The Effectiveness of Covid-19 Vaccination in Indonesian Population: A Case-Control Study Protocol

Sri Idaiani[1(✉)], Nurhayati Nurhayati[1], Delima Delima[1], Harimat Hendarwan[1], Lucie Widowati[1], Ingan U. Tarigan[1], Nurfi Afriansyah[1], Sundari Wirasmi[1], Diah Yunitawati[1], Setyo Adiningsih[1], Hadjar Siswantoro[2], Tince A. Jovina[2], Yenni Risniati[2], Rossa Avrina[2], Armaji K. Syarif[2], Nita Prihartini[2], Narendro Arifia[2], Yusi D. Nurcahyani[2], Evi I. Natalia[2], Made D. Susilawati[2], and Jarir A. Thobari[3]

[1] Research Organization for Health, National Research and Innovation Agency, Jakarta, Indonesia
sri.idaiani@brin.go.id
[2] Health Policy Agency, Ministry of Health, Jakarta, Indonesia
[3] Faculty of Medicine Public Health and Nursing, Universitas Gajah Mada, Yogyakarta, Indonesia

Abstract. It is essential to prove a vaccination program's effectiveness before initiating such a program to the entire population. Accordingly, the government of Indonesia has conducted research at the beginning of the COVID-19 vaccination program. The general objective of the current study was to assess the effectiveness of COVID-19 vaccine against symptomatic COVID-19 incidence and its severity. This is a protocol study of an unmatched case-control study design. The subjects are health workers and members of the community. The case group is symptomatic COVID-19 as confirmed by the RT PCR or Antigen rapid tests taken during the data collection time on 13 January 2021 for the health workers and in February 2021 for non-health workers. Meanwhile, the control group consisted of people who are at least 18 years old and had never been diagnosed with COVID-19. The ratio of cases and controls in the health workers group is 1:4, while the ratio for the community group is 1:1. Based on the previous effectiveness study, the city of Bandung required 4625 health workers and 3834 non-health workers. The data for the study were collected from July to October 2021 in seven provinces and 14 districts/cities. The case group data were obtained from hospital medical records, while the control group data were collected from the same hospital and community living in areas heavily affected by COVID-19. Trained enumerators filled out the patient questionnaires, while the control group filled out the questionnaires themselves. The degree of severity of COVID-19 was obtained from the doctor in charge of the patients (DPJP). This study used the Lime Survey application from the link http://bit.ly/effectiveness_vaksin_c19. Data analysis was carried out separately for the groups of health workers and community groups. We calculated the odds ratio (OR) adjusted by age, gender, and comorbid diseases; then the effectiveness of the vaccination was designated as 1-OR. Vaccine effectiveness will be calculated based on the type of vaccine as well. The Indonesian government will use the results as scientific evidence of the effectiveness of COVID-19 vaccination in Indonesia.

I. Nurlaila et al. (Eds.): ICHR 2022, AHSR 56, pp. 785–795, 2023.
https://doi.org/10.2991/978-94-6463-112-8_71

Keywords: Indonesia · COVID-19 vaccine · effectiveness · symptomatic COVID-19

1 Introduction

Corona Virus Disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The disease was first discovered in Wuhan, China in December 2019 [1, 2]. The World Health Organization (WHO) on March 11, 2020, officially declared the COVID-19 as a global pandemic. Indonesia has also been affected by the COVID-19 pandemic with the number of positive confirmed cases and deaths that continue to rise from day to day [3]. From the onset of the pandemic until the time when this protocol was compiled, i.e., in early 2021, there has been no information about the existence of a specific SARS CoV-2 variant in Indonesia, although it has been scientifically identified that there are several variants, such as alpha, beta, delta, and gamma [4].

