Philippine COVID-19 Living Clinical Practice Guidelines
Institute of Clinical Epidemiology, National Institutes of Health, UP Manila
In cooperation with the Philippine Society for Microbiology and Infectious Diseases
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EVIDENCE SUMMARY

Is CoronaVac (Sinovac) effective and safe in the prevention of COVID-19-infections?: A Rapid Review (Update)

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RECOMMENDATIONS

1. **We recommend the use of the CoronaVac (Sinovac), given as (given as 0.5 mL (600SU) to prevent symptomatic SARS-CoV-2 infection in**:
   - Healthy Adults *(Low certainty of evidence; Strong recommendation)*
   - Pregnant women in their first trimester after consultation with a physician *(Very Low certainty of evidence; Strong recommendation)*
   - Pregnant women in their 2nd and 3rd trimester and lactating women *(Very Low certainty of evidence; Strong recommendation)*
   - Adults who have medical comorbidities *(including chronic respiratory disease and infection, cardiovascular disease, chronic kidney disease, cerebrovascular disease, diabetes mellitus, obesity, neurologic disorder, chronic liver disease and others like sickle cell disease, thalassemia, or Down's syndrome, as per DOH guidelines dated April 5, 2021 on the A3 Priority Group) (Low certainty of evidence; Strong recommendation)*
   - Immunocompromised patients after medical clearance from a physician *(the immunocompromised include those diagnosed with HIV, hepatitis B and C, those with cancer undergoing chemotherapy, transplant patients receiving immunosuppression) (Low certainty of evidence; Strong recommendation)*

2. **We suggest the use of CoronaVac (Sinovac) to prevent SARS-CoV-2 infection in older adults (>60 years old)**. *(Low certainty of evidence; Weak recommendation)*

3. **We suggest against the use of CoronaVac (Sinovac) to prevent SARS-CoV-2 infection in children (3 to 17 years old)** *(Very Low certainty of evidence; Weak recommendation)*

4. **In areas where Delta is the predominant variant of concern, we recommend the use of CoronaVac (Sinovac)** *(Very Low certainty of evidence; Strong recommendation)*

5. **Under the current context of low vaccine coverage and inadequate vaccine supply, we recommend against booster vaccination using CoronaVac (Sinovac) in the healthy, adult population (18 years old and above)** *(Low certainty of evidence; Strong recommendation)*

6. **For immunocompromised patients who received primary CoronaVac (Sinovac) vaccination, we recommend for heterologous booster vaccination** *(Very Low certainty of evidence; Strong recommendation)*

Consensus Issues

In the light of new evidence since the last version of the guidelines, the panel revised the wordings and updated the strengths of the recommendations accordingly.

The panel members were divided and could not reach consensus regarding homologous booster vaccination for CoronaVac. Despite three rounds of voting and additional evidence search followed by a Delphi and a fourth round of voting, no consensus was reached. The arguments for and against homologous boosting of these 4 vaccines in the immunocompromised are as follows:

FOR:

1. The immunocompromised are vulnerable and at risk of severe COVID-19 infection and should be given the necessary protection from effective vaccination.
2. Primary vaccination has been found to result in poor immunogenic response in this population. Without a third/additional dose, these patients remain relatively unprotected and would likely have breakthrough infections.
3. Majority of the local population, and this likely includes the immunocompromised, received either ChAdOx1 or CoronaVac as their primary vaccination. Hence, despite the lack of a strong evidence of efficacy/effectiveness, giving them a booster using the same vaccine is better than not giving one.

AGAINST:

1. Homologous boosting using these vaccines for this population may turn out to be a waste of precious resources, given the lack of evidence that demonstrates clinical or even immunologic effectiveness and safety.
2. Ongoing trials and continued evidence generation may soon provide the necessary answer to the question and it may be prudent to wait for their results.
3. Heterologous boosting may be a better option, considering the current evidence of a satisfactory benefit/harm ratio.

The panel gave a strong recommendation for heterologous booster vaccination despite the low certainty of the evidence because of its significantly better immunogenic response compared to homologous boosting combined with the acceptable safety profile. More importantly, with the inconsistent supply of vaccines, and the need for the provide an effective vaccination regimen to the immunocompromised, the heterologous booster vaccination may be the only available option at this time.

What's new in this version and Key Findings

The updated search on September 7, 2021 provided additional real-world evidence on the clinical effectiveness of CoronaVac in the general, as well as the immunocompromised population, in whom immune response to the vaccine is diminished. One trial showed that CoronaVac was immunogenic and safe among children aged 3 to 17 years old. Studies among the immunocompromised population showed reduced immunologic responses after CoronaVac vaccination. Additional evidence showed sufficient protection against COVID-19 infection by the Delta variant despite decreased immunologic response elicited by CoronaVac against the variant of concern. However, available evidence suggests escape from immunity against the Gamma variant after CoronaVac vaccination. It is also uncertain whether a booster results in additional protection against infection in terms of clinical outcomes. Studies suggest declining immunologic marker levels over time with concomitant decreased vaccine effectiveness in the older population. The effect of booster vaccination in providing additional protection is limited.

Review Methods

This review searched the following resources for its evidence base (date of the last search):

1. PubMed (September 7, 2021)
2. COVID NMA (September 1, 2021)
3. Iloveevidence.com (September 7, 2021)
4. Metaevidence.org (September 1,2021)
5. WHO Situational reports (September 3, 2021)
6. IVAC-JHI Vaccine effectiveness summary reports (September 2, 2021)

Results

Clinical Efficacy

Three (3) randomized controlled trials on the clinical efficacy of CoronaVac against COVID-19 infection were identified. These were Phase 3 trials conducted in Brazil, Turkey and Indonesia.[1-3] The data from Indonesia was taken from the regulatory report. The reported vaccine efficacy values for symptomatic COVID-19 infection ranged from 50.70% (95% CI 35.90-62.00) from the Brazilian trial involving healthcare workers, to 65.3% from Indonesia and to 83.5% (95% CI 65.4-92.1) in the general population from the trial in Turkey. The VE for >60 years old was 51.1% (95% CI -166.9 to 91.0).

Three (3) additional randomized trials on the efficacy of CoronaVac presented only immunogenicity outcomes. Two (2) studies were on adults from China and from Chile [4,5] and one (1) on children from China.[6] Generally, CoronaVac immunization resulted in a significant increase in the immunogenicity markers measured at 28 days after the second dose.

Appendix 2 presents the detailed characteristics of the clinical trials on CoronaVac.

Appendix 3 presents the vaccine efficacy rates (3a) and immunogenicity outcomes (3b) from the trials on CoronaVac.

Real World Evidence: Effectiveness

Epidemiologic Studies

The search yielded two (2) epidemiologic studies from Brazil demonstrating the effectiveness of vaccination, where CoronaVac was used in a significant proportion of the population, together with other vaccines.

The first study investigated the seven-day moving average of COVID-19 cases in Brazil from March 2020 to May 2021. It compared the proportion of cases, severe cases, and deaths in each age group before the vaccine roll out for the particular age group versus two weeks after the roll out onwards. CoronaVac comprised 40.8% of all administered doses during the study period (ChAdOx1 = 46.4%, BNT162b2 = 9.9%, Ad26.CoV2.S = 2.9%). The study found moderate reduction in the number of COVID-19 cases (-0.21, 95%CI -0.01 to -0.39), and a pronounced reduction in severe cases (-0.55, 95% CI -0.34 to -0.76) and deaths associated with vaccination.[7]

The second study also from Brazil was an analysis of mortality trends among the 70-year-old and older population from January 2021, at the beginning of the national vaccination roll out (Coronavac = 65.4% of all doses given, ChAdOx1 = 29.8%) at week 1 to 4 and at week 15 to 19. The study showed that the proportionate COVID-19 mortality among the aged 80 years and older fell rapidly from week 6 onwards (from 26.1% to 11.5%), while those aged 70 to 79 years old started to drop at week 15 (from 24.1% to 18.2%), whereas proportionate mortality due to non-

COVID causes remained relatively stable throughout the study period (~30% for the 80 years and older, ~20% for the 70 to 79 years old). The decline in the mortality rate coincided with the increasing vaccination coverage in the said population groups.[8]

Observational Clinical Studies

Six (6) studies were identified providing real world evidence on the effectiveness of CoronaVac. These studies implemented a 28-day dosing interval of CoronaVac, in contrast to the 14-day interval used in most of the clinical trials.

Two (2) were population-based studies in Latin America validating the vaccine efficacy (against symptomatic COVID-19) rates ranging from 50-84% reported in clinical trials.[9,10] The prospective, national cohort study in Chile included 10,187,720 participants, aged 16 years or older who received at least one dose of the CoronaVac vaccine between February 2 and May 1, 2021, or did not receive any COVID-19 vaccination. Among the fully vaccinated (>14 days from the administration of the second dose), the adjusted vaccine effectiveness was 65.9% (95% CI 65.2-66.6) for the prevention of COVID-19 and 87.5% (95% CI 86.7-88.2) for the prevention of hospitalization, 90.3% (95% CI, 89.1-91.3) for the prevention of ICU admission, and 86.3% (95% CI 84.5-87.9) for the prevention of COVID-19 related death.[10] The retrospective cohort done in Brazil enrolled 25,752,013 individuals who received at least one dose of CoronaVac from January to April 2021. The adjusted vaccine effectiveness rates among the fully vaccinated were as follows: 52.7% (95% CI 52.1-53.4) against any infection, 72.8% (95% CI 71.8-73.7) against hospitalization, 73.8% (95% CI 72.2-75.2) against ICU admission and 73.7% (95% CI 72.3-75) against COVID-19 death.[10]

A population registry-based study on the elderly (75 years and older) from Brazil compared the deaths by COVID-19 among the unvaccinated and those who died 21 days or later after the first dose of CoronaVac. It showed significantly lower death rates among those who received the first dose and among those who received two doses compared to those who were not vaccinated (0.45% and 0.08% vs. 9.21%). The study reported attributable protection ratios of 95.1% (95% CI 94.7-95.5) after the first dose of CoronaVac and 99.1% (95% CI 98.9-99.3) after two doses. Increasing protection was also observed with increasing age: 70 to 79 years old: 86.3 (95% CI 84.7-87.7), 80 to 89 years old: 97.6 (95% CI 97.2-97.9) and 90 and older: 99.3 (95% CI 99.1-99.5).[11]

Three (3) studies were on healthcare workers from Brazil.[12,13] The first study showed an adjusted vaccine effectiveness (aVE) rate of 50.7% (95% CI 33.3-62.5) beginning at two weeks after the second dose, increasing to a rate of 73.8% (95% CI 57-84.8) 5 weeks later.[12] The second study was a test negative case control conducted during the Gamma variant surge, which showed that two doses of CoronaVac was not associated with a reduction in the odds of symptomatic COVID-19 infection (aVE = 37.1%, 95% CI -53.3 to 74.2).[13]

Finally, a cross-sectional study done among 4,260 healthcare workers in Brazil who received at least one dose of CoronaVac showed that 193 (38.7%) cases tested positive on RT-PCR within the first 9 weeks from vaccination. This rate was found to be significantly higher compared to those who received ChAdOx1 (positive rate = 30.3%).[14]

Appendix 4a outlines the characteristics and risk of bias of studies providing clinical effectiveness of CoronaVac.

