INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

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MASTHEAD

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INA-RESPOND Newsletter

TRIPOD, PROACTIVE, & ORCHID Study Updates

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

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Two papers from the TRIPOD study have been submitted to the American Journal of Tropical Medicine and Hygiene and the Frontiers in Medicine - Infectious Diseases - Surveillance, Prevention, and Treatment. Both are currently under review.

Other ongoing activities regarding TRIPOD are summarized below:

- Collaboration within the RePORT network on Epidemiology of TB Progression and Outcomes Study, using the TRIPOD data is still ongoing with the Data Transfer Agreement between INA-RESPOND Rutgers University. Meanwhile, the INA-RESPOND team will prepare the progress RePORT Data harmonization study.
- INA RESPOND reference Laboratory successfully sequenced the mTB DNA samples from 8 participants using oxford nanopore (Minion). The analysis of the sequence to find out mutations associated with drug resistance is still in process. We need to explore the software suitable for the sequencing data obtained. We are still waiting for the sub-culture process in BBLK Bandung for about 116 isolates remaining.

INA104

As of April 15, 2022, from 4336 subjects enrolled, 49.4 % of subjects have ended their study, and 50.5% are still on-going. For the end of study subjects, 1702 subjects had already completed the study until follow up visit month 36, 227 subjects died, 142 subjects were lost to follow up, 32 subjects withdrew their consent, 31 subjects moved to the city without PROACTIVE Site, five subjects with HIV negative, and one subject was suspended (imprisoned). The study progress from each site is described in Figure 1, while the detailed information on the end of study participants is available in Table 1.

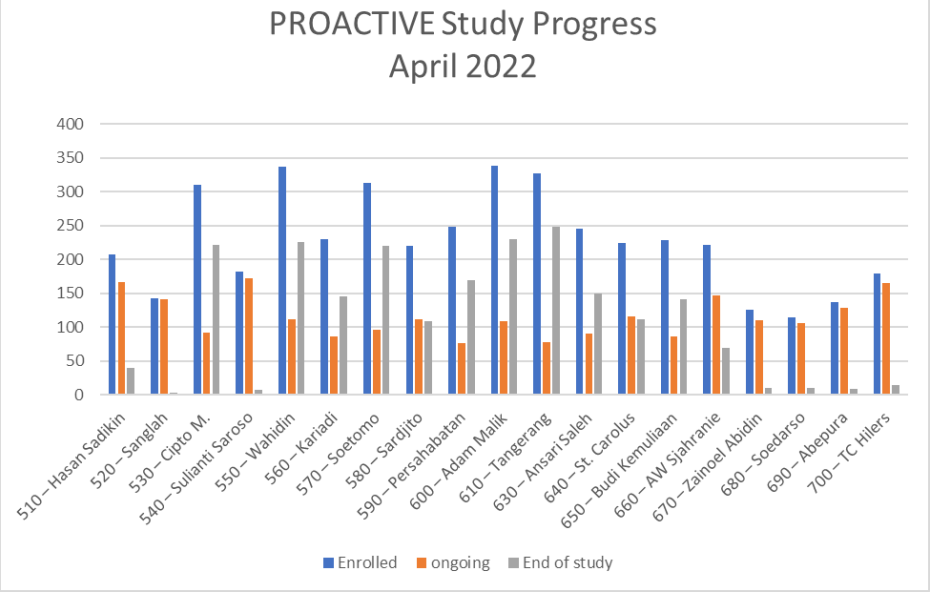

Figure 1. Site's study progress

For the monitoring activity, there are two on-site monitoring visits in April 2022, namely to Persahabatan Hospital (site 590) on 11-13 April 2022 and to Dr. H. Adam Malik Hospital (site 600) on 19-21 April 2022.

Table 1. Subjects' end of study reasons

No	Site	*End of Study Duration/ Complete*	Withdrew Consent	Participants with HIV negative	Moved	Death	Investigator Discretion	Lost to Follow Up	Other	Total
1.	510 – RSUP Dr. Hasan Sadikin	33	1	0	2	4	0	0	0	40
2.	520 - RSUP Sanglah	1	0	0	0	3	0	0	0	4
3.	530 – RSUPN Dr. Cipto Mangunkusumo	198	0	0	0	17	0	6	0	221
4.	540 – RSPI Dr. Sulianti Saroso	0	0	0	2	6	0	0	0	8
5.	550 – RSUP Dr. Wahidin Sudirohusodo	160	0	0	5	21	0	40	0	226
6.	560 – RSUP Dr. Kariadi	121	1	3	0	14	0	7	0	146
7.	570 – RSUD Dr. Soetomo	176	13	0	4	21	0	6	0	220
8.	580 – RSUP Dr. Sardjito	88	1	0	4	4	0	12	0	109
9.	590 – RSUP Persahabatan	125	0	1	0	35	0	9	0	170
10.	600 – RSUP Dr. H. Adam Malik	176	3	0	2	21	0	28	0	230
11.	610 – RSU Kabupaten Tangerang	204	7	0	3	19	0	14	1	248
12.	630 – RSUD Dr. M. Ansari Saleh	135	1	0	1	7	0	6	0	150
13.	640 – RS St. Carolus	109	0	0	0	1	0	2	0	112
14.	650 – RSU Budi Kemuliaan Batam	118	3	0	5	8	0	7	0	141
15.	660 – RSU A. Wahab Sjahranie	58	0	0	2	5	0	5	0	70
16.	670 – RSUD Zainoel Abidin	0	0	0	0	11	0	0	0	11
17.	680 – RSUD Soedarso	0	0	0	0	10	0	0	0	10
18.	690 – RSUD Abepura	0	1	1	1	6	0	0	0	9
19.	700 – RSUD TC Hillers	0	1	0	0	14	0	0	0	15
Total		1702	32	5	31	227	0	142	1	2140

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Based on uploaded CRFs as of 5 April 2022, a total of 183 participants were enrolled in the ORCHID-COVID-19 study, with 115 from site 610 (RSU Kabupaten Tangerang, Tangerang) and 68 from site 521 (RS Universitas Udayana, Denpasar). This study had 172 (94%) participants who completed the visits, with 5 (3%) participants died during the study. In terms of deaths, 2 subjects from site 610 died because of COVID-19 and heart failure, while 3 subjects from site 521 died from thromboembo-