As the disease progressed and the number of patients grew, the Indonesian government has made various efforts to control the COVID-19 pandemic by conducting regional quarantine (lockdown), imposing physical and social restrictions, implementing massive contact tracing [5], and ultimately vaccinating its population. The vaccination program was launched in early 2021 for front-line health workers, followed by adults aged 18 years and over. In general, other countries in the world also initiated their vaccination program for these groups [6–8]. The vaccines injected into the population consists of different platforms; however, in the earliest stage of the program, it was mainly vaccines manufactured by an Asian country. The objective of COVID-19 vaccination is to reduce the transmission of COVID-19, reduce the mortality and morbidity rate due to COVID-19, achieve herd immunity, and protect members of the community from COVID-19, therefore allowing them to remain socially and economically productive. Herd immunity only could be achieved if vaccination coverage is sufficiently high and evenly distributed throughout the region [9–11].

As a general rule, before initiating a comprehensive vaccination program to the general population, proof of the vaccine's effectiveness in the form of clinical test results should be made available and such vaccine should only be given to the population if it is proven to be effective. The clinical trial setting is the most ideal condition, in which the various confounding factors are controlled; however, in the real-world many things play a role. In fact, many vaccine-effectiveness studies use feasible methods, such as retrospective cohorts and case-controls [12].

The need for this study is if the vaccine effectiveness remains acceptable in the non-clinical trial setting, undoubtedly more people will be participating in the vaccination program, and consequently, the attempt to control the pandemic will be more successful [13]. In line with the preceding statement, there is a need to carry out a study to assess the effectiveness of the vaccine against the incidence of symptomatic COVID-19 and the degree of severity.

The general objectives of this study were to assess the effectiveness of COVID-19 vaccine against symptomatic COVID-19 incidence and severity. The specific objectives were as follows: (1)To assess the effectiveness of COVID-19 vaccine against the incidence of symptomatic COVID-19 among the health workers, (2)To assess the effectiveness of COVID-19 vaccine against the incidence of symptomatic COVID-19 in the

community, (3) To assess the effectiveness of COVID-19 vaccine on the severity of symptomatic COVID-19 among the health workers, (4) To assess the effectiveness of COVID-19 vaccine on the severity of symptomatic COVID-19 in the community.

2 Material and Methods

This study used an unmatched case-control design [14, 15]. The research subjects were health workers and members of the community. They were divided into two groups; i.e., the case group consisted of subjects who were confirmed to have symptomatic COVID-19, and the control group consisted of subjects who did not experience symptomatic COVID-19. The research subjects from the two groups (cases and controls) would be traced for their exposure to the variables studied, i.e., their COVID-19 vaccination status and other related variables.

The criteria inclusion of case group were (1)The subject must have a positive COVID-19 test result based on RT PCR or rapid Antigen tests, which were carried out within the time limit since the start of the vaccination program in the research location district/city (national: January 13, 2021, for health workers or February 17, 2021, for members of the community), (2) The subject must show COVID-19 symptoms when the COVID-19 test result was confirmed as positive. (3) COVID-19 categories mild, moderate, severe or critical, (4) Age 18 + years old, (5) Having a domicile in the research location or in the surrounding district/city. The criteria exclusion of case group criteria was (1) The results of COVID-19 tests by RT-PCR or rapid Antigen were positive but did not experience COVID-19 symptoms, (2) Declining to participate.

The inclusion criteria of control group were (1) The subject did not experience symptomatic COVID-19 since the start of the vaccination program in the research location district/city (national vaccination starts on January 13, 2021, for health workers and on February 17, 2021, for members of the community). (2) Age 18 + years old, (3) Having a domicile in the research location or in the surrounding district/city.

The exclusion criteria of control Group Criteria: (1) The results of COVID-19 tests by RT-PCR or rapid Antigen were positive but did not experience COVID-19 symptoms. (2) Declining to participate.

