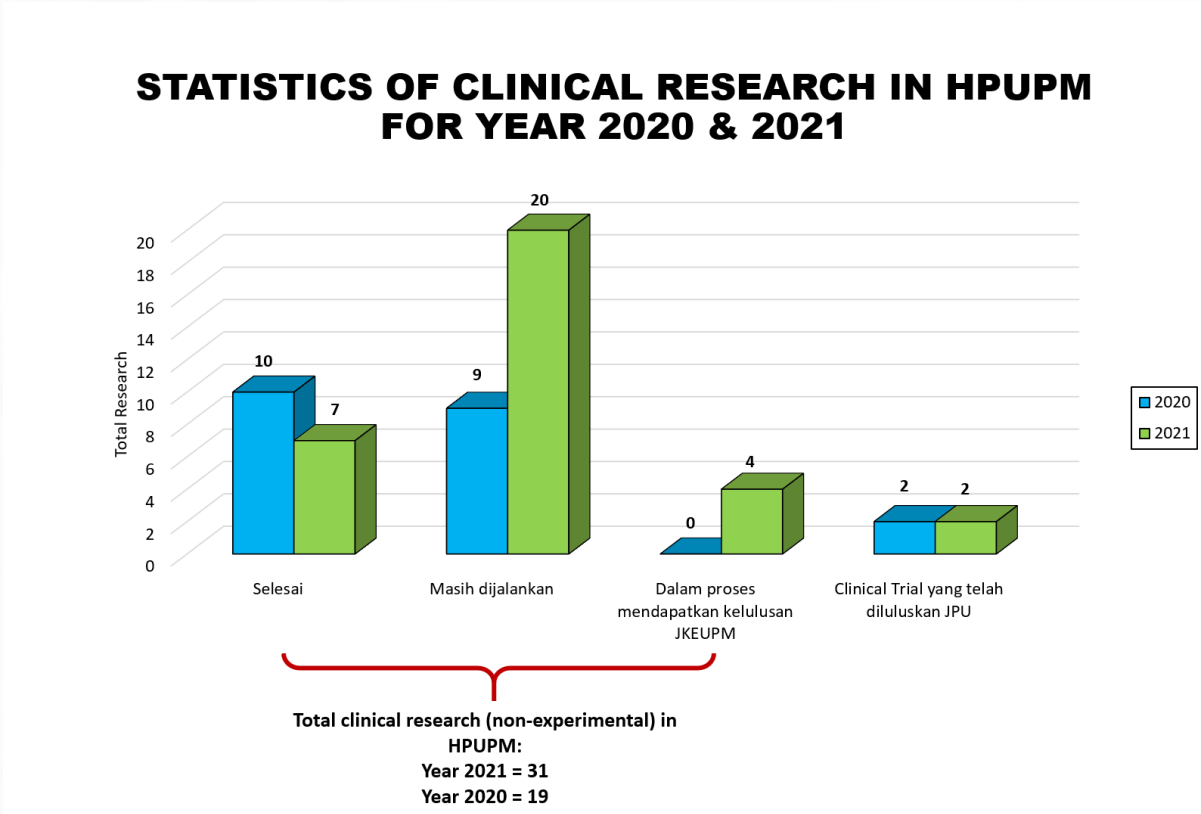
Roland LT, Gurrola JG 2nd, Loftus PA, Cheung SW, Chang JL. Smell and taste symptom-based predictive model for COVID-19 diagnosis. Int Forum Allergy Rhinol. 2020 Jul;10(7):832-838. doi: 10.1002/alr.22602. Epub 2020 Jun 7. PMID: 32363809; PMCID: PMC7267242.

CLINICAL RESEARCH UNIT

ANNUAL REPORT

By: Faridzatul Syuhada Abdul Rashid

1. CLINICAL RESEARCH IN HPUPM FOR YEAR 2021



2. CLINICAL TRIAL FOR YEAR 2020 - 2021

NO.	PRINCIPAL INVESTIGATOR	PROJECT TITLE	SPONSOR
1	ASSOC. PROF. DR. LIYANA NAJWA BINTI INCHE MAT	A Phase 3, Multi Arm, Multi Stage, Covariate-adjusted, Response-adaptive Randomised Trial To Determine Optimal Early Mobility Training After Stroke (Avert Dose)	The Florey Institute Of Neuroscience And Mental Health, Australia
2	DR. ANG JIT KIAT	A Randomized, Open-label, Rater-blinded, Active-controlled, International, Multicenter Study To Evaluate The Efficacy, Safety, And Tolerability Of Flexibly Dosed Esketamine Nasal Spray Compared With Quetiapine Extended-release In Adult And Elderly Participants With Treatment-resistant Major Depressive Disorder Who Are Continuing A Selective Serotonin Reuptake Inhibitor/Serotonin-norepinephrine Reuptake Inhibito	Janseen Pharmaceutical Companies Of Johnson & Johnson (Malaysia)

NO.	PRINCIPAL INVESTIGATOR	PROJECT TITLE	SPONSOR
3	ASSOC. PROF. DR. HOW KANG NIEN	A Comprehensive study of the Efficacy and Safety of Lichochalcone - A Containing Sun Block in the Management of Acne and Post Acne Pigmentation Among Malaysia Patients	Beiersdorf (Malaysia) Sdn Bhd
4	ASSOC. PROF. DR. WAN ALIAA BINTI WAN SULAIMAN	The Effectiveness and Tolerability of Multi Strain Probiotics for Preventive Treatment of Episodic Migraine: A Single-Center, Double-Blind, Placebo-Controlled Phase 2 Trial (PREM)	B-Crobes Laboratory Sdn Bhd (588778-K)

3. CLINICAL RESEARCH (NON-EXPERIMENTAL) FOR YEAR 2021

No.	Title	Principal Investigator & Department	Status
1	Establishing A New Approach To Clinical Communication Skills Assessment For Medical Students Using An Immersive Virtual Simulated Patient – PhD student	Dr. Siti Khadijah Adam Department of Human Anatomy, Faculty of Medicine and Health Sciences, UPM	Ongoing
2	A Developmental Model of Patient Engagement across Multiracial Society in Malaysia	Dr. Aneesa Binti Abdul Rashid Department of Family Medicine, UPM	Completed
3	Effects of COVID-19 Vaccine on Retinal Vasculature Among Healthcare Workers in Hospital Pengajar Universiti Putra Malaysia (HPUPM)	Dr. Dhashani Sivaratnam Department of Ophthalmology, UPM	Ongoing
4	Development and Evaluation of a Stage-Based Tailored Nutrition Education Package for Childhood Obesity (ST-NEPCO) (7-11 Years Old) in Petaling District, Selangor	Dr. Norbaizura Md Yusop, Department of Dietetik, UPM	Ongoing
5	Caregiver Burden and Health Related Quality of Life Among Informal Caregivers of Patients with Severe and Persistent Mental Illness	Dr. Zamzalian bt Abdul Mulud (UiTM) Dr. Chong Seng Choi Department Psychiatrics,UPM	Ongoing
6	Work Related Musculoskeletal Disorders among Healthcare Workers in Hospital Pengajar Universiti Putra Malaysia : The Prevalence and Association Factors - Master Student	Dr. Firdati Mohamed Saaid, Department of Orthopedics	Completed

No.	Title	Principal Investigator & Department	Status
7	The Evaluation of Platelet Parameters and MRI Findings in Facilitating Acute Ischemic Stroke Treatment in Hospital Universiti Putra Malaysia(HPUPM) - Master Student	Assoc. Prof. Dr. Sabariah binti Md Noor, Department of Pathology	Completed
8	Antimicrobial Stewardship - Antimicrobial Utilisation at A Newly Opened Tertiary Hospital in Klang Valley (Hospital Pengajar UPM) (Master Student)	Dr. Tengku Zetty Maztura Tengku Jamaluddin, Department of Medical Microbiology	Completed
9	Multicenter Study on Neuronal and Genetics Changes Among Alzheimer's Disease and MCI Patients in Klang Valley, Malaysia	Assoc. Prof. Dr. Subapriya Suppiah, Department of Radiology	Ongoing
10	The Effect of Acupuncture As Adjunctive Therapy On Homeostasis Model Assessment-Insulin Resistance And Health-Related Quality Of Life In Patients With Type 2 Diabetes Mellitus	Professor Dr. Zalilah Mohd. Shariff Department of Dietetics	Ongoing
11	Correlation Between The Volume of MRI Brain Infarct and Inflammatory Markers among Acute Ischemic Stroke Patients in HPUPM – Master students	Assoc. Prof. Dr. Suraini binti Mohamad Saini Department of Radiology	Completed
12	Infection Control Management Through the Integration of Conventional Antimicrobial Resistance Surveillance, Advance Biopsychosocial Assessment and Machine Learning Approaches	Dr. Azmiza Syawani Jasni Department of Medical Microbiology	Ongoing
13	Factors Associated with Malnutrition Among Geriatric Patients In Public Hospitals In The Klang Valley - Master students	Dr. Noraida binti Omar, Department of Dietetics	Ongoing
14	Performance Validation of Capillary Electrophoresis for Haemoglobinopathy Diagnosis and Verification of Normal HbA2 and HbF Values on the Sebia Capillarys 3 Octa Capillary Electrophoresis	Prof. Madya Dr. Sabariah binti Md Noor Department of Pathology	Ongoing
15	A Pilot Quasi-Experimental Study Evaluating the Feasibility and Potential Effectiveness of a Home Hazard Management Program on reducing the rate of Falls and Fear of Falling among Malaysian Community Dwelling Stroke Survivors - PhD student	Ms. Husna Ahmad Ainuddin (GS53888) Dr. Muhammad Hibatullah bin Romli, Department of Rehabilitation Medicine	Ongoing
16	Characterisation and Applications of Fabricated Germanium-doped Silica	Assoc. Prof. Dr. Noramaliza binti Mohd Nor,	Ongoing