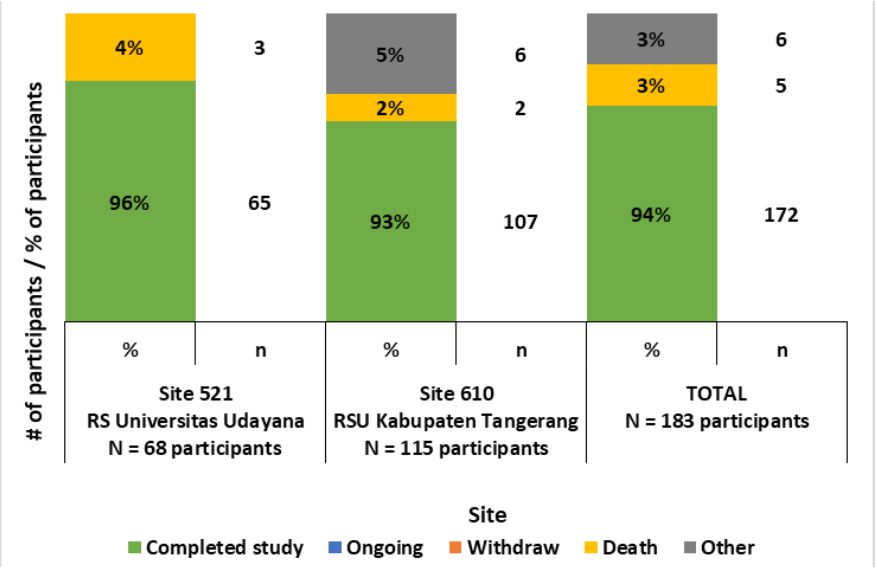


Figure 1. Participant status per site based on uploaded CRF as of 5 April 2022

lism, non-ST-segment Elevation Myocardial Infarction, and thromboembolism. On the other hand, 6 (3%) participants decided to not continue participation to the study (categorized as other) (figure 1).

As of 5 April 2022, a total of 153 (84%) participants were identified as positive COVID-19 while 30 (16%) participants were identified as negative COVID-19. In site 610, the number of participants identified as positive COVID-19 was 105 (91%) and 10 (9%) participants identified as negative COVID-19. On the other hand, in site 521, there were 48 (71%) participants identified as positive COVID-19 and 20 (29%) participants identified as negative COVID-19 (figure 2).

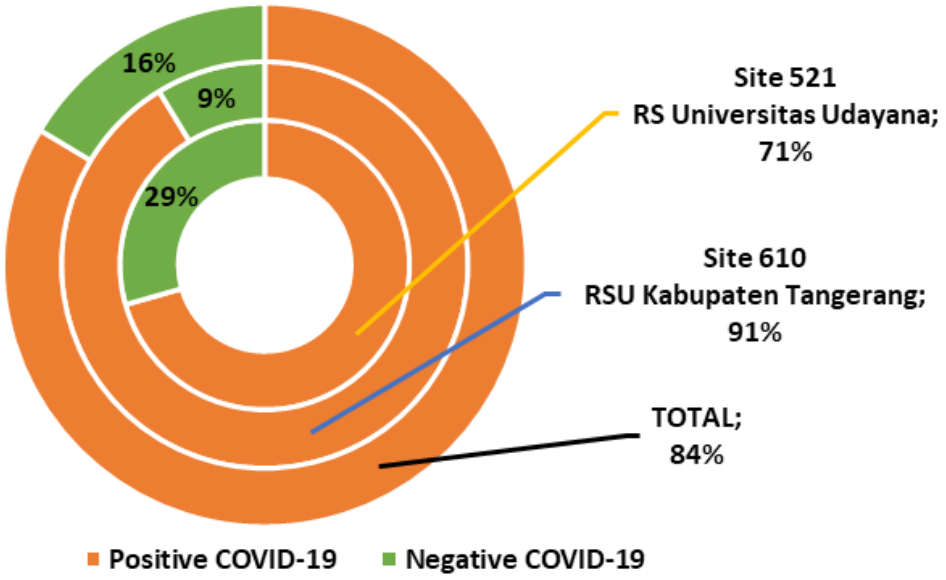


Figure 2. COVID-19 identification at enrolment based on uploaded CRF per 5 April 2022

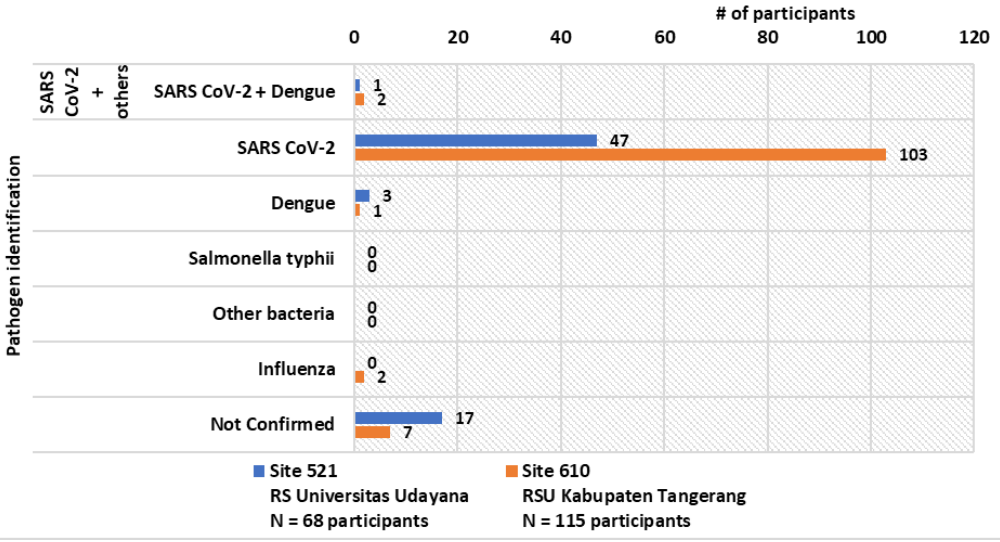


Figure 3. Pathogen identification based on uploaded CRF per 5 April 2022

In site 521, SARS-CoV-2 was identified in 47 (69%) participants based on the pathogen identification data. SARS-CoV-2 and Dengue (confirmed by PCR SARS-CoV-2 and RDT Dengue IgM) co-infection were identified in 1 (1%) participant. Dengue (confirmed by RDT Dengue NS-1) was also identified in 3 (5%) participants. Based on the data from site 610, SARS-CoV-2 was identified in 103 (90%) participants. SARS-CoV-2 and dengue (confirmed by PCR SARS-CoV-2, RDT Dengue NS-1, and RDT Dengue IgM IgG) co-infection were identified in 2 (2%) participants. Influenza (confirmed by PCR) was identified in 2 (2%) participants. Dengue (confirmed by RDT Dengue NS-1 and RDT Dengue IgM IgG) was also identified in 1 (1%) participant. Overall, the pathogen was unidentifiable among 24 (13%) participants, 17 were from Site 521 and 7 from site 610 (figure 3).