Immunogenicity Studies

The search identified 10 immunogenicity studies on CoronaVac involving different populations. In general, they showed satisfactory seroconversion after two doses of CoronaVac. The following observations regarding factors influencing immunogenicity were consistent across the different studies: (a) greater immunologic response (both seropositivity and titers) to CoronaVac is seen among those with previous history of COVID-19 infection compared to the infection naïve [15-18] and (b) immunologic response decreases with age.[15-21] The two studies that investigated the relationship between the presence of comorbidities and immune response showed conflicting results.[17,22]

Appendix 4b presents the characteristics and detailed results of immunogenicity studies on CoronaVac.

Safety

Safety outcomes in the clinical trials consistently showed significantly higher reactogenicity rates with CoronaVac compared to placebo. Local adverse reaction rates associated with CoronaVac across the trials ranged from 12% to 61%. Pain at the injection site was consistently cited as the most common local adverse event, with reported rates from 11% to 61%. Systemic reaction rates ranged from 10% to 58%. Headache, fatigue, and malaise were the most commonly reported systemic adverse reactions. Serious adverse event rates associated with CoronaVac across the trials were low (<5%) and not significantly different from placebo. Most serious adverse events (SAE) were assessed to be unrelated to the vaccination. Only one (1) trial reported vaccine-related SAEs, which included systemic allergic reaction, seizure, and encephalitis.[2]

One (1) trial reported one death in the vaccine group, caused by medication overdose, which was assessed to be unrelated to the vaccine.[1]

Appendix 5 presents the characteristics and detailed results of the studies providing safety information on CoronaVac.

Safety Reports from Regulatory Agencies

The Pan American Health Organization's report on July 12, 2021, provided the adverse events from immunization (AEFI) and serious adverse event rates for CoronaVac used in the region as of June 30, 2021. After 57,486,521 doses administered, 36,340 events were reported, of which 3,353 were classified as serious. The total AEFI events per 100,000 doses was 63.2 (range = 5.1-603.5) and the serious events per 100,000 doses was 5.8 (range = 0.0-10.3).[23] In the report on July 29, 2021, it quoted the Chilean authority report covering the period December 24, 2020 to May 14, 2021, with 2,619,095 doses of CoronaVac administered. The AEFI rate per 100,000 doses administered was 36.8 with a total of 5,103 events recorded. There were 121 reported cases of anaphylaxis, 36 cases of seizures, 28 cases of Bell's palsy, 16 thromboembolic events, and 4 cases of Guillain-Barre syndome. In the same report, the reported rate of AEFI for CoronaVac in Portugal was 915.25 per 100,000 doses administered.[24]

The Hong Kong Health Department has administered 2,253,000 doses of CoronaVac as of July 31, 2021 with a reported frequency of adverse events at 2,242. Seventeen deaths following CoronaVac vaccination were also reported but upon review, the death cases were not causally linked with vaccination.[25]

The Philippine FDA, as of September 5, 2021, reported that 20,427,037 doses of CoronaVac were administered with 24,559 reports of adverse reactions. The most reported events were increased blood pressure followed by headache and injection site pain.[26]

Specific Adverse Event: Cutaneous and Allergic Reactions

A multicenter, online questionnaire-based, cross-sectional study that enrolled 221 HCWs in Turkey enumerated the cutaneous and allergic reactions following a first dose of CoronaVac vaccine.[27] Urticaria was the most frequently reported cutaneous reaction. The study also reported one case of anaphylaxis, and three cases each of angioedema and type IV allergic cutaneous rash (including erythema multiforme). Reactivation of herpes zoster and herpes simplex were also observed in two patients each. Another published case series reported on six healthcare workers who developed cutaneous reactions following CoronaVac vaccination.[28] There were two cases of urticaria with angioedema and two cases without angioedema. The other two developed erythema multiforme and pityriasis rosea. Other case reports described one case of systemic drug-related intertriginous and flexural exanthema (SDRIFE)-like eruption [29], another case of erythema multiforme [30], and generalized pustular psoriasis following CoronaVac vaccination.[31]

Specific Adverse Event: Nephrotic Syndrome

There were two reports of nephrotic syndrome following vaccination with one dose of CoronaVac. [32,33] The first case was of a 65-year-old man from Turkey who developed pedal edema, ascites, and acute weight gain one week after receiving the vaccine.[32] Similarly, a 67-year-old woman from Turkey presented with hypertension and pedal edema 2 weeks post-vaccination.[33] A diagnosis of minimal change disease was made on both cases, based on kidney biopsy. The second case received a second dose of the vaccine and subsequently developed headache and recurrence of generalized edema. The second biopsy revealed interstitial nephritis. The authors hypothesized that the patient may have become sensitized to the components after the first dose of the vaccine.

Specific Adverse Event: Optic Neuritis and Subacute Thyroiditis

A patient who developed bilateral optic neuritis and acute thyroiditis following CoronaVac vaccination was also described in a case report.[34] The case presented with rapidly progressive low visual acuity and pain on movement of the left eye and headache. Fundus examination revealed bilateral disc swelling, more pronounced in the left eye. A diagnosis of concurrent subacute thyroiditis was made based on elevated levels of thyroid stimulating hormone with normal thyroxine (T4), increased anti-thyroglobulin, and anti-thyroid peroxidase. The report was the first case of acute thyroiditis and optic neuritis after COVID-19 vaccination.

Specific Adverse Event: Bell's Palsy

Bell's palsy following CoronaVac vaccination has been reported in post-vaccination adverse event surveillance.[35] A case series and a nested case-control study done in Hong Kong reported that the age standardized incidence of clinically confirmed Bell's palsy was 66.9 cases per 100,000 person-years (95% CI 37.2-96.6). The age-standardized incidence difference compared with the background incidence in the same period in 2020 was 41.5 (95% CI, 11.7-71.4), equivalent to additional 4.8 cases per 100,000 people within 42 days of receiving CoronaVac. In the nested case control analysis, the adjusted OR was 2.384 (95% CI 1.415-4.022) for risk of Bell's palsy following CoronaVac vaccination.

Children

Clinical Efficacy and Effectiveness

The search failed to identify a study reporting on the clinical efficacy or effectiveness of CoronaVac on children.

Immunogenicity

One (1) randomized, double-blind, placebo-controlled Phase 2/3 study reported on the immunogenicity of CoronaVac in children from 3 to 17 years.[6] The intervention group was blocked into two: (1) high dose (3.0ug) and (2) low dose (1.5ug).

The Phase 1 intervention group had 100% seroconversion rates for both doses. None of the participants in the placebo group became seropositive. In Phase 2, seroconversion rates were as follows: 1.5ug: 96.8% (95% CI 93.1-98.8), 3.0ug: 100% (95% CI 98.0-100.0), placebo: 0% (95% CI 0.0-3.9) (p value: <0.0001). CoronaVac was found to be highly immunogenic with GMTs generally higher than those found in adults. The observed GMT of the 3.0ug group was significantly higher than that of the 1.5ug across all age subgroups.

Safety

Incidences of adverse reactions were generally similar across the treatment groups with no dose-related concerns on safety. Overall adverse event rates within 28 days of vaccination were similar between the treatment groups (29% for 3.0ug vs. 24% for placebo). Only pain at the injection site was noted to occur more frequently in the vaccine group (16% for 3.0ug dose vs. 2% for placebo). No case of hypersensitivity was observed in both vaccine groups (1 case was noted in the control group).

Pregnant Women

The search did not yield any study providing information on the safety and efficacy or effectiveness of CoronaVac in pregnant women. The Brazilian regulatory trial reported one pregnancy in the vaccine group, which resulted in an abortion. The placebo group had two abortions in the three pregnancies reported.[1]

Immunocompromised Population

Available evidence on the use of CoronaVac among the immunocompromised is limited to immunogenicity and safety. The search identified three (3) studies; two involving patients with immune-mediated disease and one on cancer patients under systemic treatment. No study with vaccine effectiveness has been identified.

A Phase 4 prospective controlled trial evaluated the immunogenicity and safety of CoronaVac in a cohort that enrolled 910 adults with autoimmune rheumatic diseases (ARD) and 182 age- and sex-frequency matched healthy adults.[36] Primary outcome was the reduction of greater than 15% in anti-SARS-CoV-2 IgG seroconversion and neutralizing antibody (Nab) positivity six weeks after the second dose. Lower anti-SARS-CoV-2 IgG seroconversion (70.4% vs. 95.5%, p<0.001) and Nab positivity (56.3% vs. 79.3%, p <0.001) were noted at Day 69 among adults with autoimmune rheumatic diseases (ARD) compared to the controls. Short-term immunogenicity was still acceptable, albeit reduced. Adverse effects reported were mild.