No.	Title	Principal Investigator & Department	Status
	Optical Fibres as Thermoluminescent Dosimeters in Proton Beam Dosimetry- PhD student	Department of Radiology	
17	The Use of Fabricated Germanium-doped Optical Fibres for Computed Tomography Radiation Dosimetry - PhD student	Assoc. Prof. Dr. Noramaliza binti Mohd Nor, Department of Radiology	Ongoing
18	The Use of Real-time Fabricated Germanium Doped Optical Fibers for Clinical Computed Tomography Radiation Dosimetry - PhD student	Assoc. Prof. Dr. Noramaliza binti Mohd Nor, Department of Radiology	Ongoing
19	Occurrence of ESBL and Non-ESBLiproducing Klebsiella Pneumonia Harbouring magA and K2A Genes in Clinical Samples Isolated from Hospitals in Malaysia	Dr. Nurshahira Sulaiman, Department of Biomedical Sciences	Ongoing
20	Sociodemographic Profiles, Knowledge, Attitudes and Practices of Hospital Malnutrition Among Healthcare Workers in Universiti Putra Malaysia Teaching Hospital (HPUPM) - Degree Student	Dr. Zuriati Ibrahim (Project Supervisor)	Completed
21	Towards Development of An Individualised Screening Tool by Utilising Cervical Length Measurement in Relation to Body Mass Index(BMI) for Early Identification and Intervention of Preterm Birth	Dr. Nurul Iftida Basri Department of Obstetrics and Gyneacology	Ongoing
22	Correlating HbA1c Result between Capillary Electrophoresis (CE) and High-Performance Liquid Chromatography (HPLC) Measurement in HPUPM, 2021 – Master Student	Assoc. Prof. Dr. Intan Nureslyna Samsudin Department of Pathology	Ongoing
23	A Multicenter Study of the Relationship Between Anthropometric Measurements and Hamstring Autograft Diameter in Anterior Cruciate Ligament Reconstruction in Malaysia – Master Student	Dr. Liew Siew Khei Department of Orthopedics	Completed
24	Seroconversion Post-COVID-19 Vaccination: The Determination of KAP, Genetic Factors Using Transcriptomics Analysis and Potential Use Of Pre-Corneal Tear Film As The Non-Invasive Screening Method'	Dr. Aidalina binti Mahmud Department of Community Health	Ongoing

No.	Title	Principal Investigator & Department	Status
25	Comparison between the pro-inflammatory cytokines level in inflammatory, non-inflammatory acnes and non-lesional skin using the tape stripping method	Dr. How Kang Nien Department of Medical	Ongoing
26	Developing Smart Walker Prototype for Promoting Mobility Among Older Malaysians	En. Mohd Rizal Hussain Institut Penyelidikan Penuaan Malaysia, UPM (MyAgeing)	Ongoing
27	Discovery of genetic aberrations in paediatric patients suspected of rare genetic disorders	Assoc. Prof. Dr. Ting Tzer Hwu Department of Pediatrics	Ongoing
28	Health Technology Assessment of AIIB Spectral Device™ as the Screening Tool for Covid-19 Infection in Malaysia : A 2-Phase Pilot Study	Assoc. Prof. Dr. Chee Hui Yee, Department of Medical Microbiology	Awaiting for JKEUPM approval
29	The Effects of Music in Hospital Waiting Lounge	Dr. Yeoh Pei Sze, Jabatan Muzik, Fakulti Ekologi Manusia UPM	Awaiting for JKEUPM approval
30	A Multi-Centred Double Blind Randomized Placebo Controlled Study to Assess Aspects of Safety and Efficacy of Nuvastatic? (C5OSEE5050ESA) as an Immunomodulator Adjuvant Therapy to the Standard Care of Treatment in Covid 19 Patients	Dr. Ummi Nadira binti Daut, Department of Medical	Awaiting for JKEUPM approval
31	The Evaluation of NGAL, KIM, MCP-1 and TWEAK Biomarkers with Utilization of Electron Microscopy (EM) for Early Prediction of Outcome in Lupus Nephritis	Dr Nur Alya Binti Zainal (Master student, International Medicine, UPM)	Awaiting for JKEUPM approval

4. CRU ACTIVITIES IN YEAR 2021

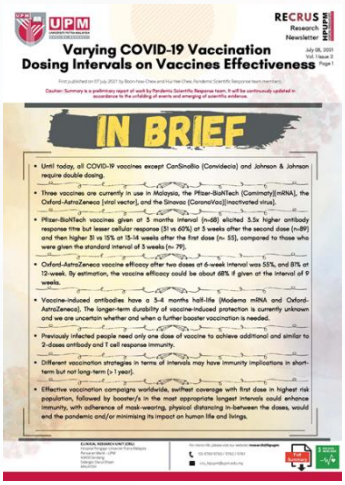
NO.	ACTIVITY	FREQUENCY	STATUS
A. RESEARCH CONSULTATION CLINIC			
1	*'Research Design Clinic (RDC)'*	Based on application	15 sessions completed
2	*'Biostatistics Clinic (BSC)'*	Based on application	17 sessions completed

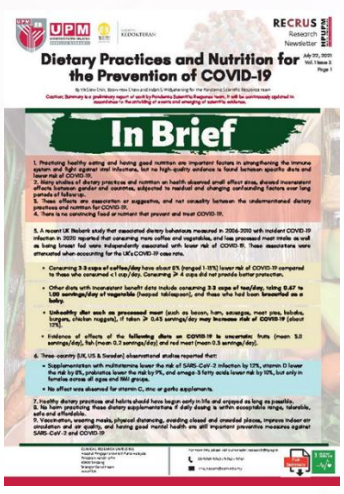
NO.	ACTIVITY	FREQUENCY	STATUS
B. WORKSHOP / COURSES / TRAINING ORGANIZED BY CRU			
1	Crash-Workshop On 'Clinical Epidemiology Research Methodology' *(Cw-Cerm)* Speaker: **Assoc. Prof. Dr. Chew Boon How** Head of Clinical Research Unit	1	Conducted virtually on 4th Mac 2021 with 40 participants.
2	The Planning and Conducting of A Prognostic Research Speaker: **Assoc. Prof. Dr. Sharmini Selvarajah** Consultant Clinical Epidemiologist MBBS (UM), MPH (Hons), MSc Clin Epi, PhD (Utrecht, NL)	1	Conducted virtually on 21st May 2021 with 51 participants.
3	Webinar Talk On Clinical Research & Data Management During The Pandemics Speaker**: Assoc. Prof. Dr. Karuthan A/L Chinna** (PhD) Taylor's University	1	Conducted virtually on 21st May 2021 with 37 participants.
4	'Meta-Journal Hour (MJH) Series'	4 series	**a. Series 1: Interpreting Systematic Review: Are We Ready To Make Our Own Conclusions?** Date: 17th September 2021 **b. Series 2: Ultraprocessed Food Consumption and Risk of Type 2 Diabetes Among Participants of the NutriNet-Sante Prospective Cohort** Date: 15th October 2021 **c. Series 3: Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality** Date: 19th November 2021 **d. Series 4: Methodological quality of COVID-19 clinical research** Date: 10th December 2021.
5	'Research Colloquium (RC) Series 1'	1	Conducted virtually on 1st December 2021 with 42 participants. These are the topics presented during RC:

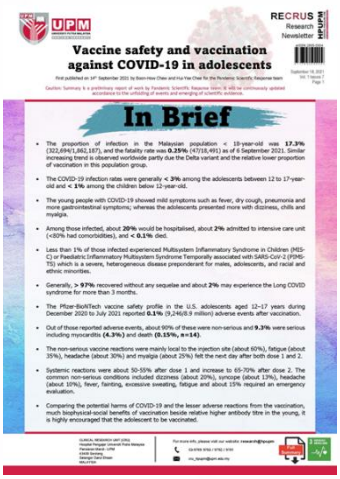
NO.	ACTIVITY	FREQUENCY	STATUS
			a. *Comparison of Automated and Manual Nucleic Acid Extraction Methods for Covid-19 Detection with RT-PCR in HPUPM* **Dr. Narcisse Mary A/P Sither Joseph** b. *The association of atherosclerosis with nutritional status measurements in non-Covid-19 adult patients admitted to HPUPM during the pandemic* **Assoc. Prof. Dr. Bahariah Khalid** c. *Antimicrobial Utilisation at A Newly Opened Tertiary Hospital in Klang Valley (Hospital Pengajar UPM)* **Dr. Tengku Zetty Maztura Tengku Jamaluddin**
6	'Webinar on The Types of Systematic Review (SR) in The Medical and Health Sciences'	1	Conducted virtually on 2nd December 2021 with 114 participants. There are 18 types of SR covered and the speakers are among CRU Associate Members (CRAMs) and CRU officers.
7	'Webinar on Key Skills in Academic Writing' Speaker: **Ms. Nurul Iman Hafizah Adanan** Research Officer, CRU Bachelor (Hons.) Nutrition and Dietetics (UiTM), MSc. (Clinical Nutrition) (UPM)	1	Will be held on 23rd December 2021 virtually.
C. RESEARCH AND PUBLICATION			
1	RECRUS Research Newsletter (eISSN 2805-5004)		Ongoing: *"Vol 1 Issue 10"*
2	Survey on Research Needs	1	Full report to be published in Newsletter.
3	Intersectoral research project: 'Research on Digital Health'	1	Questionnaire validation and proposal preparation
4	Development & Evaluation of A Research Capacity Building Training Module Among HPUPM staff	1	Proposal preparation
5	MASA Policy Development Program (MPDP): 'Improving Health through The Development of an Evidence-Based	1	Submitted the MPDP grant application on 29th October 2021. Awaiting for the feedback.

NO.	ACTIVITY	FREQUENCY	STATUS
	Smartphone Mobile Apps to Promote Healthy Behaviours During COVID-19 Endemic'		
D. OTHERS			
1.	Webpage: *Research@HPUPM*	Periodically	Ongoing
2.	Research Assistant / Enumerator Pool	-	Ongoing
3.	Recognition for Grant Success for year 2020 & 2021	-	Due date: 31st Disember 2021
4	Research Electronic Data Capture (REDCap) software	-	Awaiting for the 'open domain' access from USPK / iDEC UPM

'RECRUS RESEARCH NEWSLETTER VOL. 1'
Scientific Responses to COVID-19 Pandemic







'RECRUS RESEARCH NEWSLETTER VOL. 1'

RECRUS
Research Newsletter
Volume 1, Issue 8, October 2021, 043 - 059

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HOSPITAL PENGAJAR UPM

FROM THE EDITOR'S DESK

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Appraisal of Meta-Journal Hour Series 1 (pg. 43 - 44)

Research Achievements & Impacts
Winners of Research Grants 2020 - 2021 (pg. 45 - 59)

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2.Webinar on "Types of Systematic Reviews"

RECRUS Editorial Members
Associate Professor Dr. Chew Boon How (Editor-in-Chief)
Cik Nurul Iman Hafizah Adanan (Papers Editor)
Dr. Nur Aazifah Ilham (News Editor)
Cik Faridzarul Syuhada Abdul Rashid (Production Editor)
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RECRUS
Research Newsletter
Volume 1, Issue 9, November 2021, 060 – 079

HPUPM
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FROM THE EDITOR'S DESK

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BREAKING NEWS
The new SOPs from JKEUPM on research approvals from other ethics committees for research at non-UPM facilities.