2.1 Sample Size Justification

Research subjects were calculated using the sample size determination in the health study software from the World Health Organization using the formula for estimation of the odds ratio with a specific relative precision described in the following [16].

$$n = \frac{Z^2_{1-\alpha/2}}{[\log_e(1-\varepsilon)]^2}\left[\frac{1}{P_1(1-P_1)} + \frac{1}{P_2(1-P_2)}\right]$$

The odds ratio was obtained by referring to the CoronaVac vaccine efficacy of 65.3% based on the study by Kusnandi et al. in Bandung during the interim analysis [17]. Using the assumption of vaccine effectiveness = (1-OR) [18, 19], the OR value is 0.347. However, the percentage of vaccination coverage in the control group (P2) for the health

workers sub-study was 80% and 20% for members of the community sub-study. The confidence level α is 5%; meanwhile, the relative precision is 20% to the odds ratio. By using the above formula, the minimum sample size can be obtained = n. If the ratio of case and control groups is = c; therefore, the sample size of the case group is n1 = (c + 1) n/2c, and the size of the control group is n2 = cn. To anticipate the occurrence of non-response or the possibility of incomplete data, which is estimated to be 20%, the non-response factor is set at q = 1/(1-f) = 1.25. Therefore, the size of the case group after taking into account the non-response factors is n1 = qn1, and the size of the control group is n2 = qn2. From the description above, the sample size is determined as follows.

Sample Size for Health Workers: With α = 5%, ε = relative precision = 20%, P2 = 80%, OR = 1–0.653 = 0.347, C = 4, then n count = 800. Considering f = 20%, then n1 (case group) = 625, n2 (control group) = 4000; therefore, the total subjects = 4625 people.

Sample Size for Members of the Community: With α = 5%, ε = relative precision = 20%, P2 = 20%, OR = 1–0.653 = 0.347, C = 1, then n count = 1533. Considering f = 20%, then n1 (case group) = 1917, n2 (control group) = 1917; therefore, the total subject = 3834 people.

2.2 Time and Places

Preparation for the research strarted in February 2021; however, data collection was carried out from July to October 2021 with the assumption that the vaccination coverage at that time should be sufficiently widespread to ensure adequate samples. The subjects were from seven provinces, and each province was selected in two cities. The provinces are North Sumatra, West Java, DI Jogjakarta, East Kalimantan, South Sulawesi, Bali, and Papua, and the cities are Medan, Lubuk Pakam (Deli Serdang District), Bekasi, Depok, Jogjakarta, Sleman (Sleman District), Balikpapan, Samarinda, Denpasar, Gianyar (Gianyar District), Makassar, Sungguminasa (Gowa District), Jayapura, and Sentani (Jayapura District).

The locations were selected following discussions with the district/city and provincial Health Offices while taking into account the number of COVID-19 cases in the local hospitals and in the district/city where COVID-19 patients reside. In each city, we selected 2–3 hospitals with the highest numbers of COVID-19 patients. We then tracked the neighborhood where the highest number of these COVID-19 patients reside. The areas with the most COVID-19 patients will be designated as areas where we will find mild COVID-19 cases with symptoms and people who have never been confirmed as having COVID-19.

2.3 Sampling Method

Based on the minimum sample size, the number of subjects was allocated in line with the number of COVID-19 cases according to the national data dashboard. Consequently, the provinces and districts/city with more COVID-19 cases will receive more subject allocations.

After obtaining the required number of samples for both the case group and control group, they were divided into the designated hospitals, local health centers, and the community. The ratio for case and control groups for health workers is 1:4, whereas the ratio for the community is 1:1. The flow of sampling collection is illustrated in Fig. 1.