A cross-sectional study was conducted in Turkey among hospital workers and elderly people, which identified a subgroup with immune-mediated disease (IMD), mostly rheumatic disease.[18] It showed that they were less likely to have detectable antibodies than controls (92.7% vs. 99.7%, p < 0.001). Multivariate logistic regression analysis showed that having IMD [OR 17.31, (95% CI

3.57–85.95), p< 0.001] and being 60 years or more [OR 4.32, (95% CI 1.20–15.50), p = 0.025] were found to be independently associated with having negative antibody result.

A multicenter, prospective, observational study evaluated the immunogenicity and safety of CoronaVac vaccine in 47 patients with cancer receiving active systemic therapy.[20] More than half of the entire patient group developed immunogenicity (antibody level > 1 IU/mL) 30/47 (63.8%) four weeks after the second dose of the vaccine. Seropositivity rate was 59.5% (25/42) in those receiving at least one cytotoxic drug and 100% (5/5) for those receiving monoclonal antibodies and immunotherapy. Age was predictive of immunogenicity (OR 0.830, p = 0.043).

Appendix 6 details the characteristics and risk of bias of studies discussed in this section.

Effectiveness Against Variants

Six (6) studies provided information on the effectiveness of CoronaVac against the variants of concern. Four (4) studies provided clinical outcomes while two (2) were immunologic studies. Two of the four clinical studies dealt with the Delta variant and two were on the Gamma variant. Both immunologic studies were on the Delta variant.

Two (2) observational studies were conducted during the Delta outbreak and genomic sequencing of the infected cases was assumed.[37,38] In these two studies, other vaccines were used aside from CoronaVac. No separate vaccine effectiveness was presented for each vaccine. Both studies showed adjusted vaccine effectiveness estimates similar to the vaccine efficacy estimates in the clinical trials, such as sufficient protection against COVID-19 infection, including severe disease.

The first study was a retrospective cohort study from China among persons identified as cases or close contacts of infected patients who tested positive during the Delta outbreak.[37] Two vaccines in use in the studied population were CoronaVac (51% among partially vaccinated and 58% among fully vaccinated) and ChAdox1. The adjusted vaccine effectiveness for pneumonia in the fully vaccinated was 69.5% (95% CI 42.8–96.3). No case of severe infection was found in the vaccinated cohort.

The second study was a test negative case control study also from China among COVID-19 patients aged 150 to 59 years old and close contacts.[38] Genomic sequencing of a sample of the study population showed majority of the infections were caused by the Delta variant. In this study, the adjusted vaccine effectiveness against any infection was 59% (95% CI 15.0–81.6) for the fully vaccinated. The aVE for moderate infection was 70.2% (95% CI 29.6–89.3). Again, no case of severe infection was reported among the vaccinated cohort.

Two test negative case control studies from Brazil investigated the effect of CoronaVac during the period when the Gamma variant was the prevalent strain.[13,39] Both studies showed decreased adjusted vaccine effectiveness against any infection, hospitalization, and death due to COVID-19 disease, compared to the estimates in the clinical trials. Of particular note are the low adjusted vaccine effectiveness estimates among the elderly population aged 80 years and older in the study from Sao Paolo breaching the cutoffs for sufficient protection set by the WHO.[39] The aVE for hospitalization in this age group was at 38.9% (95% CI 21.4 -52.5) and the aVE for death with COVID was at 44% (95% CI 20.3-60.6).
The two immunogenic studies involved the investigation of CoronaVac effectiveness against the Delta variant.[40,41] The first study, from China, included sera from 20 persons who had received their second CoronaVac dose 7 to 14 days prior. In this study, 19 out of the 20 sera had substantial

serum neutralizing activity against D614G spiked pseudotyped viruses. Compared with activity against D614G, 65% (13/20) of sera from the CoronaVac recipients were decreased below the threshold of serum neutralizing ability for the Delta variant. The average neutralization potency of CoronaVac recipients were also decreased 2.5-fold (GMT 36) as compared to the D614G (GMT 89).[40]

Another immunologic study conducted in Thailand investigated the effect of SARS-CoV-2 variants of concerns to vaccine and infection-induced antibodies.[41] In this study, sera from 60 vaccinated (2 doses of CoronaVac) healthcare workers were used. Neutralizing antibodies against the wild type, Alpha, Beta, and Delta variants were measured. The study found out that relatively low neutralizing antibody titers were elicited by CoronaVac compared to natural infection. Results also showed that quantifiable antibody titers against Delta were present in only 69.17% of vaccinated sera as compared to 99.17% against the wild type. Furthermore, only 48.33% of vaccinated participants had neutralizing antibody titers of at least 20 (which is the cutoff for neutralizing antibody positivity) against the Delta variant, as compared to 98.33% against the wild type. It was noted in the study that natural infection consistently produced a greater percentage of antibody positivity as compared to CoronaVac recipients across all the tested variants. The authors state that despite a robust S1-RBD-binding IgG and 100% seropositivity sera from CoronaVac and previously infected recipients, they had significantly reduced neutralizing capacities against all the three variants of concern tested.

Appendix 7 presents the characteristics and results of the studies on CoronaVac clinical effectiveness (7a) and immune response (7b) against the variants of concern.

Duration of Protection

To answer the question of duration of protection offered by CoronaVac, the review searched for studies that presented vaccine effectiveness or immunogenicity data over time. Five studies were identified; three provided immunogenic information while two reported clinical effectiveness data.

A study from Turkey among 272 health workers who received 2 doses of CoronaVac and were assessed for anti-RBD, anti-spike, and anti-nucleocapsid IgG antibody concentrations (by CLIA reaction) at one, three, and six months post vaccination. This study found that the antibody concentrations were statistically decreased at the third month but with median concentrations still above the reactive level. However, it found that for the group of healthcare workers with a prior history of infection, the decrease in antibody concentrations was not found to be statistically significant. In terms of seropositivity rates for the anti-RBD antibodies, the study found that the decline from first to the third month was not statistically significant (98.2% vs. 97.8%). The decline in the anti-spike / anti-nucleocapsid IgG antibodies seropositivity rates from the first to the third month was 93% to 87.5%, which was statistically significant. Similarly, the decline in the median antibody levels from the 1st to the 3rd month) was significant for both anti-S-RBD IgG (29.14 to 10.46 AU/ml) and anti-spike/anti-N IgG (198 to 6.16 AU/ml).[42]
Another study reported on 158 individuals who received 2 doses of an inactivated COVID-19 vaccine (3ug dose in an Al(OH)3) adjuvant) 14 or 28 days apart and were assessed for antibody titers and positivity until 180 days after the second dose. The antibody levels peaked at day 28 after the second dose and subsequently declined. Neutralizing, anti-S and anti-N antibody seropositivity rates were generally halved by the sixth month post vaccination from 92-100% to 35-52%.[43]

A similar study in Thailand evaluated the change in immune response over a 12-week period after CoronaVac given at a 21-to-28-day interval. It showed the median SARS-CoV-2 sVNT significantly declined from 77% (95% CI 58.5-87.9) inhibition to 38.7% (95% CI 22.1-55.7).[44]

The interim report of the regulatory trial from Brazil provided the vaccine efficacies from 14 to 98 days from the first dose of CoronaVac, showing marginal change over time. The VE within 28 days of the first dose (14 days after second dose) increased from 42%, peaked at 60% on the 56th day, and gradually, but minimally, declined to 52% at 98 days post-first dose.[1]

A retrospective review of linked population-based health registries in Brazil was done among infection naive individuals who received their first COVID-19 vaccine dose (CoronaVac or ChAdOx1) between January 18, 2021 and July 24 2021.[10] The study followed these individuals to assess infection, hospitalization, admission to ICU, and death with laboratory-confirmed diagnosis SARS-CoV-2 infection until three months post-vaccination. The study found that CoronaVac vaccination was associated with decreased and maintenance of a low hospitalization incidence up to 84 days in all vaccinated individuals up to 79 years of age. However, for those 80 years and older, incidence levels were lowest 28 days after the second dose, and gradually increased afterward, but to a level that was still lower that those observed at the reference level (within 13 days after the first dose).

Appendix 8 presents the characteristics and detailed results of studies on duration of protection after CoronaVac immunization.

Booster Doses

Homologous Booster

Four (4) studies provided information on the effectiveness of CoronaVac as a booster, although outcomes were limited to immunologic response. Both studies were randomized controlled trials performed in China among healthy adults, which showed increased neutralizing antibody titers and greater positivity rates after a third dose compared to levels after the second dose.[4,45] This immunogenic response was demonstrated whether the third dose was given early (1 month after the second dose) or late (6 months after). In the older group (>/= 60 years old), the seropositivity rate was not significantly increased after the third dose compared to the second dose (100% vs. 97.7%).[4] Safety data from these trials showed generally low adverse event rates associated with the booster dose. The CoronaVac booster dose showed similar local and systemic adverse reaction rates compared with that of the second dose. Serious adverse event rates were low and similar to that of the placebo. No vaccine-related serious adverse events were reported.

A case series of 76 individuals who received a third dose of CoronaVac at an unspecified time after the second dose showed seroconversion of 100% neutralizing antibody with GMTs of 57.9 and 36.8 for S and N antibodies. Increased T cell response of the IFN-γ secretion against S and N antigens was also observed. Furthermore, a significant difference in the IFN-γ levels one month after the second and third doses was reported.[46]

Finally, a subgroup of the Phase 2/3 registration trial for CoronaVac received a booster dose six months after the second. It demonstrated a 60% higher neutralization activity after the third dose inoculation when compared with the second dose. The reported GMT values were 1,176 after the third dose compared with 660 after the second dose. It also showed lesser reductions in activity against the variants of concern (Beta, Gamma, and Delta) with the third compared with the second dose.[47]

Heterologous Booster

A cross-sectional study among healthy adults 18 to 59 years old primed with two doses of CoronaVac compared the effect of a homologous CoronaVac booster and a heterologous booster using a recombinant adenovirus type-5-vectored vaccine (Convidencia).[48] The booster doses were given 3 to 6 months after the second dose. Results showed increased immunogenicity after either booster dose, with significantly higher neutralizing antibody titers with heterologous booster at 14 days (33.6 vs. 197.4) and 28 days (35.3 vs. 150.3) compared with homologous vaccination. Seropositivity rates were 100% for both regimens at 14 days post-boost, and 99% for CoronaVac and 100% for Convidencia at 28 days. Heterologous prime-boost immunization had significantly more local (29.2% vs. 2.9%) and systemic (14.6% vs. 2.9%) reactions.