Clinical Epidemiology
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What are the world top scientists? (pg. 69 – 71)

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World top 2% scientists in HPUPM and FPSK (pg. 73)
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Announcements
1. Meta-Journal Hour Series 3
2. Webinar on "Types of Systematic Review" (update)
3. Research Colloquium
4. Webinar on "Sample Size Calculation"

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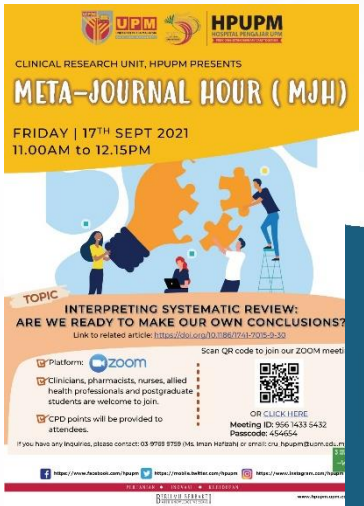
INVITING SUBMISSION TO SECTION

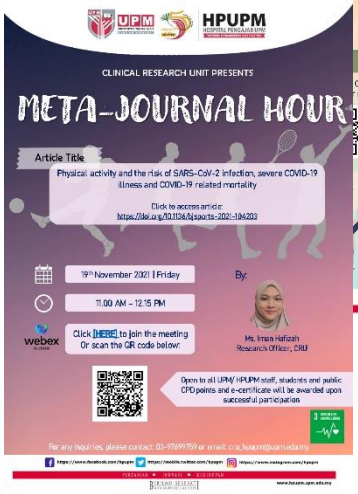
Postgraduate Students: Graduated UPM's MMed/PhD/MSc students and the importance of their research findings

'META-JOURNAL HOUR (MJH) SERIES'



HPUPM
CLINICAL RESEARCH UNIT, HPUPM PRESENTS
META-JOURNAL HOUR (MJH)
FRIDAY | 17TH SEPT 2021
11.00AM to 12.15PM
TOPIC
INTERPRETING SYSTEMATIC REVIEW: ARE WE READY TO MAKE OUR OWN CONCLUSIONS?
Platform: zoom
Clinicians, pharmacists, nurses, allied health professionals and postgraduate students are welcome to join.
CPD points will be provided to attendees.
OR CLICK HERE
Meeting ID: 966 1433 5432
Passcode: 454654

HPUPM
CLINICAL RESEARCH UNIT PRESENTS
META-JOURNAL HOUR (MJH)
ARTICLE TITLE
Ultraprocessed Food Consumption and Risk of Type 2 Diabetes Among Participants of the NutriNet-Santé Prospective Cohort
Link to article: https://doi.org/10.1001/jamainternmed.2019.5942
15TH OCTOBER 2021 | FRIDAY
11.00AM - 12.15PM
By:
webex
Open to all UPM staff
CPD points and e-certificates will be provided



HPUPM
CLINICAL RESEARCH UNIT PRESENTS
META-JOURNAL HOUR
Article Title
Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality
Click to access article:
https://bjsm.bmj.com/content/early/2021/10/20/bjsports-2021-104203
19th November 2021 | Friday
11.00 AM – 12.15 PM
webex
Click [HERE] to join the meeting
Or scan the QR code below:
By:
Ms. Iman Hafizah
Research Officer, CRU
Open to all UPM/ HPUPM staff, students and public
CPD points and e-certificate will be awarded upon successful participation

HPUPM
CLINICAL RESEARCH UNIT PRESENTS
META-JOURNAL HOUR
Join our discussion on appraising the quality of COVID-19 clinical research
ARTICLE TITLE
Methodological quality of COVID-19 clinical research
Click to access full article:
https://doi.org/10.1038/s41467-021-21220-5
10TH DECEMBER 2021 (FRIDAY) | 11.00 – 12.15PM | WEBEX
Click [HERE] to register
or scan the QR code below:
webex
To access the meeting click [HERE]
Speaker
Dr. Nur Aazifah Ilham
Medical Officer, CRU
Open to all UPM / IPPUPM staff, students and public
CPD points and e-certificate will be awarded upon successful participation

'WEBINAR / WORKSHOP / RESEARCH COLLOQUIUM'

RESEARCH STRATEGIC PLAN 2021-2025 IMPLEMENTATION

Excerpts from the presentation by

Prof Dr. Rukman Awang Hamat

Deputy Dean (Research and Internalization) FPSK, UPM

during the annual Business Meeting organised by CRU on the 9th December 2021

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WITH KNOWLEDGE WE SERVE
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TREE OF SUCCESS

VISION — To become an institution of national pride and global prestige health to humanity

MISSION — Empowering the world community to improve human health through discovery and innovation with excellence, diversity, sustainability and integrity

CORE VALUES — High research impact-translational research

MOTTO — Upholding High Performance Culture

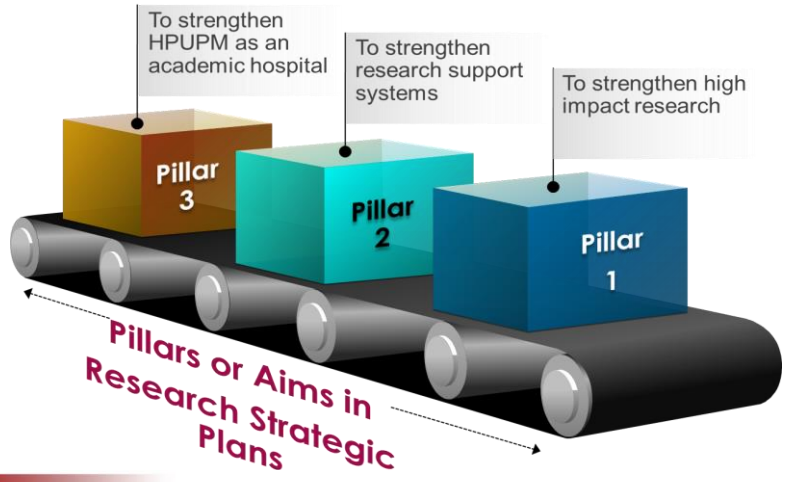
3 PILLARS — Aims that focus to achieve high research impact

9 OBJECTIVES — 4 (P1), 3 (P2), 2 (P3)

12 OUTCOMES — Within 5 years

UNIVERSITI PUTRA MALAYSIA
AGRICULTURE • INNOVATION • LIFE

Research Strategic Plan



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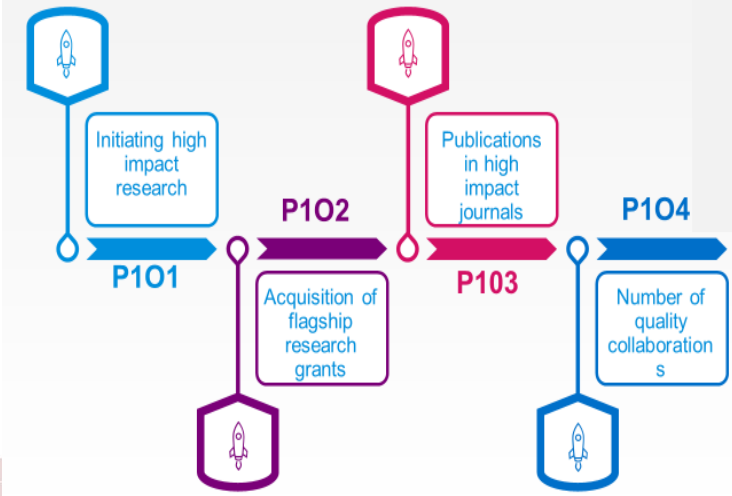
PILLAR 1: To strengthen high impact research

4 objectives

7 outcomes



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PILLAR 2: To strengthen research support systems

P2O1:

Improving the management and maintenance of equipment

Optimizing the lab space for research

P2O2:

Optimizing human resource

Pillar 2:

3 objectives

4 outcomes

P2O3:

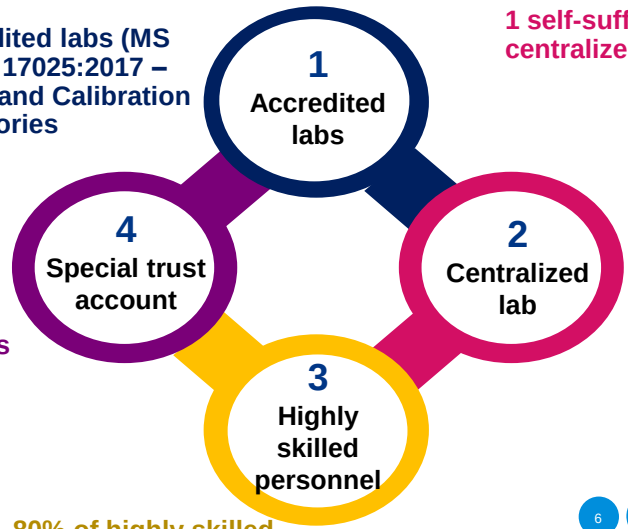
Generating income for sustainable financial support

PILLAR 2: To strengthen research support systems

2 accredited labs (MS ISO/IEC 17025:2017 – Testing and Calibration Laboratories

1 self-sufficient centralized lab

Pillar 2: 4 outcomes



Special trust account for income generation

To plan for the allocations given to research groups at all levels

80% of highly skilled personnel for handling high-end equipment

UNIVERSITI PUTRA MALAYSIA
AGRICULTURE • INNOVATION • LIFE

PILLAR 3: To strengthen the roles of HPUPM as an academic hospital

Pillar 3:

2 objectives

1 outcome

P3O1

Strengthening HPUPM Clinical Research Unit (CRU)

Developing a strategic clinical research program based on translational research (clinical to practice)

P3O2

PILLAR 3: To strengthen the roles of HPUPM as an academic hospital

Pillar 3: 1 outcome

- ✓ **1 translational research for each of clinical departments**
- ✓ **Faculty – focus on translational research; HPUPM will ensure the activities would fulfil the objectives**

1 translational research

HIGH QUALITY RESEARCH, TRUE ACADEMICS, REAL EXPERTS MOVEMENT 2021 – 2025

By: Associate Professor Dr. Chew Boon How

High-quality researches are relevant and important researches that produce credible evidence to resolve issues in clinical practices, expedite discovery of effective treatments and to innovate quality care services. This is brought about from ability to identify the right research question, to collaborate with others, to plan and conduct the most suitable clinical study which is most feasible and efficient, to properly analyse, fully report all the findings and disseminate at meetings and in reputable journals, with open-access with data-sharing in a timely manner to impact changes in practices and living.