INA-RESPOND Newsletter

RISK OF NEWLY DIAGNOSED DIABETES MELLITUS AFTER COVID-19

By: Yan Mardian

SCIENCE CORNER

Every 18 April the National Diabetes Day (or Hari Diabetes Nasional) is celebrated in Indonesia. This campaign is led by the Indonesian Ministry of Health and is intended to increase the awareness of diabetes mellitus. Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Hyperglycaemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels. In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2019, diabetes was the direct cause of 1.5 million deaths, and 48% of all deaths due to diabetes occurred before the age of 70 years (1).

Data reveal an increased risk of diabetes in the months after acute COVID-19 infection – which could have implications for stretched public health systems. A few reports have raised the possibility that COVID-19 could increase the risk of type 2 diabetes. In The Lancet Diabetes & Endocrinology, Xie and Al-Aly offer further evidence for the increased risk of diabetes beyond the first 30 days of infection (post-acute phase) by analyzing the US Department of Veterans Affairs national health-care records of those who survived the first 30 days after a positive COVID-19 test. These data raise important questions about the relationship between COVID-19 and diabetes concerning causality, biological mechanisms, and implications for clinical care and public health (2).

Incidence of diabetes and antihyperglycemic medication use was compared between 181,280 COVID-19 survivors, 4,118,441 contemporary controls without COVID-19 infection from the same year, and 4,286,911 historical controls from 2017. Diabetes was defined by the International Classification of Diseases-10 diagnosis codes or an HbA1c of more than 6·4% (46 mmol/mol). The authors used inverse probability weighted survival analyses, including predefined and algorithmically selected high dimensional variables, and reported two measures of risk; hazard ratio (HR) and burden per 1000 people at 12 months.

The study revealed that COVID-19 infection appears to significantly raise the risk for diabetes by about 40% at 1 year. Significantly increased diabetes risks compared to those not infected ranging from 31% to more than double were found in a subgroup analysis based on diabetes risk score, body mass index, age, race, prediabetes status, and deprivation level, and even after adjusting for confounding factors. Risks and burdens of post-acute out-

comes increased in a graded fashion according to the severity of the acute phase of COVID-19 (whether patients were non-hospitalized, hospitalized, or admitted to intensive care), but a significant excess diabetes burden was seen even among those with "mild" COVID-19. All the results were consistent in analyses using the historical control as the reference category.

Given the extraordinary number of COVID-19 cases globally — 480 million confirmed cases and counting — the modest increase in diabetes risk could correspond to a drastic rise in the number of people diagnosed with the disease worldwide. But the findings of the aforementioned study might not translate to other groups of people. The US veterans in the study were mostly older, white men, many of whom had elevated blood pressure and were overweight, putting them at high risk of developing diabetes. And it's possible that some people in the control group had undetected mild or asymptomatic COVID-19 but were never tested, potentially skewing the data. Other factors might also be contributing to the apparent rise in diabetes among people who recovered from COVID-19. Existing cases of diabetes might have gone undetected until people sought medical care for COVID-19.

Another study, recently published in Diabetologia, also suggested that people who recover from a mild case of COVID-19 appear to have an increased risk for subsequent new-onset type 2 diabetes but not other types of diabetes. The findings were based on a nationwide primary care database in Germany. The retrospective cohort analysis was performed using data from the Disease Analyzer, a representative panel of 1171 physician practices in Germany, from March 2020 to January 2021, with follow-up through July 2021. Individuals with a history of COVID-19 or diabetes and those taking corticosteroids within 30 days after the index dates were excluded (3).

A total of 35,865 patients with confirmed SARS-CoV-2 infection were propensity score-matched on a one-to-one basis for sex, age, health insurance, and comorbidities with those who had acute respiratory tract infections (controls) but were COVID-19 negative. Median follow-up was 119 days for the COVID-19 group and 161 days for controls. There was a 28% increased risk of type 2 diabetes for those who had COVID-19 versus controls (15.8 per 1000 person-years vs 12.3 per 1000 person-years, respectively, which was significantly different, and an incidence rate ratio [IRR] of 1.28). The incidence of other types of diabetes or unspecified diabetes for the COVID-19 and control groups did not differ significantly (4.3 per 1000 person-years vs 3.7 per 1000 person-years; IRR, 1.17).

There are many plausible theories about how COVID might cause diabetes, but none have been proven (4). One possibility is that inflammation caused by the virus could bring about insulin resistance, which is a feature of type 2 diabetes. Early in the pandemic, researchers raised concerns based on anecdotal reports in young people and children that SARS-CoV-2, like other viruses, might damage cells in the pancreas that produce insulin, triggering type 1 diabetes. But data on a link between SARS-CoV-2 infection and newly diagnosed cases of type 1 diabetes remain mixed. Several studies have found no evidence that the disease is causing the uptick in cases of type 1 diabetes in younger adults or children. And a laboratory study published in February also challenged the idea that SARS-COV-2 destroys insulin-producing pancreatic cells. In that study, leveraging comprehensive single-cell analyses of in vitro SARS-CoV-2-infected human pancreatic islets, they demonstrate that productive infection strictly depends on the SARS-CoV-2 entry receptor ACE2 and targets practically all pancreatic cancer cell types. Notably, the infection remains highly circumscribed and largely non-cytopathic and, despite a high viral burden in infected subsets, promotes only modest cellular perturbations and inflammatory responses. Similar experimental outcomes are also observed after islet infection with endemic coronaviruses. Thus, the limits of pancreatic SARS-CoV-2 infection, even under in vitro conditions of enhanced virus exposure, challenge the proposition that in vivo targeting of β cells by SARS-CoV-2 precipitates new-onset diabetes. Whether restricted pancreatic damage and immunological alterations accrued by COVID-19 increase cumulative diabetes risk, however, remains to be evaluated (5).