No study was identified using CoronaVac as a heterologous booster to another vaccine regimen.

The characteristics and the results of these booster studies are detailed in tables that may be found in Appendix 9-11.

Ongoing Trials

As of September 7, 2021, 35 trials are registered in *clinicaltrials.gov* involving CoronaVac as an intervention. Four trials included children and adolescents. Nine are observational studies, while 13 are Phase 4 trials. Eight trials are recruiting.

Appendix 12 shows the details of these registered trials.

Authorizations

The WHO issued its recommendations on the use of CoronaVac on May 24, 2021 after the SAGE meeting on April 29, 2021.[49]

The Philippine FDA issued an emergency use authorization for CoronaVac on February 22, 2021.[50]

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Appendix 1. Evidence to Decision

Summary of Initial Judgements Prior to Panel Discussion (N = 10)

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
Problem	No	Yes (10)					
Benefits	Large (6)	Moderate (3)	Small	Uncertain (1)			• Epidemiological and observational studies showed increased rates of CoronoVac vaccination coincided with a decline in COVID-19 cases, reduction in severe cases, and in mortality rates. • Immunogenicity studies showed satisfactory seroconversion after 2 doses of Coronavac.
Harm	Large	Small (10)	Uncertain				• Randomized controlled trials reported adverse reactions, ranging from local (e.g., pain at injection site) (12-61%) to systemic (headache, fatigue) (10-58%), with <5% showing serious adverse events and no reported deaths.
Certainty of evidence	High	Moderate (4)	Low (6)	Very low			• Very low to moderate
Balance of effects	Favors vaccine (10)	Does not favor vaccine	Uncertain				
Values	Important uncertainty or variability	Possibly important uncertainty or variability (6)	Possibly no important uncertainty or variability (2)	No important uncertainty or variability (2)			
Resources required	Uncertain (2)	Large cost (3)	Moderate cost (3)	Negligible cost or savings (1)	Moderate savings	Large savings (1)	• It is affordable but the total budget allocation is not proportionate to the target vaccinees.
Certainty of evidence of resources required	No included studies (8)	Very low	Low (1)	Moderate (1)	High		

Cost effectiveness	No included studies (9)	Favors the comparison	Does not favor either the intervention or the comparison	Favors the intervention (1)			
Equity	Uncertain (2)	Reduced	Probably no impact (2)	Increased (6)			• PHL FDA EUA indication is for clinically healthy people (aged 18 years old and above) susceptible to the virus. • This product is not recommended for use among healthcare workers with exposure to COVID-19 patients. • Addresses wide disparity in vaccine coverage: 85.1% fully-vaccinated senior citizens in NCR; only 28.3% in BARMM..
Acceptability	Uncertain (2)	No	Yes (8)				• CoronoVac was given EUA by the Philippine FDA on February 22, 2021
Feasibility	Uncertain (2)	No	Yes (8)				

Appendix 2. Characteristics of Randomized Clinical Trials on CoronaVac efficacy and safety

Study ID (Country)	Population	Intervention (n)	Comparator (n)	Outcomes	Methods (Risk of Bias)
Wu (China)	60 years and older Exclusion High risk history History of SARS or SARS-CoV-2 T > 37'C	CoronaVac 1.5ug / 3.0ug / 6.0 ug Administered IM on 0 and 28 days	Placebo (aluminum hydroxide only) Ph I = 36	Vaccine-related adverse events within 28 days after each dose Seroconversion rate of neutralizing antibodies at 28 days after D2 Geometric mean titer of neutralizing antibodies to SARS-COV-2 Increase of seroconversion rate Increase in GMT Severe adverse events	Ph 1 = 72 Randomization codes generated by the randomization statistician using SAS software Randomization code assigned to each participant in sequence in the order of enrollment Participants, investigators, laboratory staff masked (Low risk)
Tanriover/ Akova (Turkey)	18-59 years old No history of COVID-19 Negative PCR and antibody test for SARS-CoV-2 K1; healthcare workers K2: general population Exclusion: Immunosuppressive therapy Bleeding disorders Asplenia Receipt of any blood products or immunoglobulins within 3 months Planned follow up = 1 year	Coronavac 3ug (600SU) given at 0 and 14 days (N = 6,646) - safety	Placebo (N = 3,568) - safety	Incidence of symptomatic COVID-19 confirmed by RT-PCR at least 14 days after D2 Incidence of hospitalization or mortality COVID-19 confirmed by RT PCR Adverse events: solicited, unsolicited, systemic, local, Neutralizing antibody and IgG at 14 and 28 days after each dose: Seroconversion rate Seropositivity rate Geometric mean titer Adverse reactions from day of vaccination to 28 days after D2 Adverse reaction within 7 days Serious adverse event to 1 year after second dose	Randomized by interactive web response system Participants and practitioners masked to group allocation Incomplete follow-up (interim report with median ff-up of 90 days of ff-up after first dose) Sampling for antibody assays at least 14 days after D2 (Low risk)
Bueno (Chile)	Health care workers 18 years and older (N = 434) Excluded: history of confirmed COVID-19, pregnancy, allergy to	CoronaVac 3.0ug, 2 doses, 14 days apart (N = 270)	Placebo (N = 164)	Antibody and cell-mediated immunity results - Seroconversion (anti RBD IgG, anti-N Nab, IFN-G	Randomization using sealed enveloped system integrated into the eCRF Participants, investigators and lab staff masked to allocation

	vaccine components, immunocompromised	(N = 39 for immunogenicity study)		Safety - Solicited AE - Unsolicited AE within 7 days Any AE within 28 days of each dose Serious AE Events of special interest Falls	Interim analysis (Low risk, incomplete ff-up) Immunogenicity, specimen taken at 14, 28 and 42 days after each dose, by ELISA
Palacios (Brazil) Preprint	Healthy health professionals caring for COVID patients (N = 12,396); Only 5% were 60 years and older 55.9% with comorbidities (N = 9,823) Excluded pregnant, previous COVID-19 vaccines, acute symptoms of COVID	CoronaVac 3.0ug, 14 days apart (N = 6,195) - safety (N = 4,953) - efficacy	Placebo (N = 6,201) - safety (N = 4,870)	Symptomatic RT-PCR confirmed infection 14 days after 2nd dose 50.7 (36-62) Moderate infection 83.7 (58-93.7) Severe infection 100 (56.4-100) Adverse events up to 28 days after immunization Local, systemic, serious AEs Deaths Neutralization assays GMT and seroconversion for variants	Randomization by IWRS Coding received only by pharmacist not involved in trial Participants and study staff and lab techs unaware of product allocation Interim report Underpowered for safety (Low risk)
Han (China)	Healthy children from age 3 to 17 years old Total enrolled: Ph I = 72, Ph 2 = 480 Exclusion: ○ Travel or residence history in communities with case reports, or contact history with someone infected with SARS-CoV-2) ○ History of severe acute respiratory syndrome or SARS-CoV-2 infection (as reported by participants) ○ Axillary temperature of more than 37·0° ○ History of allergy to any vaccine component Balanced age, gender distribution, ethnicity between groups	CoronaVac inactivated vaccine 1.5 or 3.0ug in 0.5ml aluminum hydroxide adjuvant, 2 doses, 28 days apart Ph1: 36, Ph2 1.5ug: 192, 3.0ug: 192	Placebo (aluminum hydroxide only) Ph 1: 36 Ph2: 96	Safety ○ Any vaccine related AE within 28 days after administration ▪ Solicited AEs – first 7 days ▪ Spontaneous reporting of AEs – until 28 days ○ Serious adverse events (until 12 months) ○ Abnormal changes in lab measurement at day 3 Immunogenic ○ Seroconversion rate of neutralizing antibodies at day 28 after second dose ○ Seropositive rates (4-fold rise from baseline) ○ GMT of neutralizing antibodies to live SARS-CoV-2 (positive cut off was 1/8) ○ Geometric mean increase Planned follow up until 12 months after dose 2	Ph1 – age de-escalation and dose escalation study (n= 72) Ph2 – main safety/efficacy trial Randomization codes generated by the randomization statistician using SAS software Randomization code assigned to each participant in sequence in the order of enrollment Participants, investigators, laboratory staff masked Interim analysis, planned follow up to 12 months after dose 2 All planned outcomes reported (Low Risk)