2.4 Data Collection Instrument

The data were collected through the Lime Survey application with the link http://bit.ly/effectiveness_vaksin_c19. Cases treated at the referral hospital were filled in by enumerators who were trained for this study. For the control group, both the health workers and the member of the community filled out the link themselves. The link contains questionnaires that can be accessed via a cellular phone or a computer. The questionnaires for the case and control groups were differentiated in certain steps so the questions for the case group would not be asked to the control group. The questionnaire contains the following data: (1) Socio demographic data: encompassing age, gender, occupation, education, marital status, resident's ID number, (2) Hospitalization history: PCR or Antigen swab test results, degree of severity, (3) Data on risk factors: comorbid diseases, symptoms of COVID-19, history of COVID-19 vaccination.

Source of data: for the case group at the hospital, we used data from the patients' medical records, while for the control group of health workers, as well as the mild cases and community control groups we used data obtained from the questionnaires filled out by the subjects. In the study, data on the severity of COVID-19 were obtained from the results of the assessment made by the doctor in charge of the patient who would classify the patient's degree of severity as mild, moderate, severe, or critical [20].

Variables

COVID-19 symptomatic positive: Experienced COVID-19 throughout the period since the launching of the COVID-19 vaccination program until the time when data were collected and confirmed by a positive result of PCR or Antigen tests and showing COVID-19 symptoms.

Degree of severity based on Minister of Health decree Number Hk.01.07/Menkes/4641/2021

Asymptomatic: The results of the SARS CoV-2 tests are positive without any clinical signs and symptoms.

Mild: Patients with symptoms without evidence of viral pneumonia or without hypoxia. Symptoms include fever, cough, fatigue, anorexia, shortness of breath, myalgia. Other non-specific symptoms such as sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, loss of smell (anosmia) or loss of taste (ageusia) that occur before the onset of respiratory symptoms are also frequently reported.

Moderate: Patients with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing), without signs of severe pneumonia including

	SpO2 > 93% in room air. Rapid breathing criteria: age > 5 years, ≥ 30 x/minute.
Severe:	In adolescent or adult patients: patients with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) plus one of the following symptoms: respiratory rate > 30 x/minute, severe respiratory distress, or SpO2 < 93% in room air.
Critical:	The patient's condition deteriorated rapidly to acute respiratory distress syndrome (ARDS) or respiratory failure or developed shock, encephalopathy, myocardial damage or heart failure, coagulopathy, acute renal impairment, and multiple organ dysfunction or other manifestations of sepsis.

Potential variables

Vaccination status:	2 doses,1 dose, No vaccine
Type of Vaccine:	Sinovac/CoronaVac, Aztra Zeneca, Sinopharm
Gender:	Male, Female
Age:	Determined from the person's ID card
Occupation:	Health worker, Non health worker (community)
Comorbid:	Present, not present, unknown. Present, if the person has or is currently experiencing one or more of the following conditions: Hypertension, Diabetes Mellitus, Heart disease, Lung disease, Kidney disease, Autoimmune disease, Allergy, Cancer, Liver disease, Asthma, Bronchitis, Tuberculosis, Pneumonia, Overweight/obesity, or others

2.5 Data Management and Analysis

Enumerators from selected cities were tasked with checking data using the glide application until data collection was complete. Incomplete data were reconfirmed to the subject, or the medical record was checked again. Data changes and additions were recorded by enumerators in each city and reported to the central data management. Central data management did the editing based on the enumerator information.

All the data had been collected, edited, cleaned, and transferred to an excel sheet and then to SPSS dataset by the central data management. We run binary and multinomial logistic regression for calculating the effectiveness of CoronaVac against symptomatic COVID-19 and its severity with adjustment for gender, age, and presence of comorbidity. Then we measure the effectiveness of the vaccination using 1-OR; hence, for the health workers and members of the community groups.