True academics are intellectuals who are guided by scientific methods in professional activities, aware of the limitations in science, hold in high regards wisdom and value of humanity, and the sensitivities of the people of different cultures near them, and to be mindful of the directions of the fellow human beings at large as a whole, engaged in and leading/steering them out of foreseeable troubles instead of exploiting knowledge for selfish gain.

> *True academics and real experts are intellectuals who take proactive actions in steering their communities out of coming troubles and take pains to heal their present ailments. These are the callings to those who are in the academia. Fulfilling these responsibilities in trying times over the years of many similar incidences will earn the people's respect, trust and awe. Hasn't the history proven this? You know what will happen otherwise.*

Real experts are skilled workers who understand what they are doing, and able to execute right decisions with the right clients, at the right time and in appropriate manners to bring about the best outcome possible. They update their professional skills and knowledge, and these include ethical aspects related to the carrying out of the professional duty.

> *Real experts do not appear for fame and celebrity in public but when they do they speak with earnest, concern and care for the people; they base their opinion on robust data and do not over-speculate on the available data; they do not venture out of their professional training/background when provide advice or without a precautionary note.*

Research culture is the "behaviours, values, expectations, attitudes and norms" [1] of the research community. Good research culture will be cultivated to nurture high-quality researchers in HPUPM. This is expected to lead many to become true academics and real experts.

Bland CJ et al [2] enlisted a consistent set of 12 characteristics in research-conducive environments:

(1) Clear goals that serve a coordinating function,
(2) Research emphasis,
(3) Distinctive culture,
(4) Positive group climate,
(5) Assertive participative governance,
(6) Decentralized organization,
(7) Frequent communication,
(8) Accessible resources, particularly human,
(9) Sufficient size, age, and diversity of the research group,
(10) Appropriate rewards,
(11) Concentration on recruitment and selection, and
(12) Leadership with research expertise and skill in both initiating appropriate organizational structure and using participatory management practices.

The following are proposed steps and actions [1-4] that can be taken in small strides in the movement to achieve the goals. The bigger steps and actions will be drawn with wider support from all. The table below suggests some of the important and early actions that to be taken by different stakeholders in HPUPM and Faculty of Medicine and Health Sciences (FPSK) to start off the movement. These are concerted efforts that require individual staff to be quicken and activated to research activity, and to thrive in supportive micro-environment of respective departments, to grow in conducive larger environment of the hospital and faculty.

CRU in HPUPM plays the roles of **facilitator** to experienced and active researchers towards higher quality conducts of clinical research, and to translate all researches to clinical practice in HPUPM; **coach** to eager staff who want to learn about research and to become high-quality researchers now; **recruiter and caller** to high-quality research to all users and prospective producers of quality clinical evidence.

STEPS to Improve High-quality Research, True Academics, Real Experts

<table>
<tr><th>Clinical Research Unit (CRU) HPUPM
• Investigator quality
• Analytic accuracy</th><th>Department / Academic Staff
• Research mix
• Passion</th><th>HPUPM Management
• Institutional efficiency</th><th>FPSK / RMC
• funding</th></tr>
<tr><td>Workshops on essential research knowledge and skills:
1. Systemic review
2. Academic writing
3. Clinical epidemiology & research methodology
4. Statistical principles
5. Etc…</td><td colspan="2">Staff self-management support:
1. Improve awareness of the importance of high-quality research
2. Identify strengths and weakness of personal styles in research
3. Establish and communicate about career plan
4. Define and negotiate personal roles in the department
5. Motivate with regular program (engage CRU)</td><td>Integrate research and teaching throughout curriculum (eg, undergraduate research fellowships, structured postgraduate research modules)</td></tr>
<tr><td>Invited expertise & talks:
1. External consultants with grant success record
2. External reviewers with current NIH funding
3. Compensated external reviews of applications
4. Professional editing</td><td colspan="2">1. Staff assignment with equal time for research & teaching until funded
2. Minimize service activities of grant- writing academic staff
3. Reduced teaching assignments during funded projects
4. Teaching/service assignments increased when research productivity low</td><td>Reward research, education & service successes</td><td>1. Increase or maintain funding opportunity
2. Subscribe to FREE publication with certain publishers eg. BMC/Springer Nature</td></tr>
<tr><td>Grant specialist & administrative assistant/s with skills in managing all forms, have knowledge of funders', NMRR and ethical rules</td><td colspan="2">1. Make compulsory every academic staff to have a 4-hour academic- focused protected time every week for reading (primarily) and writing.
2. Suggest and encourage another 4-hour slot on Saturday for the 'young' academic staff.</td><td></td><td></td></tr>
<tr><td colspan="4">Research output recognition:
1. Hospital meeting announcements of submitted/funded grants
2. Broadcast emails regarding funded grants
3. Announcements about research honours/research publications</td></tr>
</table>

10 ACTIONS for Successful Implementation of High-quality Research/Researchers

Primary actions

At least,

1. **1** academic-focused 4-hour protected slot for research activities* on weekday per week per staff,
   and
   1 academic-focused 4-hour protected slot research activities* per weekends per week per staff (highly recommended for 'young' academicians)
2. **1** journal paper is read/appraised per month per staff
3. **1** training/course/workshop on clinical epidemiology/research methodology/meta-research/medical statistics/academic writing per staff per year
4. **1** written-up study protocol, ever-fresh (a new study protocol will replace the old one that has progressed/succeeded in getting a grant) per staff
5. **1** on-going clinical research per staff
6. **1** research manuscript is being written-up as a SA/CA/PA† per staff (original report, review, case report, commentary, etc.) (a new manuscript will be written replacing the old one that has progressed/succeeded in getting published)
   and
   1 research manuscript as a SA/CA/PA† is under a journal's peer-review per staff
   or
   1 research manuscript as a co-author is under a journal's peer-review per staff
7. **1** systematic review is published in own's area of specialty per staff

Central actions

At least,

8. **1** active internal collaborative research project per staff
   and
   1 active external collaborative research project per staff
9. **1** active research grant as the principal investigator per staff
10. **1** active MSc student supervised as the Chairman of the supervisory committee (may begin with co-supervising) per staff

* research activities= reading and writing about scientific research, attending research-related trainings
† SA/CA/PA= senior author / corresponding author / primary author

10 ACTIONS for Successful Implementation of True Academics

At least,

1. **1** peer-review for a reputable journal per staff per quarter-year
2. **1** critical contribution‡ to scientific societies, own and others per staff per year
3. **1** timely input to the public communities on national or international issues with insights (media publication/live telecast) per staff per year
4. **1** ownership of a teaching module/program (refreshing and updating teaching materials on regular basis) per staff
5. **1** active PhD student supervised as the Chairman of the supervisory committee (may begin with co-supervising) per staff
6. **1** active membership in an esteemed national committee of a professional body
7. **1** active membership in an esteemed international committee of a professional body
8. **1** trip to external collaborator per staff per year
9. **1** trip to a new collaborator / an international academy per staff every 2-3 years
10. Works are cited by clinical practice guidelines, professional society's declaration/statements, policy papers and protocols

‡ transforming practices, creating new services, introducing new values
Passive indicator

10 ACTIONS for Successful Implementation of Real Experts

1. Clinical opinion / service is highly sought after by patients
2. Expertise is highly sought after by students
3. Leading developments of clinical practice guidelines, policy papers and protocols

At least,

4. **1** MMed student supervised as the Chairman of the supervisory committee who become an excellent clinical specialist

   Or/and

   1 MSc student supervised as the Chairman of the supervisory committee who become an excellent and successful professional

   Or/and

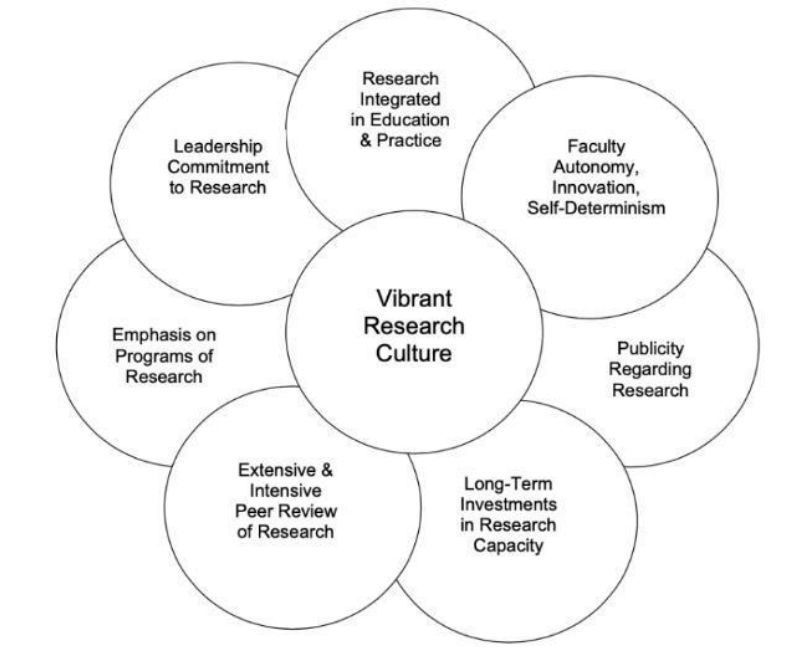
   1 PhD student supervised as the Chairman of the supervisory committee who become an excellent researcher
5. **1** leadership role in an esteemed national committee
6. **1** leadership role in an esteemed international committee
7. **1** innovation in teaching and learning
8. **1** innovation in own clinical specialty / discipline