In COVID-19 patients, insulin resistance seems to be abnormal when compared to patients with other critical conditions. This could be a factor affecting the process of new-onset hyperglycemia or diabetes in COVID-19. Montefusco and colleagues demonstrated hyperglycemia and insulin resistance in COVID-19 patients without diabetes. The persistence of hyperglycemia and insulin resistance

was documented six months after acute COVID-19 infections. Furthermore, regarding glucose homeostasis in patients with coronavirus infection, the gut is less focused than the pancreas, liver, skeletal muscle, and adipose tissue. However, increased intestinal glucose absorption via the sodium-dependent glucose transporter (SGLT1) in the intestinal epithelium, which is mediated by the downregulation of ACE2 with a SARS-CoV-2 infection, might also be involved in hyperglycemia in COVID-19 patients (6).

Assessing the diabetogenic and ketosis-prone potential of SARS-CoV-2 variants is an additional challenge. The pandemic variants of SARS-CoV-2 have been reported to change the viral characteristics, including the transmissibility and antigenicity. However, most of the currently available data were based on studies conducted before the major variants of SARS-CoV-2 were circulated. The Omicron variant is associated with a more attenuated disease severity compared to previous circulating variants. Its cellular entry is reported to be less dependent on TMPRSS2. Replication is reduced in the lower respiratory tract that highly expresses TMPRSS2, whereas the infectivity of the Omicron variant is not affected in non--expressing cells in the upper respiratory tract. Moreover, the Omicron variant is characterized by a higher ACE2 binding affinity and increased immune evasion. The expressions of ACE2 and TMPRSS2 under steady-state conditions have different distributions. The tissue tropism of variants and their impact on glycometabolism might be affected (6).

We are amidst dual pandemics of COVID-19 and diabetes and face the threat of the emergence of SARS-CoV-2 variants, including the Omicron variant. These are intricately interrelated, and it is particularly important to reveal the precise mechanism underlying the association between COVID-19 and diabetes as well as to dissolve the vicious circle of hyper inflammation and hyperglycemia. The incidence and etiology of new-onset diabetes remain to be fully elucidated, and the diabetogenic properties of SARS-CoV-2 depending on the variants is a subject for future investigation. A lingering question is also whether the metabolic changes observed in people who had COVID-19 persist after one year. More research is needed to clarify long-term trends in new-onset diabetes at a population level and to tease apart what might be causing them.

Reference:

1. World Health Organization. Diabetes [Internet]. 2021 [cited 2022 Apr 13]. Available from: https://www.who.int/news-room/fact-sheets/detail/diabetes#:~:text=In 2014%2C 8.5%25 of adults,age of 70) from diabetes.
2. Xie Y, Al-Aly Z. Risks and burdens of incident diabetes in long COVID: a cohort study. lancet Diabetes Endocrinol. 2022 Mar;
3. Rathmann W, Kuss O, Kostev K. Incidence of newly diagnosed diabetes after Covid-19. Diabetologia. 2022 Mar;1–6.
4. Watson C. Diabetes risk rises after COVID, massive study finds. Nature. England; 2022.
5. van der Heide V, Jangra S, Cohen P, Rathnasinghe R, Aslam S, Aydillo T, et al. Limited extent and consequences of pancreatic SARS-CoV-2 infection. Cell Rep. 2022 Mar;38(11):110508.
6. Yonekawa A, Shimono N. Clinical Significance of COVID-19 and Diabetes: In the Pandemic Situation of SARS-CoV-2 Variants including Omicron (B.1.1.529). Biology (Basel). 2022 Mar;11(3).

INA-RESPOND Newsletter

THE IMPACT OF THE COVID-19 ON THE CIRCULATION OF OTHER RESPIRATORY VIRUSES

By: Katy Shaw-Saliba

During the COVID-19 pandemic, symptoms such as headache, sore throat, runny nose, cough, fever, and general malaise trigger a SARS-CoV-2 diagnostic test. However, prior to COVID-19, these symptoms were usually associated with the common cold or an acute upper respiratory tract infection (URI). URIs are incredibly common throughout all parts of the globe. In 2019, it was estimated that there were 17.2 billion cases of URIs globally [1]. While many URIs are not life-threatening, they do impact general life quality and can result in severe disease and complications. Additionally, URIs put a strain on health systems, including nosocomial outbreaks and surges in emergency department visits, especially for seasonal URIs.

URIs are most commonly caused by viruses including influenza viruses, respiratory syncytial virus, parainfluenza viruses, metapneumoviruses, rhinovirus/enteroviruses, non-SARS-CoV-2 coronaviruses, respiratory adenoviruses, and bocaviruses. Most respiratory viruses have some seasonal cadence in circulation, particularly as you move away from the equator into temperate regions [2, 3]. The COVID-19 pandemic began during the respiratory virus season in the Northern Hemisphere. Nonpharmaceutical interventions (NPIs), including decreasing global travel, physical distancing, contract tracing, closure of schools, and use of facemasks, had profound, immediate, and unprecedented impacts on the circulation of other non-SARS-CoV-2 respiratory viruses [2, 4-13]. Almost immediately after NPIs were put in place, the circulation of most respiratory viruses ceased (Fig 1).

The question has been posed: what will happen to non-SARS-CoV-2 respiratory viruses as NPIs lift and life returns to "normal" or the new normal? There is a concern given the potential for low population immunity and the stress on the health system that surges of both SARS-CoV-2 and other respiratory viruses could cause. During the 2009 H1N1 pandemic, circulation of other respiratory viruses was shifted temporally, and very little seasonal influenza was observed [14-16]. However, there was no dramatic impact on the magnitude of other respiratory viruses as observed with SARS-CoV-2.