Appendix 3: Vaccine efficacy results of Clinical Trials on CoronaVac

A. Vaccine efficacy (Clinical outcomes)

VACCINE EFFICACY / EFFECTIVENESS PARAMETERS VE (95% CI)	STUDIES		
	TANRIOVER (Turkey)	**PALACIOS* (Brazil)**	**Indonesia Regulatory**
	18-59 years old 3.0ug, 0, 14d	18-59 years old; >= 60 years old	18-59 years old;
SYMPTOMATIC COVID-19 Infection (as defined by trialist), complete dosing, seronegative ONLY, after 14 days	83.5% (65.4-92.1)	50.5%	65.3%
SYMPTOMATIC COVID-19 Infection (as defined by trialist), complete dosing, seronegative AND seropositive, after 14 days		50.7% (35.7-62.2); >+ 60: 51.1% (-166.9-91.0	
SYMPTOMATIC COVID-19 Infection (as defined by trialist) occurring after 1st dose, seronegative ONLY			
- >=10 days after dose 1 before dose 2	46.4% (0.4-71.2)		
SYMPTOMATIC COVID-19 Infection (as defined by trialist), after 1st dose, seronegative AND seropositive, after 14 days		57.9% (46.3-66.9)	
Severe COVID-19 Infection, complete dosing, seronegative AND seropositive, after 14 days		100% (56.4-100.0)	
Asymptomatic COVID-19 infection, complete dosing, seropositive AND seronegative, after 14 days			
ANY COVID-19 Infection (as defined by trialist), complete dosing, seronegative AND seropositive, after 14 days			
Hospitalization due to COVID, complete dosing, seronegative only, after 14 days	100% (20.4-100.)		
Hospitalization due to COVID, complete dosing, seropositive AND seronegative after 14 days			
ICU admission due to COVID, complete dosing, seronegative AND seropositive, after 14 days			
Death due to COVID, complete dosing, seronegative ONLY, after 14 days			
SPECIAL POPULATIONS: COVID 19 infection, complete dosing, seronegative only			
>=65 years old, after 14 days of 2nd dose			
< 18 years old			
At high risk for COVID, at 14 days after 2nd dose		48.9% (26.6-64.5)	
Seropositive at baseline		49.5%	
Asian		66.0% (-226.8-96.5)	
Healthcare workers		50.7% (35.7-62.2)	
Children			

B. Vaccine efficacy (Immunologic outcomes)

Immunologic Outcomes	STUDIES		
	Wu (China)	**Bueno (Chile)**	**Han (Chan)**
	60 years and older	18 years and older	3-17 years old
Neutralizing antibody seroconversion	Phase 1 Day 28 after 1st dose - 3ug: 54.2% (95% CI 32.8-74.5) - 6ug: 62.5% (95% CI 40.6-81.2) Not significant (p = 0.058) Day 28 after 2nd dose - 3ug: 100% (95% CI 85.8-100.0) - 6ug: 95,7% (95% CI 78.1-99.9) Not significant (p = 0.489) Phase 2 Day 28 after 2nd dose - 1.5ug: 90.7% (95% CI 83.1-95.7) - 3ug: 98% (95% CI 92.8-99.8) - 6ug: 99% (95% CI 94.5-100.0) No significant difference in between groups	Anti-S1-RBD IgG 18 to 59 years old After 14 days: 47.8% After 28 days: 95.6% After 42 days: 95.6% >/= 60 years Anti-S1-RBD IgG After 14 days: 18.1% After 28 days: 100.0% After 42 days: 87.5% Anti N protein 18 to 59 years old After 14 days: 8.7% After 28 days: 17.4% After 42 days: 13.0% >/= 60 years Anti-S1-RBD IgG After 14 days: 0% After 28 days: 20.0% After 42 days: 37.5%	Phase 1 Day 28 1.5ug: 100% (95% CI 87.2-100.0) 3.0ug: 100% (95% CI 86.8-100.0) Placebo: 0% (95% CI 0.0-20.6) Phase 2 1.5ug: 96.8% (95% CI 93.1-98.8) 3.0 ug: 100% (95% CI 98.0-100.0) Placebo: 0% (95% CI 0.0-3.9)
Geometric mean titer (GMT) of neutralizing antibody	Phase 1 Day 28 after 1st dose - 3ug 6.9 (95% CI 4.6-10.2) - 6ug 9.1 (95% CI 6.4-13.0) Not significant (p = 0.278) Day 28 after 2nd dose - 3ug 54.9 (95% CI 38.6-78.2) - 6ug 64.4 (95% CI 41.5-99.7) Not significant (p = 0.560) Phase 2 Day 28 after 2nd dose - 1.5ug: 23.4 (95% CI 19.4-28.3) - 3ug: 42.2 (95% CI 35.2-50.6) - 6ug: 49.9 (95% CI 42.2-58.9) 1.5ug vs 3ug p<0.0001 1.5ug vs 6ug p<0.0001	Anti-S1-RBD IgG 18 to 59 years old After 14 days: 23.1 After 28 days: 1755 After 42 days: 1878 >/= 60 years After 14 days: 45.1 After 28 days: 1860.2 After 42 days: 1878 Anti N protein 18-59 years old After 14 days: 5.3 After 28 days: 8.0 After 42 days: 9.2 >/= 60 years After 14 days: 5.5 After 28 days: 9.6 After 42 days: 32.6	Phase 1 Day 28 1.5ug: 55 (95% CI 38.9-77.9) 3.0 ug: 117.4 (95% CI 87.8-157) p = 0.0012 Phase 2 Day 28 1.5ug: 86.4 (95% CI 73.9-101.0) 3.0ug: 142.2 (95% CI 124.7-162.1) P<0.0001
Cell-mediated immunity		No significant difference was observed between 18 to 59 and >/= 60 years old groups	

Appendix 4. Real World Effectiveness Studies

A. Characteristics and Results of Studies on the Clinical Effectiveness of CoronaVac

Study ID	Design Risk of Bias	Population	Intervention/ Exposure	Control	Follow up	Outcomes Reported
Alencar (Brazil)	Retrospective cohort Linked databases Poorly defined unexposed group Limited control of confounders (HIGH RISK)	Elderly population (age >/=75 y/o) (N = 132,777)	At least 1 dose of CoronaVac	Unvaccinated population Number of unvaccinated people was calculated as the difference between estimated population and the number of vaccinated individuals	Unclear	Protection ratio against death After 1st dose Deaths: 778/174,006 (0.45%) Protection ratio: 20.59 (19.07-22.22) Attributable protection ratio: 95.1 (94.7-95.5) After 2 doses Deaths: 108/132,777 (0.08%) Protection ratio: 113.17 (93.5-136.99) Attributable protection ratio: 99.1 (98.9-99.3) Unvaccinated Deaths: 3769/40,941 (9.21%) Increasing protection with increasing age 70-79 y/o: 86.3 (84.7-87.7) 80-89: 97.6 (97.2-97.9) 90 and older: 99.3 (99.1 – 99.5)
Cerquiera-Silva (Brazil)	Retrospective Cohort Adjusted for age, sex, region of residence, socioeconomic status, month of 1st dose	General population (N = 75,919, 840) CoronaVac = 25,752,013 Excluded: vaccinated besides ChAdOx1 or CoronaVac; inconsistent records; confirmed COVID-19 before vaccine administration; missing data for covariates	CoronaVac, 2 doses, median interval = 27 days (IQR 21-28)	Unvaccinated population		VE for infection, hospitalization, ICU admission, death Fully Vaccinated: VE vs Infection: 52.7% (95%CI 52.1-53.4) VS vs Hospitalization: 72.8% (95%CI 71.8-73.7) VE vs ICU admission: 73.8% (95%CI 72.2-75.2) VE vs Death: 73.7%, (95%CI 72.3 to 75.) Partially vaccinated - 18.6% (95% CI, 17.6-19.6) against infection - 28.1% (95% CI, 26.3-29.9) against hospitalization - 28.5% (95% CI, 25.4-31.4) against ICU admission - 29.4% (95% CI 26.7-31.9) against COVID-19 related death Effectiveness declined with increasing age 90y and older: VE against death: 33.6% Effectiveness declined over time (by 84 days) in those 90y/o and older

De Faria (Brazil)	Retrospective cohort Compared actual and predicted infection rates (based on population)	Healthcare workers N1 = 22,402 N2 = 21,652	Coronavac 2 doses, 2-4 weeks apart	Predicted infection rate based on general population infection rates	2-5 weeks post vaccination	VE for lab-confirmed symptomatic COVID infection 2wks post D2: 50.7% (95%CI 33.3-62.5) 3wks post D2: 51.8% (95%CI 30.0-66.0) 4wks post D2: 68.4% (95%CI 51.03-80.8) 5wks post D2: 73.8% (95%CI 57.0-84.8)
Jara (Chile)	Prospective cohort Controlled for age, sex, region of residence, income, nationality, underlying conditions Follow-up relatively short, may not account for late outcomes but similar to the duration of follow up in efficacy trials	Aged 16 years or older who received at least one dose of the CoronaVac vaccine during the mass national vaccine campaign or no receipt of COVID-19 vaccination; affiliated to the national public health insurance Excluded probable / confirmed COVID on or before study period; received BNT162b2 N = 10,187,720 Unvaccinated: 5,471,728 (53.7%)	At least 1 dose of CoronaVac Partially vaccinated: 70million person days 524,418 (5.3%) Fully vaccinated: 92 million days 4,173,574 (41.0%)	Unvaccinated		COVID-19 cases: 218,784 Hospitalizations: 22, 866 ICU admissions: 7873 Deaths: 4042 Fully vaccinated: VEs (Note: VEs similar in 60yo and older) Infection: 65.9 (65.2-66.6) Hospitalization: 87.5 (86.7-88.2) ICU admission: 90.3 (89.1-91.4) Death: 86.3 (84.5-87.8) Partially vaccinated Infection: 15.5 (14.2-16.8) Hospitalization: 37.4 (34.9-39.9) ICU admission: 44.7 (40.8-48.3) Death: 45.7 (40.9-50.2)
Hitchings (Brazil)	Test negative case control	Healthcare workers	CoronaVac	Negative RT PCR	Not mentioned	2 doses, 14 days later aVE for any infection: 37.1%, 95% CI, -53.3 to 74.2)
Toniasso (Brazil)	Cross-sectional study	Healthcare workers suspected of having COVID-19 infection	CoronaVac at least 1 dose N = 399	NA	Not mentioned	38.7% positive diagnosis (breakthrough)