References

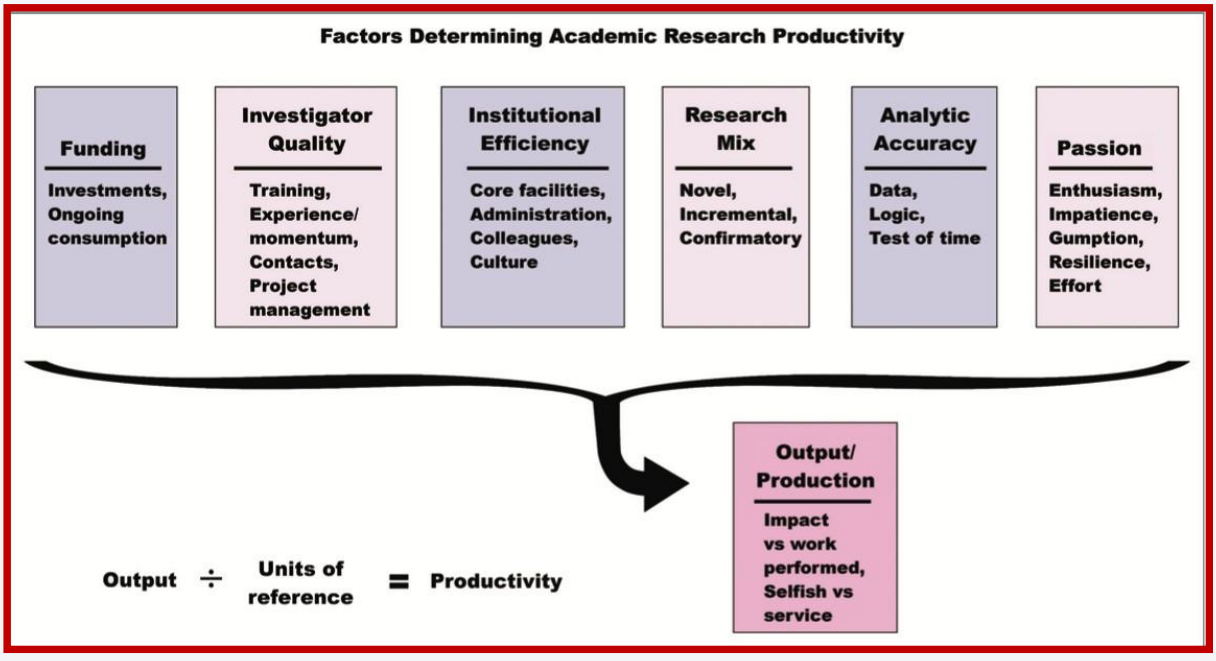
1. Conn VS, et al. Building research productivity in an academic setting. Nurs Outlook. 2005;;53(5):224-31.
2. Bland CJ, Ruffin MT 4th. Characteristics of a productive research environment: literature review. Acad Med. 1992 Jun;67(6):385-97. doi: 10.1097/00001888-199206000-00010. https://pubmed.ncbi.nlm.nih.gov/1596337/
3. Bogdewic SP, et al. Leadership and organizational skills in academic medicine. Fam Med. 1997;29(4):262-5.
4. Kern S. Analytic model for academic research productivity having factors, interactions and implications. Cancer Biol Ther. 2011;12(11):949-56.

Appendix:

Informative and instructive diagrams on factors that may influence research productivity in an academic setting like that in HPUPM.



References: Conn VS, et al. Building research productivity in an academic setting. Nurs Outlook. 2005;;53(5):224-31.



References: Kern S. Analytic model for academic research productivity having factors, interactions and implications. Cancer Biol Ther. 2011;12(11):949-56.

What clinician should know on sensitivity, specificity and predictive value?

By Nur Aazifah and Nurul Iman Hafizah
CRU HPUPM

Predictive value relies on prevalence of disease in the population. Prevalence is a measure of disease burden for the specific time point or during a specified time period not to confuse with incidence which is the rate of new cases or event during specified time period of population at risk. As prevalence increases, PPV also increases while NPV decreases. In contrast, Se and Sp are independent of prevalence. Se and Sp can be influenced by differences in disease characteristic such as clinical severity, laboratory value cut-offs and etc. Receiver operating characteristic (ROC) curve displays graphically the trade-off between Se and Sp and its useful in assigning the best cut-offs for the best Se and Sp levels.

Clinically relevant parameter for screening test is NPV while confirmatory test is PPV. Any confirmatory test is often mandatory not to produce any false positive result – they should be as specific as possible. Usually, what patient interested to know is what is the probability they would have the disease if the test is positive, this is what PPV can offer.

So, let us start with definition first.

Sensitivity (Se) is a probability of a positive test result given the presence of disease can be written as :
P (positive test | disease present)

Specificity (Sp): probability of a negative result given the absent of disease which can be written as :
P (negative test| absent disease)

Positive predictive value (PPV): probability of the present disease given a positive test result which can be written as :
P (disease present| positive test)

Negative predictive value (NPV) : probability of the disease absent given a negative test result which can be written as :
P (disease absent|negative test)

Notation (|) means given an event already happened

Figure 1

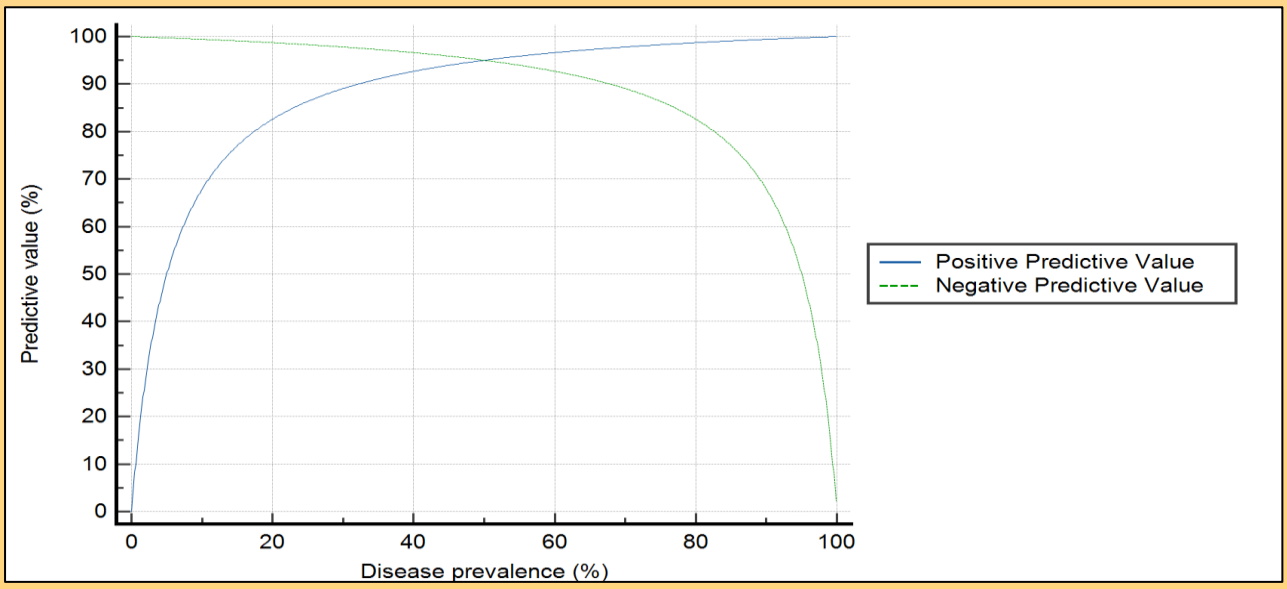


Figure 1 illustrates the effect of disease prevalence when both sensitivity and specificity are fixed at 95%. PPV and NPV are directly related to the prevalence of the disease in a population. The higher the disease prevalence, the higher the value of PPV. When the disease prevalence is low, PPV will still be low while NPV increases.

We will go through an example on how to calculate Se and Sp using 2x2table. Se and Sp can be calculated using 2x2 table directly provided we have true positive (TP), true negative (TN), false positive (FP) and false negative (FN) result.

	RT-PCR Covid-19/ Disease status		Total results
Rapid Ag Test X	Positive	Negative	
Positive	52 (TP)	2 (FP)	54
Negative	5 (FN)	185 (TN)	190
Total Results	57 (Se)	187 (Sp)	244

Sensitivity (Se): Test positive (TP) / Disease present (TP + FN) = 52/52+5= 0.912
Specificity (Sp): Test Negative (TN)/ Disease absent (TN+ FP) = 185/185+2 =0.98

Differ with PPV and NPV, we need to take account on prevalence in the calculation. Here, we will calculate PPV and NPV using two different prevalence values.

i) Prevalence from 2x2 table :
= 57 (total number of positive cases) / 244 (total population at risk) =0.23

ii) Let say the **prevalence COVID-19 in Malaysia**:
= 56989 (total number Covid-19 in Malaysia) / 33119118 (Total Malaysia population) = 0.0017

PPV: P (disease present| positive test)
NPV: P (disease absent|negative test)

Using the Bayes' theorem and after taking into consideration the prevalence using multiplication and reciprocal rule, the PPV and NPV can be appropriated and expressed as below:

$$PPV = \frac{\text{Prevalence} \times \text{Sensitivity}}{(\text{Sensitivity} \times \text{Prevalence}) + (1\text{-specificity}) \times (1\text{- prevalence})}$$

$$NPV = \frac{\text{Specificity}(1\text{- Prevalence})}{(\text{Specificity})\ (1\text{- prevalence}) + (1\text{-sensitivity}) \times \text{Prevalence}}$$

i) Using prevalence by 2x2 table :

PPV = (0.23 x 0.912)/((0.23x 0.912) + (1-0.98).(1-0.23))= 0.93
(Thus, the chance the patient has COVID-19 given a positive test is 93%)

NPV = (1-0.23)(0.98) / ((0.98)(1-0.23) + (1-0.912)(0.23)) = 0.97

ii) Using prevalence of Covid-19 in Malaysia :

PPV = (0.0017 x 0.912)/((0.0017x 0.912) + (1-0.98).(1-0.0017))= 0.072
(Thus, the chance the patient has COVID-19 given a positive test is 7.2%)

NPV = (1-0.0017)(0.98) / ((0.98)(1-0.0017) + (1-0.912)(0.0017)) = 0.99

Bayes' theorem is stated as below:
P (B|A) = P(A and B) / P (A)

There are two most important rule in understanding of conditional probability.