2.6 Ethical Clearance

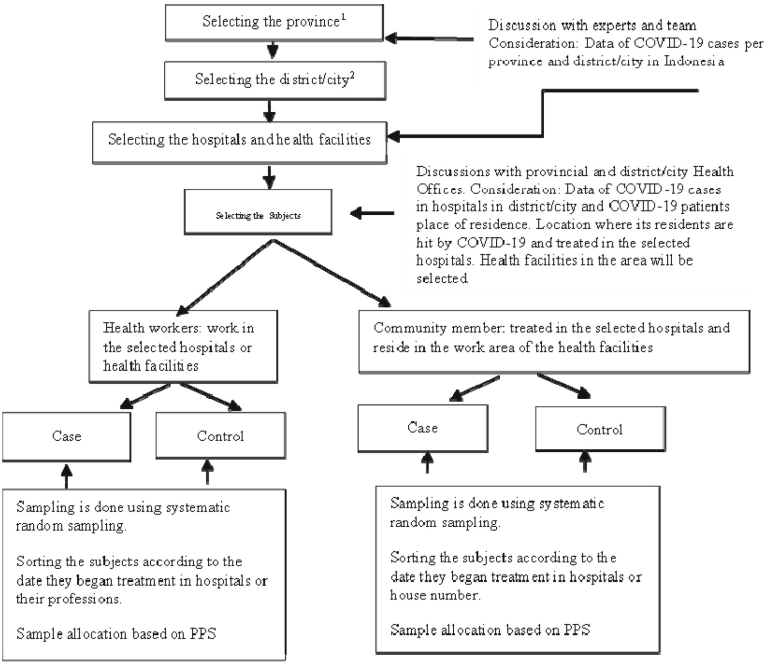
Ethical clearance was obtained from the Health Research Ethics Commission of the National Institute of Health Research and Development (NIHRD) of the Ministry of Health in a document numbered LB 02.01/2/KE 237/2021 and its amendment numbered LB 02/01/KE 391/2021. All methods were carried out in accordance with the Helsinki

Declaration. Subjects' participation was entirely voluntary, and informed consent was obtained from all participants using the online link. As for the data collected through the medical records, a permission was obtained from the director of the hospitals.

3 Results

The results of this study will be presented in 3 parts, namely the effectiveness of CoronaVac vaccine in health workers in Indonesia, the effectiveness of CoronaVac vaccine in adult population in Indonesia and the effectiveness of Astra Zeneca COVID-19 vaccine in adult population in Indonesia. In the current proceeding, one of these articles will be presented.

3.1 Procedure



Notes:

1. Provinces of North Sumatra, West Java, DI Jogjakarta, East Kalimantan, South Sulawesi, Bali and Papua.
2. Medan City, Deli Serdang District (Lubuk Pakam), Bekasi City, Depok City, Jogjakarta City, Sleman District (Sleman City), Balikpapan City, Samarinda City, Denpasar City, Gianyar District, Makassar City, Gowa District (Sungguminasa), Jayapura City and Sentani District.

Fig. 1. Sampling collection flow

4 Discussion

This study chose an unmatched case-control design because it was considered appropriate, and this design can be implemented in Indonesia despite the limited data or an unavailable registry. Most of COVID-19 vaccine effectiveness studies use retrospective cohort designs; nonetheless, there are also one or two COVID-19 vaccine effectiveness studies using case-control designs [12].

The effectiveness of vaccines in the real-world tests is more appreciated than the results of effectiveness tests obtained from clinical trials, and the real-world results are more anticipated [7, 21, 22]; however, research on vaccine effectiveness in the real-world is mostly carried out in European countries, or the USA and only a few have been carried out in Asia. The vaccine platforms used in the USA and Europe are predominantly those that utilize mRNA and only a very few utilize inactivated virus [7]. The effectiveness of vaccines that are not based on inactivated platforms is generally higher than the vaccine that is developed from an inactivated virus. For example, CoronaVac is rated to provide a general effectiveness of 65.7% based on studies carried out in Chile and Brazil [7].