B. Characteristics and Results of Observational Studies on the Immunologic Response of CoronaVac

Study ID (Country)	Population	N	Timing of Extraction (After D2)	Outcomes Reported (Test used) Result
Bayram (Turkey) March 4 and 10, 2021 Preprint	Healthcare workers, 18 years and older, received 2 doses at 28-day interval	1012	21 days	Anti-spike IgG (CLIA) Seropositivity (cut of = 50AU/ml) 1008/1012 (99.6%) overall By hx of COVID-19: 703/706 (99.66%) - no hx of COVID-19 259/259 (100%) - with hx of COVID-19 the rest had unknown status By age group: 18-34: 100% 35-59: 99.2% ≥60: 95.7% Titers (median, range) 1022.40 (10.10-66923.70)
Bichara (Brazil) March to April 2021	patients who voluntarily sought care (no reason indicated)	358 (205 - Anti-S 153 - Anti-RBD)	30 days	Anti-S1 and S2 (CMIA/CLIA) Seropositivity 159/205 (77.6%) overall By age group: 21-40 years old: 91% 41-60 years old: 83% 61-80 years old: 73% >80 years old: 62% Anti-RBD (surrogate virus neutralization test) Seropositivity 111/153 (72.6%) overall By age group: 21-40 years old: 93% 41-60 years old: 76% 61-80 years old: 72% >80 years old: 47%
Bochnia Bueno (Brazil) Preprint	healthcare workers	133	20 days (D40 since 2nd dose was given at D20)	Anti-N (Architect-I System) 69/133 (51.87%) Anti-S1 (CMIA/CLIA and EIA) 129/133 (97%) [1 of 4 who did not seroconvert had seroconverted by D60]

Appendix 5. Characteristics of Studies Reporting Safety Outcomes of CoronaVac and their Results

Study ID (Country)	Population (design)	CoronaVac dosing regimen	Results
Wu (China)	60 years and older (RCT-Ph1/2)	1,5, 3.0, 6.0ug 2 doses 28-day interval	Adverse reaction rates (28days): Vaccine (3.0ug) vs Placebo Any: 20% s 21% Local reaction: 12% s 4% Most common: pain (11% vs 4%) Systemic reaction: 10% vs 16% Most common: fever (4% vs 1%), fatigue (3% vs 1%) Serious adverse events: 1% vs 0% (Pancreatitis) All unrelated to vaccine
Bueno (Chile)	Adults 18 years and older (RCT- Ph3)	3.0 ug 2 doses 14-day interval	Adverse reaction rates: Vaccine vs Placebo Pain at injection site: 55.6% vs 40.0% Most were mild and resolved in 2 days Headache most frequent systemic AE: 48.8% vs 48.5% Followed by fatigue (27.5% vs 26.8%) and myalgia (23.8% vs 22.6%) No serious adverse event or event of special interest occurred in the trial 3 COVID-19 cases (breakthrough)
Tanriover (Turkey)	18 to 59 years old (RCT-Ph3)	3.0ug 2 doses 14-day interval	Adverse event rates: Vaccine vs Placebo Total: 18.9% vs 16.9% (p=0.011) Solicited: 17.3% vs 15.1% (p=0.0039) Systemic AE: 17.7% vs 16.0% (p=0.0263) Most common: fatigue (8.2% vs 7.0%, p = 0.02), headache (5.9% vs 5.9%) Local AE: 2.7% vs 1.5% (p=<0.001) Most common: Pain (2.4% vs 1.1%) Serious AE: 6 vs 5 events
Palacios (Brazil)	Healthcare workers (RCT-Ph3)	3.0 ug 2 doses 14-day interval	Adverse event rates: Vaccine vs Placebo Adverse reaction = 77.1% vs 66.4% Local AER = 61.5% vs 34.6% Mainly pain at injection site = 60.3% vs 32.5% Systemic reaction = 48.4% vs 47.6% Most common: Headache and fatigue Unsolicited AE = 36.8 % vs 35.8% SAE = 33 vs 31 patients 2 deaths not related to vaccination - CP arrest (placebo) - Medication overdose (CoronaVac)
Han (China)	Children aged 3 to 17years old	1.5ug or 3.0ug 2 doses	Adverse event rates: 1.5ug vs 3.0ug vs placebo Any adverse reaction 0-7d: 23% vs **27%** vs 19% (p=0.28)

	(RCT-Ph1/2)	28 days apart	Pain at injection site: 16% vs **16%** vs 2%, (p<0.001) Fever: 4% vs 5% vs 4% Hypersensitivity 0 vs 0 vs 1% (p=0.93) Any unsolicited AE (28d): 26% vs **29%** vs 24% (p=0.55)
Indonesia RCT	18-59 years old N = 1620 Safety analysis – 540 (RCT- Ph3)	3.0 ug 14-28 days interval	Adverse event rates: Vaccine vs placebo Overall: 71.6% vs 71.1% Solicited Local: 51.3% vs 44.4% Solicited Systemic: 58.5% vs 54.8% Unsolicited Local: 2.4% vs 0.7% Unsolicited Systemic: 43.7% vs 43.7% Local pain: 32.3% vs 21.5% / 30.5% vs 30.1%
Karachin (Turkey)	With solid organ tumors receiving active systemic therapy >18 years old with no previous COVID-19 (Case series)		Local reactions (1st & 2nd dose, respectively): pain at injection site (94.2%; 6.3%); swelling (2.1%; 0%); itchiness (2.1%; 0%); erythema (0%; 4.2%) Systemic reactions: fever (2.1%; 2.1%); myalgia (2.1%; 0%); fatigue (4.2%; 10.5%); headache (2.1%; 0%) No serious side effects or deaths
Riad (Jordan)	Healthcare workers who received at least one dose within 30 days prior to the survey (Cross-sectional study)		Local SE: injection site pain (41.5%), site swelling (2.6%), and redness (1.4%) Systemic: fatigue (23.6%) was the most common followed by headache, muscle pain, joint pain, and nausea. Fever and lymphadenopathy were not commonly reported

Appendix 6. Characteristics and Results of Studies on CoronaVac among Immunocompromised Patients.

Study	Design	Population	Outcomes	Results
Medeiros-Ribeiro	Phase 4, prospective non-randomized controlled trial Controlled for sex and age	910 adults with autoimmune rheumatic diseases and 182 age- and sex- frequency matched health adults	Primary Reduction of >/= 15% in anti-SARS-CoV-2 IgG seroconversion (SC) and neutralizing antibody (Nab) positivity 6 weeks after the second dose Secondary outcomes IgG SC and Nab positivity at Day 28 IgG titers and neutralizing activity at Day 28 and Day 69 Vaccine safety	Lower anti-SARS COV2 IgG SC (70.4 vs 95.5% p<0.001) and Nab positivity (56.3 vs 79.3%, p <0.001) at Day 69 among adults with autoimmune rheumatic diseases (ARD) compared to the controls IgG titers (12.1 versus 29.7, *P* < 0.001) and median neutralization activity (58.7 versus 64.5%, *P* = 0.013) were also lower at Day 69 in patients with ARD. At Day 28, patients with ARD presented with lower IgG frequency (18.7 versus 34.6%, *P* < 0.001) and Nab positivity (20.6 versus 36.3%, *P* < 0.001) than that of the CG. There were no moderate/severe adverse event
Karacin (Turkey)	Multicenter, prospective, observational study (unmatched) Controlled for confounders	47 cancer patients receiving systemic therapy who received 2 doses CoronaVac, 28 days apart Titers taken 4 weeks after the last dose of the vaccine	Immunogenicity antibody level more than 1 IU/mL	Immunogenicity rate 63.8% (30/47) in the entire patient group 59.5% (25/42) among those receiving at least one cytotoxic drug 100% (5/5) among those receiving monoclonal antibody or immunotherapy alone Age was independent risk factor (OR 0.830, p -0.043)

Appendix 7: Characteristics and Results of Studies on Effectiveness of CoronaVac on Variants of Concern

A. Characteristics and Results of Studies on the Clinical Effectiveness of CoronaVac against Variants of Concern

Study ID	Design *(Risk of Bias)*	Population	Variants Tested	Outcomes Reported Results
Kang (China)	Retrospective Cohort Adjusted for age, sex, occupation, street, contact frequency *(Serious Risk / Low Certainty)*	Person identified as cases or close contacts of infected patients who tested positive (N = 10,813) during Delta outbreak Unvaccinated = 5,888 Immed D1 Partially vaccinated = Immed D2 = Fully vaccinated = 1,407 Vaccines in use included ChAdOx1 D1 = 2,526 (51.29% CoronaVac) D2 = 1,046 (58.29% CoronaVac)	Delta	<u>aVE for pneumonia</u> Unvaccinated: n = 85 Partially Vaccinated: n =12 aVE = 8.4% (95% CI -47.6 to 64.4) Fully Vaccinated: n = 5 aVE = 69.5% (95% CI 42.8-96.3) <u>aVE for severe illness</u> Unvaccinated: n = 19 No event in vaccinated (NOTE: aVEs are for the combined effects of ChAdOx1 and CoronaVac. No separate analysis for each of the vaccine)
Li (China)	Test negative case control Adjusted for age and gender (cases were older) Exposure risk considered balanced between groups *(Serious Risk/ Low Certainty)*	18 to 59 year olds among COVID-19 patients and close contacts SARS-CoV-2 positive cases (N = 74) Test-negative controls (N = 292) Fully vaccinated – at least 14 days after D2 Partially vaccinated – at least 14 days from D1 and <14 days after D2 Unvaccinated – included those at <14days after D1 Two vaccines used: CoronaVac (61.3%) and CNBG	Delta (population-based and genomic sequencing of partial sample of study population)	<u>aVE for any infection</u> Partially Vaccinated: 13.8% (95% CI -60.2 to 54.8 Fully Vaccinated: 59.0% (95% CI 16-81.6) <u>aVE for mild infection</u> Fully Vaccinated: -29.4% (95% CI -369.4 to 67.9) <u>aVE for moderate infection</u> Partially Vaccinated: 11.2% (95% CI -72.5 to 55.5) Fully Vaccinated: 70.2% (95% CI 29.6-89.3) <u>aVE for Severe infection</u> No case among vaccinated, 2 cases in unvaccinated Noted higher VEs in the younger population (NOT : aVEs are for the combine effects of ChAdOx1 and CoronaVac. No separate analysis for each of the vaccine)
Hitchings (Manaus, Brazil)	Test negative, matched case control Matched by sample collection date, age, neighborhood residence	Health care workers >/= 18 years old residing in Manaus, received CoronaVac Cases = positive SARS-CoV-2 RT-PCR test and absence of a positive test in the preceding 90-day period N1 = 590 symptomatic	Gamma (population-based)	aOR symptomatic infection at least 14 days after D2: 0.62 (0.26-1.46) (37.1%, -53.3 to 74.2) aVE asymptomatic infection 100%