1. Reciprocal rule
P (Event A |Event B) ≠ P (Event B| Event A)
= Which means sensitivity is not equal to PPV.

2. Multiplication rule
P (Event A and Event B) = P (A) x P (B| A)

We have shown mathematically that predictive values are determined by the Se and Sp of a test as well as the prevalence of a disease in the population. In contrast, Se and Sp are independently affected by prevalence. Given this mathematical property, the measures of Se and Sp can be used and computed across different populations with difference prevalence rate with the assumption that the disease characteristics such as clinical severity or laboratory cut-offs does not differ much depending on the measures and extent of a disease.

For clinicians, sensitivity and specificity may still be useful to rule conditions (i.e illnesses) in or out during the course of a patient's differential diagnosis. On the other hand, predictive values are more clinically useful and intuitive. For a patient to be 'predicted' (diagnosed) as negative confidently, a highly sensitive diagnostic test is required in a low disease prevalent population. Although it is desirable to have tests with high sensitivity and specificity, the values for those two metrics should not be relied on making decisions about individual people in screening situations. PPV and NPV is more appropriate to indicate the likelihood that a test can successfully identify whether people do or do not have the target condition/disease base on the result.

References

1/ Annette M. Molinaro Diagnostic Test: How to estimate the positive predictive value Neuro-oncology Practice 2(4), 162-166. 2015
2/Christopher M Sensitivity, Receiver -Operating Characteristic (ROC) Curves and Likelihood Ratios Clinical Biochem Review Vol 29 2008
3/ Hwee B. W. Measures of Diagnostic Accuracy: Sensitivity, Specificity, PPV and NPV Proceedings of Singapore Healthcare Volume 20 Number 4 2011
4/ Fierz W Problems of Serological Laboratory Diagnosis Molecular Biotechnology Volume 13 1999

Polemics in the Lancet volume 398, issue 10301 (August 21, 2021) on the evidence presented in **Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis.** *Lancet.* 2020; **395**: 1973-1987
(View in Article: Scopus (1168); PubMed; Summary; Full Text; Full Text PDF; Google Scholar).

Author: Willem Marten Lijfering
Revisiting the evidence for physical distancing, face masks, and eye protection.
CORRESPONDENCE| VOLUME 398, ISSUE 10301, P659-660, AUGUST 21, 2021.
"Derek Chu and colleagues' 2020 meta-analysis was epidemiologically flawed. In a comparison of countries where face mask wearing was mandatory (eg, China) with countries where it was not (eg, Italy), they find a lower rate of COVID-19 in countries where masks were mandatory. Many variables can explain such a finding, so it is clearly a case of correlation not causation. …."
Full-Text HTML
PDF

Author: John Conly, Roger Chou, Mitchell J Schwaber, Andreas Voss
Revisiting the evidence for physical distancing, face masks, and eye protection
CORRESPONDENCE| VOLUME 398, ISSUE 10301, P660, AUGUST 21, 2021
"Derek Chu and colleagues1 concluded, based on an analysis of a subgroup of observational studies, that health-care workers might afford greater protection against SARS-CoV-2 infection from N95 respirators than from surgical masks. They acknowledge substantial limitations and rated certainty of effect as low. We would argue it is lower still, as several studies seem to have been misclassified with regard to mask type…"
Full-Text HTML
PDF

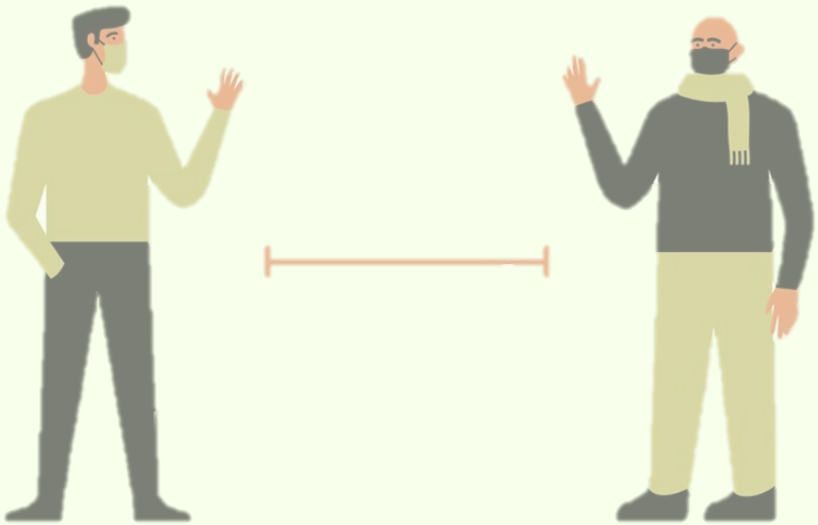
Author: Luca Scorrano, Ilaria Baglivo, Domenico Maria Cavallo, Francesco Cecconi, Sara Gandini
Revisiting the evidence for physical distancing, face masks, and eye protection
CORRESPONDENCE| VOLUME 398, ISSUE 10301, P660-661, AUGUST 21, 2021
"Derek Chu and colleagues reported that face mask wearing in hospitals and health-care settings reduces risk of respiratory infection.1 Surprisingly, this recommendation was extended to the general population. Summary estimates were calculated using results of three severe acute respiratory syndrome studies, of which only two yielded statistically significant results…"
Full-Text HTML
PDF

Author: Qi Zhou, Xiaoqin Wang, Janne Estill, Kehu Yang, Yaolong Chen
Revisiting the evidence for physical distancing, face masks, and eye protection
CORRESPONDENCE| VOLUME 398, ISSUE 10301, P661, AUGUST 21, 2021
"Derek Chu and colleagues1 examined whether physical distancing, face masks, and eye protection could prevent transmission of SARS-CoV-2. We are concerned that some of the data from the included preprints were out of date, affecting the results of the meta-analysis…"
Full-Text HTML
PDF

Author: Mohamed Abbas, Michihiko Goto, Ermira Tartari, Eli Perencevich, Didier Pittet
Revisiting the evidence for physical distancing, face masks, and eye protection
CORRESPONDENCE| VOLUME 398, ISSUE 10301, P661-663, AUGUST 21, 2021
"We read with great interest the results of the systematic review1 on the effect of personal protective equipment (PPE) to prevent SARS-CoV-2 infection, predominantly based on evidence from other betacoronaviruses. As this work raised many more questions than it answered, and because its implications are far-reaching, we highlight several salient concerns…"
Full-Text HTML
PDF

Author: Peter Jüni, Bruno R da Costa, Pavlos Bobos, Nicolas S Bodmer, Allison McGeer
Revisiting the evidence for physical distancing, face masks, and eye protection
CORRESPONDENCE| VOLUME 398, ISSUE 10301, P663, AUGUST 21, 2021
"The systematic review and meta-analysis by Derek Chu and colleagues1 has several problems. First, the investigators combine data on SARS-CoV-2, SARS-CoV, and MERS-CoV.… Second, even if combining data from different diseases were valid, the assumed linear association between distance and the log risk ratio of disease in the meta-regression of physical distancing appears inappropriate…Third, only three studies on SARS-CoV-2 contributed to the meta-analysis of masks versus respirators…"
Full-Text HTML
PDF

The response from the authors to the concerns raised by the others above.
Author: Derek Chu, Assem Khamis, Elie Akl, Ignacio Neumann, Karla Solo, Holger Schunemann
Revisiting the evidence for physical distancing, face masks, and eye protection – Authors' reply
CORRESPONDENCE| VOLUME 398, ISSUE 10301, P663-664, AUGUST 21, 2021
"We appreciate the comments we received on our urgent evidence synthesis addressing use of masks, eye protection, and distancing early on in the COVID-19 pandemic…"
Full-Text HTML
PDF



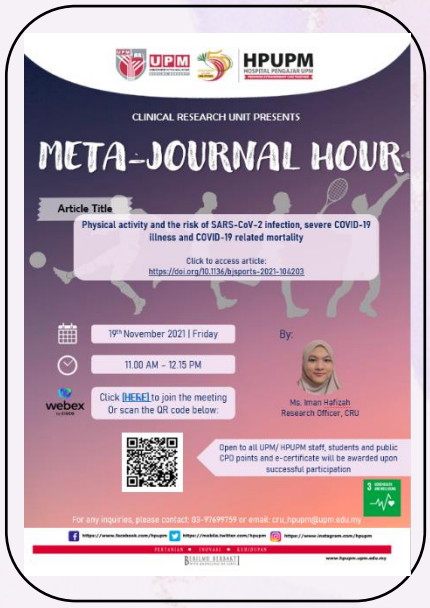
Appraisals in Meta-journal Hour 3

By Nurul Iman Hafizah, Nur Aazifah Ilham and BH Chew



The paper:
Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality in South Korea: a nationwide cohort study. doi: 10.1136/bjsports-2021-104203

Why was this study conducted?
Previous studies have showed protective health benefits of sufficient physical activity in reducing the risk for all-cause and disease-specific mortality, non-communicable chronic diseases such as metabolic syndrome, type 2 diabetes and cardiovascular disease as well as improved physical functioning, cognition and quality of life. However, the impact of physical activity on infectious disease particularly COVID-19 infectivity and its clinical outcomes remained unclear. This study aimed to investigate the hypothesis that sufficient physical activity may reduce the risk of COVID-19 infectivity, severity and its related mortality among patients who underwent SARS-CoV-2 testing and its association with length of hospital stay.



How was it done?

Study Population and Data Source
The study included all Korean individuals aged ≥20 years who underwent SARS-CoV-2 testing between 1st January 2020 to 30th May 2020 (n=212 768) in which their data were subsequently linked to Korean national general health examination data between 1 January 2018 and 31 December 2019 to obtain the assessment on their level of physical activity and other relevant data such as socioeconomic background, lifestyle habit, comorbidities and medication history and health assessment.

Exposures and Outcomes
For the classification of exposures and outcomes, please refer figure below.