There are several output to measure in assessing vaccine effectiveness, such as mortality, hospitalization, ICU care, COVID-19 symptoms, and antibody levels [6, 23–27]. In this study, the output criteria were determined as follows; the patients should have COVID-19 symptoms accompanied by a positive PCR or Antigen swab results. Several effectiveness studies have used a case-control design using a negative test result [28, 29]. Even though performing the PCR test on all research subjects is the proper course of action, and because not all research sites were able to carry out PCR tests quickly and cheaply, this study did not conduct PCR tests during the study, but it used existing data plus the subject's declaration.

It should also be noted that this research was carried out when the whole genome sequencing (WGS) was not carried out extensively, because there had not been an outbreak of SARS-CoV-delta, gamma, and even omicron variants [4, 30–32]. It is possible that the delta variant already existed in Indonesia at that time, but it had not been officially declared because there were no official data yet.

The limitation of this study apart from not performing PCR tests on all subjects is also disregarding certain side effects or certain populations, such as Bell's Palsy, Guillain barre syndrome, and immunological disorders [33–35]. Potential bias might occur because not all subjects were PCR or Antigen tested and were not checked for antibody levels prior to vaccination.

The results of this study will be used by the government of the Republic of Indonesia as scientific evidence of the effectiveness of COVID vaccination for the adult population in Indonesia during the COVID-19 pandemic. This will be useful for formulating recommendations on the health policy in Indonesia.

5 Conclusion

The Indonesia government has piloted a particular protocol to allow a thorough and comprehensive evaluation upon the implementation of anti-COVID19 vaccination in 2022. The design of this protocol was deemed to be adequate in addressing the dynamics

appeared throughout the vaccination. However, reports on the unprecedented emergence of new variant referred to as delta variants will be a correcting or mediating variable one should take into consideration when interpreting our protocol.

Acknowledgements. This study was supported by the Ministry of Health, Republic of Indonesia. We are grateful to the Director-General for The National Institute of Health Research and Development, Ministry of Health, Director of Center for Research and Development of Health Resources and Services, NIHRD, Ministry of Health,

References

1. Naming the coronavirus disease (COVID-19) and the virus that causes it [Internet]. [cited 2022 Jan 28]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it
2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020;382(8):727–33. doi:https://doi.org/10.1056/NEJMOA2001017
3. Situasi COVID-19 | Covid19.go.id [Internet]. [cited 2022 Jan 28]. Available from: https://covid19.go.id/situasi
4. Duong D. Alpha, Beta, Delta, Gamma: What's important to know about SARS-CoV-2 variants of concern? CMAJ. 2021;193(27):E1059. doi:https://doi.org/10.1503/CMAJ.1095949
5. Ariawan I, Jusril H. COVID-19 in Indonesia: Where Are We? Acta Med Indones. 2020;52(3):193–5.
6. Meng Z, Zhang J, Shi J, Zhao W, Huang X, Cheng L, et al. Immunogenicity of influenza vaccine in elderly people: a systematic review and meta-analysis of randomized controlled trials, and its association with real-world effectiveness. Hum Vaccin Immunother. 2020;16(11):2680–9. doi:https://doi.org/10.1080/21645515.2020.1747375.
7. Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. Int J Infect Dis. 2022;114:252–60. doi:https://doi.org/10.1016/j.ijid.2021.11.009
8. Zhang MX, Zhang TT, Shi GF, Cheng FM, Zheng YM, Tung TH, et al. Safety of an inactivated SARS-CoV-2 vaccine among healthcare workers in China. Expert Rev Vaccines. 2021;20(7):891–8. doi:https://doi.org/10.1080/14760584.2021.1925112.
9. Kwok KO, Lai F, Wei WI, Wong SYS, Tang JWT. Herd immunity – estimating the level required to halt the COVID-19 epidemics in affected countries. J Infect. 2020;80(6):e32–3. doi:https://doi.org/10.1016/J.JINF.2020.03.027.
10. Randolph HE, Barreiro LB. Herd Immunity: Understanding COVID-19. Immunity. 2020;52(5):737–41. doi:https://doi.org/10.1016/J.IMMUNI.2020.04.012.
11. Fontanet A, Cauchemez S. COVID-19 herd immunity: where are we? Nat Rev Immunol. 2020;20(10):583–4. doi:https://doi.org/10.1038/S41577-020-00451-5.
12. Teerawattananon Y, Anothaisintawee T, Pheerapanyawaranun C, Botwright S, Akksilp K, Sirichumroonwit N, et al. A systematic review of methodological approaches for evaluating real-world effectiveness of COVID-19 vaccines: Advising resource-constrained settings. PloS one. 2022;17(1):e0261930. doi:https://doi.org/10.1371/journal.pone.0261930.
13. Harapan H, Wagner AL, Yufika A, Winardi W, Anwar S, Gan AK, et al. Acceptance of a COVID-19 Vaccine in Southeast Asia: A Cross-Sectional Study in Indonesia. Front Public Health. 2020;8:381. doi:https://doi.org/10.3389/FPUBH.2020.00381.