As the COVID-19 pandemic has continued, despite the relaxation of many NPIs, most respiratory virus activity has remained relatively low. Incredibly, global influenza activity has remained the lowest it has been by historical record [2, 5-7, 11, 13, 17]. This is even despite the very low to non-existent efficacy of the influenza vaccine against the predominant A/H3N2 virus in the Northern Hemisphere [18] and the potential for many susceptible hosts [19].

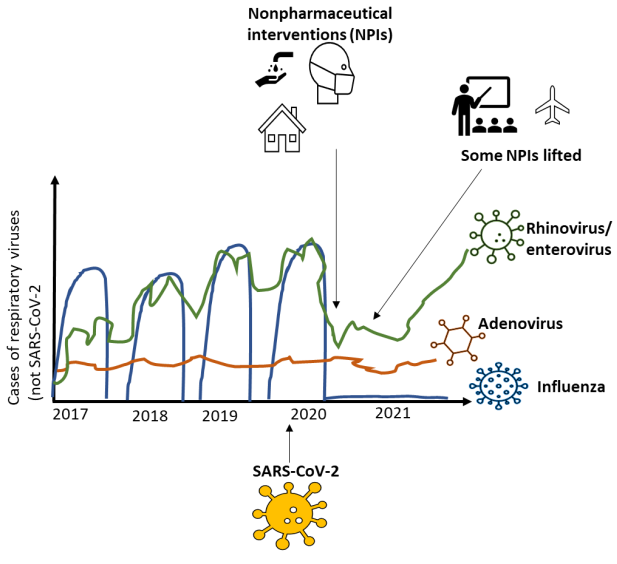


Figure 1. Impact of the COVID-19 pandemic and non-pharmaceutical interventions (NPIs) on other respiratory viruses. Influenza, adenovirus, and rhinovirus/ enterovirus are shown for illustrative purposes.

In contrast to influenza, the circulation of rhinovirus/enteroviruses and respiratory adenoviruses has been less impacted by SARS-CoV-2 [2, 5-7, 11, 13, 17] (Fig 1). Circulation was lower during periods with stringent NPIs, but it was not completely zero, as was the case for other respiratory viruses [2, 5-7, 11, 13, 17]. While adenovirus maintained a consistent level of activity, resurgence and increases in cases have only been observed with rhinovirus/enterovirus following the reopening of schools and easing of travel restrictions, even with facemask mandates and other NPIs still in place [1, 5, 7, 12, 13]. Rhinovirus/enterovirus is a non-enveloped virus that gives it greater environmental stability and better fomite transmission than other respiratory viruses. Additionally, rhinovirus/enterovirus can be transmitted via a fecal-oral route which bypasses facemasks. An expectation would then be that increased case numbers would be observed for other non-enveloped viruses (non-respiratory) that are transmitted via the fecal-oral route with the lifting of certain NPIs. However, this has largely not been observed [5, 7]. There are more than 100 rhinovirus and more than 100 enteroviruses virus types that circulate and infect all age groups. They provide very little cross-immunity [1, 5, 7, 12, 13]. Thus, this combined with differences in transmissibility and stability may explain why rhinovirus/enterovirus did not follow the same pattern as influenza.

While the decreased activity of respiratory viruses has been welcome given the continued COVID-19 pandemic, monitoring the return of influenza and other non-SARS-CoV-2 viruses that cause URIs is important as a larger portion of the population may be very highly susceptible. For respiratory syncytial virus, parainfluenza viruses, metapneumoviruses, and non-SARS-CoV-2 coronaviruses, circulation remains low. However, it does appear activity of these viruses may be increasing and even with some returning out of season [1, 5, 7, 12, 13], which was observed with other respiratory viruses following the 2009 H1N1 pandemic [14-16].

Thus, symptoms of URIs should trigger testing both for SARS-CoV-2 and other respiratory pathogens. Targeted campaigns for an updated influenza vaccine for the 2022-2023 season and understanding of currently circulating respiratory viruses for hospital cohorting to prevent nosocomial infections will be important. Studies such as the InVITE study or ORCHID, where specimens are collected from participants with symptoms consistent with a URI that are negative for SARS-CoV-2 could provide helpful information on the return and circulation of non-SARS-CoV-2 URIs. Finally, it is important to continue NPIs for vulnerable populations who may be highly susceptible to both SARS-CoV-2 and other respiratory viruses.

References

1. Jin, X., et al., Global burden of upper respiratory infections in 204 countries and territories, from 1990 to 2019. eClinicalMedicine, 2021. 37.
2. Zeng, Z., et al., Different Circulation Pattern of Multiple Respiratory Viruses in Southern China During the COVID-19 Pandemic. Frontiers in Microbiology, 2022. 12.
3. Nickbakhsh, S., et al., Epidemiology of Seasonal Coronaviruses: Establishing the Context for the Emergence of Coronavirus Disease 2019. J Infect Dis, 2020. 222(1): p. 17-25.
4. Huang, Q.S., et al., Impact of the COVID-19 nonpharmaceutical interventions on influenza and other respiratory viral infections in New Zealand. Nature Communications, 2021. 12(1): p. 1001.
5. Groves, H.E., et al., The impact of the COVID-19 pandemic on influenza, respiratory syncytial virus, and other seasonal respiratory virus circulation in Canada: A population-based study. Lancet Regional Health. Americas, 2021. 1: p. 100015-100015.
6. Olsen, S.J., et al., Changes in Influenza and Other Respiratory Virus Activity During the COVID-19 Pandemic - United States, 2020-2021. MMWR Morb Mortal Wkly Rep, 2021. 70 (29): p. 1013-1019.
7. Oh, D.-Y., et al., Trends in respiratory virus circulation following COVID-19-targeted nonpharmaceutical interventions in Germany, January - September 2020: Analysis of national surveillance data. The Lancet Regional Health – Europe, 2021. 6.
8. Lee, H., et al., Impact of Public Health Interventions on Seasonal Influenza Activity During the COVID-19 Outbreak in Korea. Clinical Infectious Diseases, 2020. 73(1): p. e132-e140.
9. Cowling, B.J., et al., Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: an observational study. The Lancet Public Health, 2020. 5(5): p. e279-e288.

10. Yeoh, D.K., et al., Impact of Coronavirus Disease 2019 Public Health Measures on Detections of Influenza and Respiratory Syncytial Virus in Children During the 2020 Australian Winter. Clinical Infectious Diseases, 2020. 72(12): p. 2199-2202.