	Logistic regression covariates: sex, occupation category, race, number of health interactions, COVID infection since start of pandemic	N2 = 218 asymptomatic Controls = test negative		
Ranzani (Sao Paolo, Brazil)	Matched test negative case control Matching by date of testing, age, sex, race, residence, previous COVID-19 status 1 case to 5 controls	>/= 70 years old Cases – test positive within 10 days of symptoms, no positive result in the preceding 90 days Controls – test negative, no positive result within the preceding 90 days and subsequent 14 days Coronavac 2-to-4-week interval	Gamma (population based)	Confirmed symptomatic infection 14 days after D2 aVE = 46.8% (38.7 to 53.8%), declining with increasing age. For >80y/o: 32.7% (17 to 45.5%) Hospitalization aVE = 55.5% (46.5 to 62.9), declining with age >/= 80: 38.9% (21.4% to 52.5) death with COVID aVE = 61.2% (48.9 to 70.5%), declining with age >/=80: 44% (20.3 to 60.6)

B. Characteristics and Results of Immunogenicity Studies on the Immune Response to CoronaVac against Variants of Concern

Study ID	Population	Timing of Extraction	Reference Strain	Variant/s Tested	Outcome (Test Used) Result
Hu (China)	Sera from 20 vaccinated patients	7 to 14 days post D2	D614G	Delta	Neutralizing antibody response (Pseudovirus-based neutralization assay): Neutralizing activity (positivity) 65% (13/20) below the threshold Decline in neutralization potency compared to control: 2.5- fold – reduction
Vacharathit (Thailand)	Health workers who received 2 doses of Coronavac (N = 60)	Not mentioned	WT Sera from unvaccinated and naturally infected COVID-19 patients (Mar –May 2020 and Apr-May 2021)	Delta	Live virus neutralization: GMT for Nab (Table 1) WT: 640 (95% CI 320-1280) Alpha: 40 (95% CI 17.5-40) Beta: 20 (95% CI 10-40) Delta: 10 (95% CI 10-40) % NaB positivity WT: 98.33% Alpha: 75% Beta: 70% Delta: 48.33% GMT IgG (s-1-RBD binding IgG WT: 774.48 (95% CI 607.22-987.82) Alpha: 44.64 (95% CI 35-56.94) Beta: 35.03 (95% CI 27.46-44.68) Delta: 24.48 (95% CI 19.2-31.23) Fold-reduction: 3.0

Appendix 8. Characteristics and Results of Studies on Duration of Protection after CoronaVac Immunization

Study ID	Population	N	Vaccine Regimen	Outcomes / Results
Jantarabenjakul (Thailand) Preprint	Healthcare workers 18 years old and above with no history of COVID-19: - SV grp (21 to 28 days interval) (N = 94) - AZ grp (8 to 10 weeks interval) (N = 91) COVID-19 group (hospitalized March to April 2020) (N = 111) - Mild (N = 58) - COVID-19 pneumonia (N = 53)	94 91 111 58 53	SV grp: 4 & 12 weeks [IQR 23 (22-24) days] AZ grp: 4 weeks [IQR 19 (16-21) days] COVID-19 grp: 4±2 weeks after dx [IQR 35 (30-38) days]	Neutralizing Ab (blocking ELISA) (% inhibition) (cut-off ≥68%inhibition) • SV (4 weeks after): 77.0 (58.5-87.9) (no significant difference in age; p=0.18); 57/94 (60.6%) [≥68%inhibition] - 20-30 y/o: 83.2% (58.5-87.9) - 31-50 y/o: 77.3% (59.1-87.5) - 51-60 y/o: 73.4% (49.3-83.2) • SV (12 weeks after): 38.7 (22.1-55.7) (significant decrease from 4 weeks; p<0.001); 11/90 (12.2%) - 20-30 y/o: 40% (31.7-66) - 31-50 y/o: 43.7% (21.2-57.4) - 51-60 y/o: 32.4% (15.3-43.3) • AZ: 90.4 (75.2-96.2) %inhibition; 78/91 (85.7%) - 20-30 y/o: 88.2% (76.6-95.8) - 31-50 y/o: 95.8% (75.6-97.9) - 51-60 y/o: 90.2% (72.5-95.3) • mild COVID-19: 80.8 (61.5-92.1) • COVID-19 pneumonia: 94.5 (88.1-95.8) ➡ the SV group had a level of SARS-CoV-2 neutralizing antibodies comparable to the mild COVID-19 group. In contrast, the AZ group had a higher level of neutralizing antibodies comparable to the COVID-19 pneumonia group

				SARS-CoV-2 total Ab (ECLIA) [1 U/ml = 0.972 BAU/ml] (cut-off ≥132 U/ ml) • SV: 188.6 (115.6-312.2) U/ml (no significant difference in age; p=0.28); 194 (118.9-321.2) BAU/ml [67/94 (71.3%)] - 20-30 y/o: 275.8 U/ml; 283.7 (104-596.9) BAU/ml - 31-50 y/o: 193 (118.9-290.4) BAU/ml - 51-60 y/o: 185.6 U/ml; 190.9 (133.6-294.5) BAU/ml • AZ: 794.2 (497.9-1383.0) U/ml; 817.1 (512.2-1422.8) BAU/ml [91/91(100%)] - 20-30 y/o: 599.8 (472.9-889.6) BAU/ml - 31-50 y/o: 960.5 (531.1-2005.1) BAU/ml - 51-60 y/o: 865.4 (512.2-1704.7) BAU/ml • mild COVID-19: 66.9 (19.7-170.2) U/ml • COVID-19 pneumonia: 794.2 (497.9-1383) U/ ml • the anti-SARS-CoV-2 total antibodies of the AZ group were significantly higher than the COVID-19 pneumonia group (P<0.001) • There was a significant decrease in neutralizing antibody levels from 4 weeks to 12 weeks for Sinovac, which was seen in the 3 age groups

Kara (Turkey) Preprint	Healthcare workers 45 (16.5%) had previous COVID-19 5 (1.8%) infected after the 2nd dose (mild)	272	1 month & 3 months	Anti-S-RBD-IgG (CLIA) (AU/ml) [significant decrease, p<0.001] 1 month vs 3 months • median: 29.14 vs. 10.46 • mean: 44.60 vs. 27.80 Seroconversion rates [significant decease, p=0.004] 1 vs 3 months 1 month vs 3 months: 98.2% vs 97.8% total anti-spike/anti-nucleocapsid-IgG antibody (CLIA) [significant decrease, p<0.001], 1 month vs. 3 months • median: 19.80 vs. 6.16 • mean: 36.95 vs. 30.55 Seroconversion rates [not significant decrease, p=1.000] 1 month vs 3 months: 93% vs. 87.3% • antibody concentrations were statistically significantly decreased at the third month among those with no previous infection, but with the median concentrations never falling below the reactive level.
Liao (China)	adult volunteers aged 18–59 years	158	2 doses (3ug in an Al(OH)3) adjuvant 14 or 28 days apart	Neutralizing antibody peaked at day 28 after the second dose and subsequently exhibited a gradual declining tendency Antibody positivity rates: 0/14 dosing at 6 months : Anti-S IgG declined to 52.1% Anti-N IgG declined to 50.7% 0/28 dosing at 6 months Anti-S IgG: declined to 52.4% Anti-N IgG: declined to 45.3%

Palacios (Brazil) Preprint	Healthy health professionals caring for COVID patients (N=12396); only 5% were 60yrs and older 55.9% with comorbidities (n = 9823) Excluded pregnant, previous COVID-19 vaccines, acute symptoms of COVID	CoronaVac (n=6195) - safety (n= 4953) - efficacy Placebo (n=6201) -safety (n=4870) - efficacy	CoronaVac 3.0ug, 14 days apart	VE 28 days after 1st dose: 42.5% (32.9-50.7) 56 days after 1st dose: 60.4% (56.5-63.9) 98 days after 1st dose: 52.5% (55.1-99.2)
Cerquiera-Silva (Brazil)	General population (N – 75,919, 840) enrolled 25,752,013 Excluded ; vaccinated besides ChAdOx1 or CoronaVac; inconsistent records; confirmed COVID-19 before vaccine administration; missing data for covariates	General population (N – 75,919, 840) enrolled 25,752,013	CoronaVac, 2 doses, median interval = 27 days (IQR 21-28)	79 years and younger: decreased in (and maintenance of low) hospitalization incidence up to 84 days 80-89 and >/= 90 years: decreased incidence 28 days (lowest) Incidence increased afterward but were lower than those observed during the reference period or for partially vaccinated individuals.