14. Verani JR, Baqui AH, Broome C V., Cherian T, Cohen C, Farrar JL, et al. Case-control vaccine effectiveness studies: Data collection, analysis and reporting results. Vaccine. 2017;35(25):3303–8. doi:https://doi.org/10.1016/J.VACCINE.2017.04.035.
15. Verani JR, Baqui AH, Broome C V., Cherian T, Cohen C, Farrar JL, et al. Case-control vaccine effectiveness studies: Preparation, design, and enrollment of cases and controls. Vaccine. 2017;35(25):3295–302. doi:https://doi.org/10.1016/j.vaccine.2017.04.037.
16. Sample size determination in health studies : a practical manual / S. K. Lwanga and S. Lemeshow [Internet]. [cited 2022 Jan 29]. Available from: https://apps.who.int/iris/handle/10665/40062
17. BPOM: Efikasi Vaksin Sinovac 65,3%, Efektivitas Terlihat Usai Vaksinasi | kumparan.com [Internet]. [cited 2022 Jan 29]. Available from: https://kumparan.com/kumparannews/bpom-efikasi-vaksin-sinovac-65-3-efektivitas-terlihat-usai-vaksinasi-1uxTGu0ajfC
18. Guidelines M medical. Vaccine effectiveness [Internet]. [cited 2022 Oct 10]. Available from: https://medicalguidelines.msf.org/en/viewport/mme/english/7-6-vaccine-effectiveness-32408146.html
19. Andrews N, Stowe J, Kirsebom F, Toffa S, Rickeard T, Gallagher E, et al. Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant. New England Journal of Medicine [Internet]. 2022 Apr 21 [cited 2022 Oct 10];386(16):1532–46. Available from: https://www.nejm.org/doi/https://doi.org/10.1056/NEJMoa2119451
20. Buku Saku Protokol Tata Laksana COVID-19 Edisi 2 – chpm.fk.ugm.ac.id [Internet]. [cited 2022 Jan 30]. Available from: https://chpm.fk.ugm.ac.id/buku-saku-protokol-tata-laksana-COVID-19-edisi-2/
21. Lasky T, McMahon AW, Hua W, Forshee R. Methodologic approaches in studies using real-world data to measure pediatric safety and effectiveness of vaccines administered to pregnant women: A scoping review protocol. JBI Evid Synth. 2020;18(10):2164–70.
22. Lasky T, McMahon AW, Hua W, Forshee R. Methodologic approaches in studies using real-world data (RWD) to measure pediatric safety and effectiveness of vaccines administered to pregnant women: A scoping review. Vaccine. 2021;39(29):3814–24. doi:https://doi.org/10.1016/j.vaccine.2021.05.071.
23. Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. Lancet. 2021;397(10293):2461–2.
24. Erol Ç, Yanık Yalçın T, Sarı N, Bayraktar N, Ayvazoğlu Soy E, Yavuz Çolak M, et al. Differences in Antibody Responses Between an Inactivated SARS-CoV-2 Vaccine and the BNT162b2 mRNA Vaccine in Solid-Organ Transplant Recipients. Exp Clin Transplant. 2021;19(12):1334–40. doi:https://doi.org/10.6002/ect.2021.0402
25. Karamese M, Tutuncu EE. The effectiveness of inactivated SARS-CoV-2 vaccine (CoronaVac) on antibody response in participants aged 65 years and older. J Med Virol. 2022;94(1):173–7. doi:https://doi.org/10.1002/jmv.27289
26. Rotshild V, Hirsh-Raccah B, Miskin I, Muszkat M, Matok I. Comparing the clinical efficacy of COVID-19 vaccines: a systematic review and network meta-analysis. Sci Rep. 2021;11(1):22777. doi:https://doi.org/10.1038/s41598-021-02321-z.
27. Medeiros-Ribeiro AC, Aikawa NE, Saad CGS, Yuki EFN, Pedrosa T, Fusco SRG, et al. Immunogenicity and safety of the CoronaVac inactivated vaccine in patients with autoimmune rheumatic diseases: a phase 4 trial. Nat Med. 2021;27(10):1744–51. doi:https://doi.org/10.1038/s41591-021-01469-5.
28. Hitchings MDT, Ranzani OT, Torres MSS, de Oliveira SB, Almiron M, Said R, et al. Effectiveness of CoronaVac among healthcare workers in the setting of high SARS-CoV-2 Gamma variant transmission in Manaus, Brazil: A test-negative case-control study. Lancet Reg Health Am. 2021;1:100025. doi:https://doi.org/10.1016/j.lana.2021.100025.