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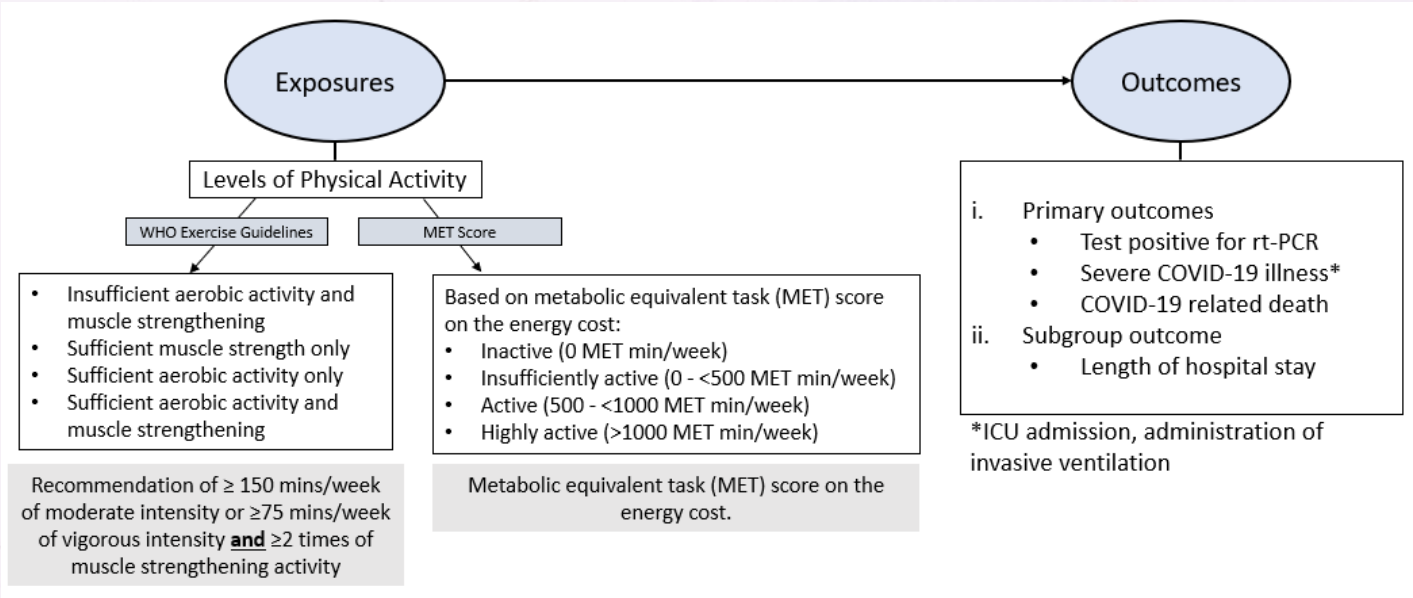
Or click [HERE] and don't forget to subscribe to our channel!



Eight Cohorts Studied

The researchers generated eight cohorts for robustness and generalization of the results. Cohort A was the main study whereby physical activity level of the participants was classified according to WHO exercise guidelines. The characteristics of participants in each cohort as shown in table below:

Cohort	Characteristics	No. of participants
Cohort A	Participants who received general health examination between 2018 and 2019 whom the physical activity was classified according to WHO exercise guidelines.	76 395
Matched cohort A	Propensity score matching of two groups (insufficient aerobic and muscle strengthening vs aerobic and muscle strengthening)	5298
Cohort B	COVID-19 confirmed patients in cohort A	1293
Cohort C	Physical activity was categorised based on MET Score	76 395
Matched cohort C	Propensity score matching of two groups (insufficient physical activity group (0–500 MET min/week) vs sufficient physical activity group (more than 500 MET min/week)	59 986
Cohort D	Participants who received general health examination between 2015 and 2019	118 768
Matched cohort D	Propensity score matching of two groups (insufficient physical activity group (0–500 MET min/week) vs sufficient physical activity group (more than 500 MET min/week)	23 860
Cohort E	COVID-19 confirmed patients in cohort C	3882

Refer to supplemental paper for detailed explanation for each cohort entries.

Sample Size Calculation

There was no study on association between SARS-CoV-2 infectivity and physical activities. Therefore, the sample size was calculated using previous study on the relationship between COVID-19 severity and physical activity [1]. They had calculated for each group to have 80% power to show a 2.8-fold improvement of severity among COVID-19 patient at 5% significant level which they need 900 patients at each group. They able to include 1293 patients with COVID-19 who had insufficient physical activity 1002 patients with COVID-19 who had sufficient muscle strengthening, aerobic or both physical activities.

Statistical Analysis

To assess the different confounding effects, researcher used three sequential inclusion adjusting model by modified Poisson regression presented by adjusted relative risk (aRR) with 95% CI or multivariate analysis of covariance presented by adjusted mean difference with 95% CI. The covariate adjustment was done using three model as below:

Model	Adjustments
Model 1	Adjusted for age (20–39, 40–59 and ≥60 years) and sex.
Model 2	Adjusted for age; sex; region of residence (Seoul Capital Area, Daegu/Gyeongbuk area and other area); Charlson comorbidity index (0, 1 and ≥2); history of diabetes mellitus, tuberculosis, stroke and cardiovascular disease; body mass index (continuous, using the cubic spline function); systolic blood pressure (continuous); diastolic blood pressure (continuous); fasting blood glucose (continuous); serum total cholesterol (continuous); glomerular filtration rate (≥90, 60–89 and ≤59 mL/min); household income (low, middle and high); smoking (never, ex and current); alcoholic drinks (<1, 1–2, 3–4 and ≥5 days per week); and medication for hypertension, diabetes mellitus and cardiovascular disease.
Model 3	Adjusted for minimal selected potential confounders by directed acyclic graph approach.

The stability and reliability of the result researcher performed several analyses with multiple condition.

1. Analysed two differential conditions of exposure such as using the physical activity guidelines (cohorts A and B) and MET score (cohorts C-E).
2. Performed propensity score matching to reduce confounding effects and to balance the baseline characteristic.
3. Sensitivity analysis was conducted by generating cohorts B and E, including only patients with COVID-19 only.
4. Directed acyclic graph approach was used to confirm adequate potential mediator in order to avoid overfitting issues.
5. Subgroup analysis was done by stratification according to age, gender, smoking status and Charlson comorbidity index.
6. Sidak's correction for multiple comparisons was done to reduce probability type 1 error.

Statistical analysis was performed using SPSS V.25.

What was the finding?

The authors presented the findings by each cohort in the paper. In the main study (cohort A), it was identified that 41 293 (54.1%), 5036 (6.6%), 18 994 (24.9%) and 11 072 (14.5%) adults with insufficient aerobic and muscle strengthening, muscle strengthening only, aerobic only and aerobic and muscle strengthening, respectively. Table 1 in the paper shows the baseline characteristics of patients who performed the SARS-CoV-2 testing in the Korean nationwide cohort (cohort A). In general, the results of the study indicated that those who engaged in both aerobic and muscle strengthening activity according to the exercise recommendations had a lower risk of SARS-CoV-2 infection (adjusted relative risk [aRR), 0.85; 95% CI 0.72 to 0.96), severe COVID-19 illness (aRR 0.42; 95% CI 0.19 to 0.91) and COVID-19 related death (aRR, 0.24; 95% CI 0.05 to 0.99) than those who did not. It was also found that the recommended key target range of metabolic equivalent task (MET; 500–1000 MET min/week) was associated with reduced risk of SARS-CoV-2 infection (aRR 0.78; 95% CI 0.66 to 0.92), severe COVID-19 illness (aRR 0.62; 95% CI 0.43 to 0.90) and COVID-19 related death (aRR 0.17; 95% CI 0.07 to 0.98). The length of stay in hospital was shortened about approximately 2 days in patients with both aerobic and muscle strengthening or with 500–1000 MET min/week.

How much can we take out from this research/paper?

The protective effect of physical activity on SARS-CoV-2 infection, severe COVID-19 and deaths were around 15%, 50% and 80% (less consistent due to low event rates), respectively. Overall, it is a good research and report that used credible data sources and measurements, and multiple statistical analyses to verify the results. Physical activity as classified according to the level of intensity in minutes (150 mins moderate or 75 mins vigorous) per week and frequency of muscle strengthening per week are practically useful for most users. However, this may not be the case with MET classification although it is a more accurate and informative measurement to some professionals. The observed protective effects of physical activities on the outcomes were quite huge and large on some COVID deaths and severe diseases. It was well discussed of residual confounding from inaccurate measurement of some the included factors, and missed factors (dietary habits, etc) [2]. The MET classification of the physical activity suggested that active instead highly active physical activity category conferred best benefits from suffering from the adverse outcomes. Unfortunately, MET is not a useful measurement that is practical to many people, and it was also not properly defined in the paper.

The researchers noted some possible interaction between some sociodemographic and the physical activity categories. Further subgroup analyses revealed interesting results of differential effects of different physical activity groups in different age groups, gender, smoking and comorbidity status on the outcomes (refer to Table 3 in the paper) [3]. For example, compared to those doing less than 150 mins moderate or 75 mins vigorous physical activity per week, physical activity when done at that level or higher prevented infection only in those aged 40-56 year-old and lowered the severe COVD-19 in those ≥ 60 year-old; combined aerobic and muscle strengthening done at or higher than that defined benefited only men from infection but female require only the aerobic exercises to lower risk of severe COVID-19 significantly. Lastly, physical activity has no observed effects among smokers (ex- and current) and those who scored other than zero on the Charlson comorbidity index.

The external validity of the findings from this study may become less due to the vaccination against COVID-19 assuming that the vaccines provided a relative large protective effects on the studied outcomes in the paper. Nonetheless, the actual benefits from physical activity in the presence of the vaccination is unknown and this require a repeat of the study by the researchers. However, the indirect effects of physical activity on health and from COVID-19 are believed to be presence.

References

1. Sallis R, Young DR, Tartof SY, et al. Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients. Br J Sports Med 2021. doi:10.1136/bjsports-2021-104080.
2. Chin YS, Chew BH and Widyahening IS. Dietary Practices and Nutrition for the Prevention of COVID-19. RECRUS Res. Newsl. 2021;1 (3): 1-5. Access on 19 November 2021, https://hpupm.upm.edu.my/upload/dokumen/20210722171045Dietary_Practices_and_Nutrition_for_the_Prevention_of_COVID-19_The_Brief_&_Summary.pdf
3. Lee SW, Lee J, Moon SY, et al. Physical activity and the risk of SARS-CoV-2 infection, severe COVID-19 illness and COVID-19 related mortality in South Korea: a nationwide cohort study. Br J Sports Med. 2021 Jul 22:bjsports-2021-104203. doi: 10.1136/bjsports-2021-104203.