11. Marriott, D., et al., Concomitant Marked Decline in Prevalence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Other Respiratory Viruses Among Symptomatic Patients Following Public Health Interventions in Australia: Data from St Vincent's Hospital and Associated Screening Clinics, Sydney, NSW. Clinical Infectious Diseases, 2020. 72(10): p. e649-e651.

12. Friedrich, F., et al., Early Impact of Social Distancing in Response to Coronavirus Disease 2019 on Hospitalizations for Acute Bronchiolitis in Infants in Brazil. Clinical Infectious Diseases, 2020. 72(12): p. 2071-2075.

13. Poole, S., et al., Physical distancing in schools for SARS-CoV-2 and the resurgence of rhinovirus. The Lancet Respiratory Medicine, 2020. 8(12): p. e92-e93.

14. Gröndahl, B., et al., The 2009 pandemic influenza A(H1N1) coincides with changes in the epidemiology of other viral pathogens causing acute respiratory tract infections in children. Infection, 2014. 42(2): p. 303-8.

15. Meningher, T., et al., Relationships between A(H1N1) pdm09 influenza infection and infections with other respiratory viruses. Influenza and Other Respiratory Viruses, 2014. 8(4): p. 422-430.

16. Yang, L., et al., Impact of the 2009 H1N1 Pandemic on Age-Specific Epidemic Curves of Other Respiratory Viruses: A Comparison of Pre-Pandemic, Pandemic and Post-Pandemic Periods in a Subtropical City. PLOS ONE, 2015. 10(4): p. e0125447.

17. Yuan, H., A. Yeung, and W. Yang, Interactions among common non-SARS-CoV-2 respiratory viruses and influence of the COVID-19 pandemic on their circulation in New York City. Influenza and Other Respiratory Viruses. n/a(n/a).

18. Chung, J.R., et al., Interim Estimates of 2021-22 Seasonal Influenza Vaccine Effectiveness - United States, February 2022. MMWR Morb Mortal Wkly Rep, 2022. 71(10): p. 365-370.

19. Rubin, R., Influenza's Unprecedented Low Profile During COVID-19 Pandemic Leaves Experts Wondering What This Flu Season Has in Store. JAMA, 2021. 326(10): p. 899-900.

INA-RESPOND Newsletter

BEING PROACTIVE EVERY DAY KEEPS DIABETES AT BAY

By: Caleb Leonardo

SPORTS & LIFESTYLE

Diabetes is a chronic metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which over time leads to serious damage to the heart, blood vessels, eyes, kidneys, and nerves. The most common is type 2 diabetes (T2DM), which usually occurs in adults when the body becomes resistant to insulin or doesn't make enough insulin. Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin by itself.

Around 422 million people worldwide have diabetes, and Indonesia ranks fifth in the country with the most Diabetes Mellitus (DM) after China, India, Pakistan, and the United States. In 2021, 19.47 million Indonesian had DM, and according to the International Diabetes Federation (IDF), in 2045, it can reach 28.57 million.

People with diabetes have insulin resistance in their bodies, so they can no longer respond to insulin as it should. Insulin is needed to help glucose enter the body's cells to be used as energy. When the body is no longer sensitive to the presence of insulin, glucose cannot enter the body's cells to be broken down into energy, so it remains in the bloodstream/ blood circulation. If the blood sample is checked, we will find high blood glucose, but the person is weak because no energy is produced.

You might not know that you have type 2 diabetes until it affects your health. About 1 in 4 people with the condition don't know that they have it. Symptoms can come up slowly. They may include:

1. You become more/easily thirsty. When sugar builds up in your blood, your kidneys work overtime to get rid of it. This pulls fluids from your tissues and dehydrates you, so you feel thirsty.
2. You quickly become hungry. Because diabetes can stop glucose from getting to your cells, you feel hungry, even after eating.

3. Peeing often. You'll pee more often because your kidneys are working on getting rid of extra sugar in your system.
4. Dry mouth. Dehydration and peeing a lot can drain moisture from your mouth as well.
5. Weight loss without trying. When you lose sugar from peeing a lot, you also lose calories. You might lose weight even though you're eating as usual.
6. Fatigue. When your body can't use energy from food, you could feel weak and tired. Dehydration can make you feel this way, too.
7. Blurry vision. High blood sugar levels can make you have trouble focusing.
8. Headaches. High blood sugar levels can cause your head to hurt.
9. Loss of consciousness. After you exercise, skip a meal, or take too much medication, your blood sugar could go too low, and you could pass out.
10. Infections or sores that don't heal. High blood sugar can slow blood flow and make it harder for your body to heal.
11. Tingling hands and feet. T2DM can affect nerves in your hands and feet.
12. Red, swollen, tender gums. You might be more likely to get infections in your gums and the bones that hold your teeth in place. Your gums may get infected or pull away from your teeth. Your teeth might become loose.

Luckily, you can control and even prevent T2DM with lifestyle changes. Lifestyle modifications, both from diet and exercise, are the most crucial thing in the management of diabetes. Regular physical activity in the form of physical exercise improves insulin sensitivity to control blood sugar levels, helps lose weight, reduces the risk of cardiovascular disease, and improves the quality of life for people with diabetes.

Benefits of exercise:

1. Aerobic exercise. Short-term aerobic exercise improves insulin sensitivity in adults with T2DM, paralleling improved mitochondrial function. Short-term aerobic exercise in individuals with obesity and T2DM improves whole-body insulin action through gains in peripheral insulin sensitivity more so than hepatic insulin sensitivity. Regular training improves insulin sensitivity, lipids, blood pressure, other metabolic parameters, and fitness levels even without weight loss.
2. Resistance exercise. Resistance training improves 10%–15% in strength, bone mineral density, blood pressure, lipid profiles, skeletal muscle mass, and insulin sensitivity in adults with T2DM. High-intensity training is more beneficial than low-to-moderate intensity training for overall glucose management and insulin levels in adults with T2DM.
3. Combined exercise. A combination of aerobic and resistance training may be superior to either mode alone. A more significant reduction in A1C has been noted in adults with T2D undertaking a combined training program compared with either type alone. All three exercise modalities favorably impact glycemia and insulin sensitivity, and combined training may produce more significant reductions in A1C than either training modality alone.
4. High-Intensity Interval Exercise. Higher intensities of aerobic training are generally considered superior to low-intensity training. High-intensity interval exercise (HIIE) training is a regimen that involves aerobic training done between 75%-95% of maximum heart rate for 10s to 4 min with 12s to 5 min of active or passive recovery and can be repeated up to 10 times per session. The maximum heart rate is 220- age. HIIE training also significantly improves fitness levels and reduces A1C and body mass index (BMI) in adults with T2D. Compared with continuous walking for energy expenditure, HIIE training resulted in more excellent fitness, better body composition, and improved blood glucose.