29. Chua H, Feng S, Lewnard JA, Sullivan SG, Blyth CC, Lipsitch M, et al. The use of test-negative controls to monitor vaccine effectiveness: a systematic review of methodology. Epidemiology. 2020;31(1):43–64. doi:https://doi.org/10.1097/EDE.0000000000001116.
30. Ranzani OT, Hitchings MDT, Dorion M, D'Agostini TL, De Paula RC, De Paula OFP, et al. Effectiveness of the CoronaVac vaccine in older adults during a gamma variant associated epidemic of covid-19 in Brazil: Test negative case-control study. BMJ. 2021;374. doi:https://doi.org/10.1136/bmj.n2015.
31. Lopez Bernal J, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, et al. Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. N Engl J Med. 2021;385(7):585–94. doi:https://doi.org/10.1056/NEJMOA2108891.
32. Li XN, Huang Y, Wang W, Jing QL, Zhang CH, Qin PZ, et al. Effectiveness of inactivated SARS-CoV-2 vaccines against the Delta variant infection in Guangzhou: a test-negative case–control real-world study. Emerg Microbes Infect. 2021;10(1):1751–9. doi:https://doi.org/10.1080/22221751.2021.1969291.
33. Wan EYF, Chui CSL, Lai FTT, Chan EWY, Li X, Yan VKC, et al. Bell's palsy following vaccination with mRNA (BNT162b2) and inactivated (CoronaVac) SARS-CoV-2 vaccines: a case series and nested case-control study. Lancet Infect Dis. 2022;22(1):64–72. doi:https://doi.org/10.1016/s1473-3099(21)00451-5.
34. Tutar NK, Eyigurbuz T, Yildirim Z, Kale N. A variant of guillain-barre syndrome after sars-cov-2 vaccination: Amsan. Ideggyogy Sz. 2021;74(7–8):286–8. doi:https://doi.org/10.18071/ISZ.74.0286.
35. Ramirez GA, Asperti C, Cucca V, Yacoub M-R. Challenges to Vaccination against SARS-CoV-2 in Patients with Immune-Mediated Diseases. Vaccines (Basel). 2021;9(10):1147. doi:https://doi.org/10.3390/vaccines9101147.