CONGRATULATION TO ASSOCIATE PROFESSOR NIZLAN AND THE TEAM! AWARDED FOR 1ST RUNNER UP OF THE SANUSI GHANI AWARD

No.	Content	Investigator/Collaborator
1.	*The PUTRA Technique for Chronic Acromio-clavicular (AC) Joint Reconstruction - When AC Ligament Matters*	 1. **Associate Professor Dr Mohd Nizlan bin Mohd Nasir** Co-Investigators: 2. Dr Raymond Yeak Dieu Kiat 3. Dr Azlan Sulaiman 4. Dr Johan Abdul Kahar
2.	*Award* The 1st Runner Up of the Sanusi Ghani Award at the Malaysian Arthroscopy Society Annual Scientific Meeting 2021	
3.	*What the project aims to achieve?* To come up with a more stable technique for Chronic AC Joint reconstruction.	
4.	*Why is it important?* • There is a high incidence of failure of coraco-clavicular ligament reconstruction without incorporation of the AC ligament • There has also been reports of high incidence of pin-site infection with usage of Kirchner wires to stabilize the AC joint post-reconstruction • The PUTRA technique uses an **internal brace** for better stability of our biological CC and AC reconstruction	
5.	*How will it be done?* This technique has been used for AC joint reconstruction in HPUPM since 2020.	
6.	*Expected output?* The clinical outcome is promising	

The PUTRA Technique for Chronic Acromio-clavicular (AC) Joint Reconstruction - When AC Ligament Mat

Chronic acromio-clavicular (AC) joint disruption poses a challenge to the treating surgeons due to the fact that coraco-clavicular (CC) restoration alone resulted in sub-optimal stability and subsequent loss of reduction. Techniques have evolved from simple CC fixation, reconstruction using synthetic devices and, of late, reconstruction with **biological augmentation**. Biological reconstructions which include acromio-clavicular (AC) ligament reconstruction have shown promising result as horizontal stability is also restored, and this is the technique used by UPM together with **TWO additional augmentation** procedures, as depicted in this case report.

Three patients with chronic AC joint disruption (def: post-traumatic period of more than 4 weeks) were seen at HPUPM's Orthopedic Clinic. All patients showed complete disruption of their CC and AC ligaments with **two (2) displaying Rockwood Type 5 and one (1) with Type 4** disruption. All three patients consented and underwent biological reconstruction of their CC and AC ligaments using hamstring autograft harvested from their left lower limbs. The construct of all three cases was done according to Figure1.

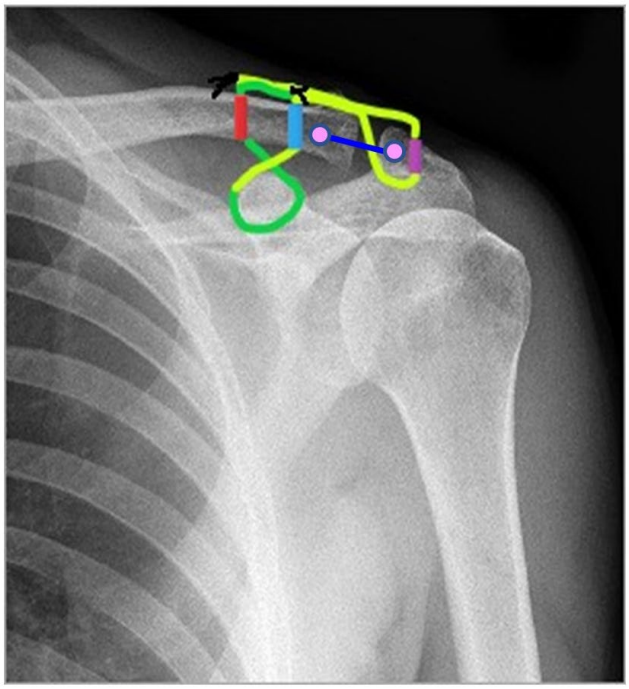


Diagram: The PUTRA AC Joint Reconstruction technique. The bright and dark green tracing represents the graft construct and the dark blue line with the pink dots represent the internal brace (IB) construct

Figure 1

Additional AC ligament reconstruction has been incorporated into CC ligament reconstruction following further understanding of its role in the stability of the AC joint[1]. Unfortunately, there is paucity of AC ligament reconstruction techniques in the literature[2] and we have created the technique mentioned above. The residual length of the semitendinosus tendon was adequate to **extend the procedure laterally** to incorporate the acromio-clavicular articulation.

In conclusion, Additional AC ligament reconstruction is a crucial step in the reconstruction of the AC joint stability with end-to-end graft suturing and additional usage of internal bracing to augment the construct.

Figure 1 shows the construct of the AC joint reconstruction done for all 3 patients. Two 5-mm tunnels were created at the distal clavicle 3.5 cm (conoid) and 2.5 cm (trapezoid) from the distal end. The graft's end was fixed in the ***conoid tunnel*** *(**red colour**) using a* ***4-mm biotenodesis screw (picture)*** *with its end left free around 1 - 1.5 cm. The graft was then looped under the coracoid process and passed in a figure-of-eight fashion towards the* ***trapezoid tunnel*** *(**blue**). The distal clavicle was then reduced with slight over-reduction and the trapezoid tunnel graft fixed using another 4-mm screw.*

The graft is then passed over the distal clavicle and under the acromial medial edge, subsequently ***passed from inferior to superior*** *surface of the acromion through another 5-mm tunnel (**purple**); the graft is then looped back, overlapped and* ***sutured to the free end of the graft*** *on the other side of the construct (white arrow). This* ***end-to-end suturing*** *is* ***one of our modifications*** *to this technique.*

After that, ***internal brace fixation*** *was added using a 2-mm fiber-tape which was fixed at the clavicle side of the construct using a 4.75-mm swivel-lock anchor and another at the acromion side with a 3.5-mm anchor. The orientation of the internal brace varies, depending on the type of AC joint disruption. The usage of internal brace is the other* ***additional augmentation procedure*** *practiced by UPM team.*

WINNER OF RESEARCH GRANT 2020 – 2021

December 2021
Vol. 1 Issues 10
Page 135

Molecular mechanism of Centella asiatica-enriched Exosomes in Mediating Neural Stem Cell activity in vitro: A fundamental understanding towards cell-free therapy for brain diseases.

- 1 November 2020 - 31 October 2023
- 3 years

Allocation

RM 185, 200

What the project aims to achieve?

This study investigates the therapeutic potential of exosomes originating from neural stem cells (NSCs) transdifferentiated from Centella asiatica (CA)-enriched amniotic fluid stem cells (AFSCs).

Why is it important?

- Presently, there is no cure for brain defects such as neurodegenerative diseases (NDs) and brain injury.
- One possible approach for the treatment of these diseases is through neuro-transplantation. Unfortunately, the low survival, migration, differentiation and integration efficiency of transplanted NSCs in the brain remains poor.
- Recent studies have suggested the possibility of exogenous NSCs to execute their therapeutic effects through secreting exosomes. These naturally occurring lipid-bound nano-vesicles protect, transport and deliver bioactive molecules from stem cells to target cells in the brain as they can pass through the blood-brain barrier.
- These exosomes could be the answer for treating neurodegenerative diseases and brain injury, particularly from high-quality exogenous NSCs, through treatment using exosomes delivering pharmaco-molecules for future cell-free or acellular therapy.
- Herbal extract such as CA, known for its antioxidant and neurogenic properties, could be utilised to stimulate the production of valuable therapeutic molecules from NSC-derived AFSCs as cargo in the exosomes.

How will it be done?

This study Involves *in vitro* study of the exosomes from CA-enriched AFSC-derived NSCs using a cell line established in-ho rat full-term amniotic fluid stem cell (R3).
We are interested in unravelling the valuable factors in the exosomes and understanding the mechanism by which the exosomes mediate their effect on endogenous rat brain-derived NSCs in culture conditions.

INVESTIGATOR:
ASSOCIATE PROFESSOR DR. NORSHARIZA NORDIN

Co-investigators:
- AP Dr. Lim King Hwa (UPM)
- AP Dr. Asilah binti Ahmad Tajudin (UPM)
- AP Dr. Cheah Pike See (UPM)
- Prof. Dr. Mohd Ilham bin Adenan (UiTM)

International Collaborator:
- Professor Dr John O. Mason (University of Edinburgh)

Industrial Collaborator:
- Genomax Technologies Sdn. Bhd

The study is divided into three parts:
a) To isolate the exosome and identify the factors cont exosomes secreted from AFSC-derived NSCs treated wi
b) To assess how these exosomes promote proliferatio (neurospheres) at cellular and molecular levels.
c) To determine how these exosomes affect the differe NSCs at cellular and molecular levels.

Expected output?

- Novel therapeutic cell-free therapy approach in treating brain defects. Fundamental knowledge for the generation of high quality exogenous neural stem cells where a continuous supply of cell sources for neuro-transplantation could be initiated. This study would have a high impact on the well-being of not only humankind but also of animals.
- Publications: Two research articles.
- PhD student: One.
- Intellectual Property (IP): One IP on generating CA-treated amniotic fluid stem cell-derived neural stem cell exosomes.

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Speaker

Ms. Iman Hafizah
Research Officer, CRU

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TENTATIVE PROGRAM

Time	Title	Speaker*
0830-0915	Determination of a minimum required sample size: Concept and application	SHN
0915-1000	Sample size determination in interventional studies	SHN
1000-1015	**Break**	
1015-1100	Sample size determination in observational descriptive studies	SHN
1100-1145	Sample size determination in observational analytical studies	SHN
1145-1230	Sample size determination using risk estimates	SHN
1230-1300	Tips and tricks, dos and don'ts in sample size determination	SHN
1300 -1430	**Lunch and prayers**	
1430-1500	Sample size for common statistical tests (correlation, Cronbach's alpha)	MAB
1500-1600	Sample size using rule of thumb - for multivariate statistical tests	MAB
1600- 1630	Summary of the process on sample size calculation & estimation	MAB
1630-1700	Open Forum / Question and Answer	SHN MAB

* **SHN** PROF DR SYED HATIM NOOR

MAB DR MOHAMAD ADAM BUJANG

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