Dietary restriction and increased Physical Activity are the cornerstones of intensive lifestyle interventions (ILS) that are typically used to induce weight loss. Such interventions may prevent or delay the onset of T2DM in at-risk populations and reduce cardiovascular disease risk in individuals with T2DM. The US Diabetes Prevention Program multicenter trial utilized ILS with a goal of achiev-

ing modest (5%–7%) weight loss in 6 months. It led to the important observation that for every 1 kg of body weight lost, T2DM risk was reduced by 16%.

In addition to increased physical activity and dietary restriction, reduced prolonged sitting time also lowers the risk of developing T2DM. In sedentary adults with 9 hours of sedentary behavior per day, 1 hour extra of sedentary time daily over eight days is associated with a 22% increase in developing T2DM. The interruption of prolonged sitting with activity breaks, such as light intensity walking or simple resistance activities for 3 min every 30 min over 8 hours, decreases postprandial glucose, insulin, C-peptide, and triglyceride levels. Short 5 min breaks every hour over 12 hours are more effective to lower glucose and insulin levels than 1 hour of moderate -intensity continuous exercise at the beginning of the day in people with impaired glucose tolerance.

For overall health benefits and not just diabetes, moving always has good health benefits compared to sitting still or being sedentary.

Physical activity recommendation

Moving more and sitting less throughout the day is highly recommended.

Aerobic exercise at least 150 minutes to 300 minutes a week at a moderate intensity, or 75 minutes to 150 minutes at a vigorous intensity, or a combination of moderate and heavy intensity.

Perform moderate or vigorous muscle strengthening exercises involving all major muscle groups 2-3 times per week on non-consecutive days if working on the same muscle groups.

For the elderly group, added balance exercises to reduce the risk of falling in the future.

If you cannot do 150 minutes of exercise per week due to your physical condition, do as much physical activity as you can according to your condition.

Reference:

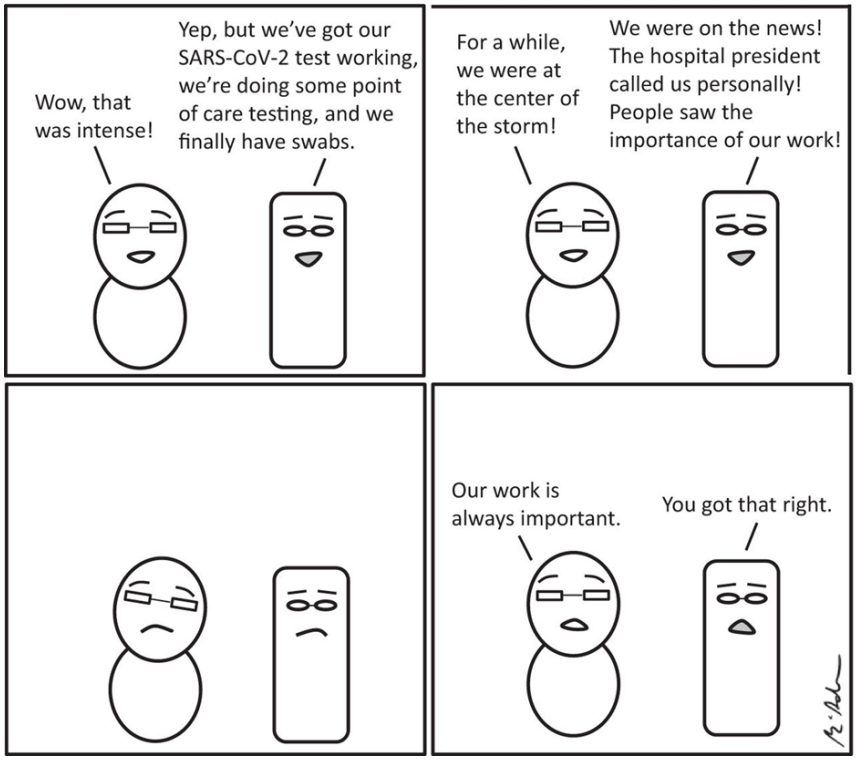
- Kanaley JA, Colberg SR, Corcoran MH, Malin SK, Rodriguez NR, Crespo CJ, et al. Exercise/Physical Activity in Individuals with Type 2 Diabetes: A Consensus Statement from the American College of Sports Medicine. Med Sci Sports Exerc. 2022. 1;54(2):353-68.
- Kirwan JP, Solomon TPJ,Wojta DM, StatenMA, Holloszy JO. Effects of 7 days of exercise training on insulin sensitivity and responsiveness in type 2 diabetes mellitus. Am J Physiol Endocrinol Metab. 2009;297 (1):151–6.
- Gordon BA, Benson AC, Bird SR, Fraser SF. Resistance training improves metabolic health in type 2 diabetes: a systematic review. Diabetes Res Clin Pract. 2009;83(2):157–75.
- Liu Y, YeW, Chen Q, Zhang Y, Kuo CH, KoriviM. Resistance exercise intensity is correlated with attenuation of HbA1c and insulin in patients with type 2 diabetes: a systematic review and metaanalysis. Int J Environ Res Public Health. 2019;16(1):140.
- Sigal RJ, Kenny GP, Boule NG, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. Ann Intern Med. 2007;147(6):357–69.
- Grace A, Chan E, Giallauria F, Graham PL, Smart NA. Clinical outcomes and glycaemic responses to different aerobic exercise training intensities in type II diabetes: a systematic review and metaanalysis. Cardiovasc Diabetol. 2017;16(1):37.
- Gillen JB, Little JP, Punthakee Z, Tarnopolsky MA, Riddell MC, Gibala MJ. Acute high-intensity interval exercise reduces the postprandial glucose response and prevalence of hyperglycaemia in patients with type 2 diabetes. Diabetes Obes Metab. 2012;14 (6):575–7.
- Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care. 2006;29(9):2102–7.

INA-RESPOND Newsletter

BIOBANKING FROM THE PAST TO THE COVID-19 ERA

By: Aly Diana

A Micro-Comic, Journal of Clinical Microbiology



Source: https://journals.asm.org/doi/10.1128/JCM.00661-20

A biobank is a biorepository that accepts, processes, stores, and distributes biospecimens and associated data for use in research and clinical care. The field of biobanking has changed tremendously over the past thirty years. It started with small, predominantly university-based repositories developed for the research needs of specific projects. They gradually evolved into institutional and government-supported repositories, commercial (for profit) biorepositories, population-based biobanks, and most recently, virtual biobanks. Time magazine featured biobanks in "10 Ideas Changing the World Right Now" in 2009, highlighting biobanks as an opportunity for scientists and alike to derive knowledge from thousands of samples. The data associated with stored biospecimens have increased in complexity from basics, such as date of collection and the diagnosis, to extensive information sets encompassing many aspects of the participant or patient phenotype, now rapidly extending into genetic, proteomic, and other "omics" information.

Human specimens have been collected and stored at institutions in the United States and elsewhere for over 100 years. One of the earliest examples of a disease-centric biobank is the University of California, San Francisco, AIDS Specimen Bank (ASB). The ASB started in December 1982 in response to the early challenges of the AIDS epidemic, without knowledge of the causative agent for AIDS. A most recent example relevant to the current condition is the development of biobanks to understand more about COVID-19, with the UK Biobank as one of the leading institutions. UK Biobank has taken swift strides to help tackle the global pandemic by undertaking five major initiatives – the serology study, COVID-19 repeat imaging study, coronavirus self-test antibody study, coronavirus infection study, and health data linkage. The 20,000 volunteers, a combination of existing UK Biobank participants and their children and grandchildren aged over 18, have helped produce findings that represent the UK population.

One of the study's most significant findings so far is that 99% of participants who had tested positive for previous infection retained antibodies to SARS-CoV-2 for three months after being infected, and 88% did so for the first six months of the study. This discovery provides an early indication that the antibodies produced following natural infection may protect most people against subsequent infection for at least six months. Other studies have looked into risk factors for COVID-19 -related morbidity and mortality. Alongside demographic covariates, being a healthcare worker, current smoker, having cardiovascular disease, hypertension, diabetes, autoimmune disease, and oral steroid use at enrolment were independently associated with COVID-19 mortality. These results suggest that previously reported associations of COVID-19 mortality with body mass index, low vitamin D, air pollutants, and renin-angiotensin-aldosterone system inhibitors may be explained by the aforementioned factors. In addition, prior acute kidney failure, urinary tract infection, pneumonia, neurogenerative disease, history of smoking, and high consumption of processed meat have also increased COVID-19 incident/morbidity/mortality.

Above are only a few examples of important results from studies using biobanking samples/data. However, maintaining biobanking in the COVID-19 era is not an easy task. A survey performed by a Task Force organized by members of the International Society for Biological and Environmental Repositories (ISBER) Standards Advisory Committee identified a wide range of challenges for biobanks globally, including those related to COVID-19 handling, operations, infrastructure support/ resources, business/communications, ethical, legal, and social issue, research progress, and personnel well-being. Many biobanks were unprepared for the full force and effects of the pandemic. Although many biobanks had prepared an emergency preparedness plan, it is clear that the majority of these plans were insufficient for responding to a pandemic with such profound and long-lasting effects. The development and continual revision of such a biobank emergency preparedness plan, to include long-term shutdowns due to pandemics or other causes, can better position biobanks to address this problem. Advanced planning, risk awareness, preparedness, mitigation, and crisis management for response and recovery are essential in formulating emergency management strategies. The challenges, gaps, and proposed solutions brought forward here may be helpful in better preparing the biobanking community for future emergencies, thereby underpinning the viability and sustainability of biobanks.

References:

1. Allocca CM, Bledsoe MJ, Albert M, Anisimov SV, Bravo E, Castelhano MG, et al. Biobanking in the COVID-19 Era and Beyond: Part 1. How Early Experiences Can Translate into Actionable Wisdom. Biopreservation Biobanking. 2020 Dec 1;18(6):533–46.
2. Allocca CM, Snapes E, Albert M, Bledsoe MJ, Castelhano MG, De Wilde M, et al. Biobanking in the COVID-19 Era and Beyond: Part 2. A Set of Tool Implementation Case Studies. Biopreservation Biobanking. 2020 Dec 1;18(6):547–60.
3. Clift AK, von Ende A, Tan PS, Sallis HM, Lindson N, Coupland CAC, et al. Smoking and COVID-19 outcomes: an observational and Mendelian randomisation study using the UK Biobank cohort. Thorax. 2022 Jan;77(1):65–73.
4. Dabbah MA, Reed AB, Booth ATC, Yassaee A, Despotovic A, Klasmer B, et al. Machine learning approach to dynamic risk modeling of mortality in COVID-19: a UK Biobank study. Sci Rep. 2021 Dec;11(1):16936.
5. Hu Y, Yang H, Hou C, Chen W, Zhang H, Ying Z, et al. COVID-19 related outcomes among individuals with neurodegenerative diseases: a cohort analysis in the UK biobank. BMC Neurol. 2022 Dec;22(1):15.
6. Vu T-HT, Rydland KJ, Achenbach CJ, Van Horn L, Cornelis MC. Dietary Behaviors and Incident COVID-19 in the UK Biobank. Nutrients. 2021 Jun 20;13(6):2114.
7. Yates T, Razieh C, Zaccardi F, Davies MJ, Khunti K. Obesity and risk of COVID-19: analysis of UK biobank. Prim Care Diabetes. 2020 Oct;14(5):566–7.
8. Elliott J, Bodinier B, Whitaker M, Delpierre C, Vermeulen R, Tzoulaki I, et al. COVID-19 mortality in the UK Biobank cohort: revisiting and evaluating risk factors. Eur J Epidemiol. 2021 Mar;36(3):299–309.
9. UK Biobank. https://www.ukbiobank.ac.uk/learn-more-about-uk-biobank/covid-19-hub

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