Appendix Table 9. Characteristics of Studies on the Effect of CoronaVac booster dose

STUDY ID (Country)	STUDY DESIGN	STUDY POPULATION	INTERVENTION / EXPOSURE	CONTROL	FOLLOW UP	OUTCOMES
Wu (China) Preprint	RCT Randomized – code by a statistician, assignment in sequence, Participant, investigator, lab staff masked to group allocation Balanced drop out with reason (in original trial), Balanced drop out from original study to current trial but not clear reason for drop out	Healthy adults >/=60 years old, participants in the Phase 2 trial N = 303	3rd dose at 8 months or more after V2 1.5ug N = 85 3ug N = 90 6ug N = 81	Placebo = 47	28 days	GMT of NAb to live SARS-CoV-2 on D180 after V2 and 7, 14, 28 days after V3 Seropositivity rate (cut off at 1/8) Safety: local and systemic adverse event rates(days 0-7), spontaneous recording of adverse event rate till day 28 Serious adverse events till 6 months after V2
Pan (China) Preprint	RCT Randomized Sealed envelopes Triple blinded	Adults 18 to 59 years old N = 504	3ug and 6ug, 14 or 28 day interval, V3 at 28 days after V2	Placebo, 14 or 28 day interval, Placebo V3 at 6mos after V2	Planned 1 year for safety Actual follow up 6 months	GMT of NAbs to live SARS CoV 2 Seropositivity / seroconversion At 6 months after V2, 14 days after V3 and 6 months after V3 Reactogenicity Serious adverse event
Liao (China)	Case series	Adult volunteers aged 18 to 59 years who received third dose N = 76	3ug, 14 or 28 day interval, V3 at an unspecified time	NA (self-control at D2)		Both the 0/14 and 0/28 schedules showed seroconversion of 100% neutralizing antibody with GMTs of 57.9 and 36.8
Wang (China)	subgroup analysis of Phase I/II	16 to 69 years old	3rd dose 6 months after 2nd (schedule: months 0, 1, and 7) N = 38 volunteers	22 COVID-19 convalescents 6 health participants	4 weeks after the final vaccination 1.3 months after infection (convalescents)	After the 3rd dose, there was robust recall humoral response to efficiently neutralize circulating variants NAb titer surged by ~8-fold (from 7 to 53) at week 1, peaked by ~25-fold increase (up to 177) at week 2

						after the 3rd-booster and slowly decreased over time 3rd dose had minimal reduction in neutralization titers against VOCs when compared to 2 doses
Li M (China)	RCT IWRS Observer blinded	Heathy 18 to 59 years old primed with 2 doses of CoronaVac	Ad5 at 3-6 months after V2 (N = 50)	3rd dose of CoronaVac 3-6 months after V2 (N = 51)	14 and 28 days after 28 days (AE)	Neutralizing antibodies (cytopathic effect (CPE)-based microneutralization assay) <u>14 days GMT</u> 3 doses (Ad5): 197.4 (167.7, 232.4) 3 doses (SV): 33.6 (28.3, 39.8) p<0.001 <u>28 days GMT</u> 3 doses (Ad5): 150.3 (128.6, 175.7) 3 doses (SV): 35.3 (29.4, 42.4) p<0.001 Seropositivity (titer ≥1:4) <u>14 days</u> 3 doses (Ad5): 100.0 (1.0, 1.0) 3 doses (SV): 100.0 (1.0, 1.0) p<0.001 28 days 3 doses (Ad5): 100.0 (1.0, 1.0) 3 doses (SV): 99.0 (0.9, 1.0) p<0.001 <u>SAFETY (28 days)</u> Local: 3 doses (Ad5): 28 (29.2%) 3 doses (SV): 3 (2.9%) Systemic: 3 doses (AD5): 14 (14.6%) 3 doses (SV): 3 (2.9%)

Appendix 10. Details of Immunologic Results of Studies on CoronaVac booster dose

GEOMETRIC MEAN TITERS									
Study	Vaccine (Dose)	Units	3rd dose				No 3rd dose / 2nd dose only		
			N	Interval from D2	Testing Interval from D3	GMT (95% CI)	N	Testing Interval from D2	GMT (95% CI)
Neutralizing antibody titers (GMT)									
Wu	CoronaVac (3µg)	Mean antibody titer	86	8m	28d	342.8 (266.4-441.1)	43	28d	2.0 (2.0-2.1)
Pan	CoronaVac (3µg, D0, 28, 56)	Mean antibody titer	53	28d	28d	49.7 (39.9-61.9)	59	28d	39.6 (30.1-52.2)
% POSITIVITY									
Study	Vaccine (Dose)	Units	3rd dose				No 3rd dose / 2nd dose only		
			N	Interval from D2	Testing Interval from D3	% (%95 CI)	N	Testing Interval from D2	% (%95 CI)
% Neutralizing antibody positivity									
Wu	CoronaVac (3µg)	Number of seropositives	86	8m	28d	100% (95.80-100.00)	43	28d	0 (0%) (0.00-8.22)
Pan	CoronaVac (3µg, D0, 28, 56)	Seropositivity rate	53	28d	28d	98.1% (89.9-100.0)	59	28d	94.9% (85.9-98.9)
Pan	CoronaVac (3µg, D0, 28, 208)	Seropositivity rate	49	180d	28d	100% (92.7-100.0)	56	28d	100% (93.8-100.0)

Appendix 11. Details of Safety Results of Studies on CoronaVac booster dose

Safety Outcome Parameter	Study	Follow up	3rd Dose	2nd Dose
			n/N (%)	n/N (%)
Local adverse reaction (within 28 days)	Wu	28d	3/90 (3.33%)	1/47 (2.13%)
	Pan (S1)	28d	3/55 (5.45%)	0/26 (0%)
	Pan (S2)	28d	8/55 (14.55%)	2/30 (6.67%)
	Pan (S3)	28d	2/54 (3.7%)	0/26 (0%)
	Pan (S4)	28d	8/52 (15.38%)	1/28 (3.57%)
Systemic adverse reaction (within 28 days)	Wu	28d	2/90 (2.22%)	2/47 (4.26%)
Any adverse event (within 28 days)	Wu	28d	5/90 (5.56%)	2/47 (4.26%)
	Pan (S1)	28d	5/55 (9.09%)	0/30 (0%)
	Pan (S2)	28d	10/55 (18.18%)	3/30 (10%)
	Pan (S3)	28d	3/54 (5.56%)	0/30 (0%)
	Pan (S4)	28d	8/52 (15.38%)	2/28 (7.14%)
Any adverse event (within one year)	na	na	na	na
Severe adverse event	na	na	na	na
Serious adverse event	Wu	28d	5/101 (4.95%)	2/49 (4.08%)
	Pan	6m	1/60 (1.67%)	0/30 (0%)
	Pan	6m	0/60 (0%)	0/30 (0%)
Related serious adverse event	na	na	na	na
Deaths	na	na	na	na

Appendix 12. Characteristics of Ongoing Trials

NCT Number	Title	Status	Age	Phases	Study Type	Study Designs	Completion Date	URL
NCT04801667	Evaluate the Impact, Safety, Tolerability and Immunogenicity of the Coronavac Vaccine in Kidney Transplant Recipients	Active, not recruiting	18 Years to 100 Years Â (Adult, Older Adult)	Phase 4	Interventional	Allocation: N/A|Intervention Model: Single Group Assignment|Masking: None (Open Label)|Primary Purpose: Health Services Research	1-Mar-23	https://ClinicalTrials.gov/show/NCT04801667
NCT04754698	COVID-19 CoronaVac in Patients With Autoimmune Rheumatic Diseases and HIV/AIDS	Active, not recruiting	18 Years and older Â (Adult, Older Adult)	Phase 4	Interventional	Allocation: Non-Randomized|Intervention Model: Parallel Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	31-May-22	https://ClinicalTrials.gov/show/NCT04754698
NCT04854408	Evaluation of the Effect of Coronavac Vaccine (Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 Vaccine) on Healthcare Workers' Menstrual Patterns	Completed	18 Years to 45 Years Â (Adult)		Observational	Observational Model: Other|Time Perspective: Prospective	9-May-21	https://ClinicalTrials.gov/show/NCT04854408
NCT04789356	Effectiveness of the Adsorbed Vaccine COVID-19 (Coronavac) Among Education and Public Safety Workers With Risk Factors for Severity	Active, not recruiting	18 Years to 49 Years Â (Adult)	Phase 4	Interventional	Allocation: Non-Randomized|Intervention Model: Parallel Assignment|Masking: None (Open Label)|Primary Purpose: Treatment	Mar-22	https://ClinicalTrials.gov/show/NCT04789356
NCT04942405	Efficacy, Immunogenicity, and Safety of the Inactivated COVID-19 Vaccine (TURKOVAC) Versus the CoronaVac Vaccine	Recruiting	18 Years to 55 Years Â (Adult)	Phase 3	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Triple (Participant, Care Provider, Investigator)|Primary Purpose: Prevention	31-Mar-23	https://ClinicalTrials.gov/show/NCT04942405
NCT04974164	Effectiveness of COVID-19 Vaccine for Prevention of COVID-19 in the Dominican Republic	Not yet recruiting	18 Years and older Â (Adult, Older Adult)		Observational	Observational Model: Case-Control|Time Perspective: Prospective	11-Apr-22	https://ClinicalTrials.gov/show/NCT04974164
NCT04756830	A Study to Assess the Safety and Immunogenicity of the Coronavac Vaccine Against COVID-19	Active, not recruiting	18 Years and older Â (Adult, Older Adult)	Phase 4	Interventional	Allocation: N/A|Intervention Model: Single Group Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	Jun-23	https://ClinicalTrials.gov/show/NCT04756830
NCT04765215	Investigation of the Effectiveness of CoronaVac Vaccine in Cancer Patients With Active Chemotherapy and Comparison With Healthy People.	Active, not recruiting	18 Years to 90 Years Â (Adult, Older Adult)		Observational	Observational Model: Case-Control|Time Perspective: Prospective	31-Mar-22	https://ClinicalTrials.gov/show/NCT04765215

NCT Number	Title	Status	Age	Phases	Study Type	Study Designs	Completion Date	URL
NCT04884685	Safety of an Inactivated SARS-CoV-2 Vaccine (CoronaVac) in Children and Adolescents	Active, not recruiting	3 Years to 17 Years Â (Child)	Phase 2	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Double (Participant, Investigator)|Primary Purpose: Prevention	3-Jan-22	https://ClinicalTrials.gov/show/NCT04884685
NCT04894227	Lot-to-lot Consistency of an Inactivated SARS-CoV-2 Vaccine for Prevention of COVID-19 in Healthy Adults	Active, not recruiting	26 Years to 45 Years Â (Adult)	Phase 4	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Double (Participant, Investigator)|Primary Purpose: Prevention	30-Nov-21	https://ClinicalTrials.gov/show/NCT04894227
NCT04979949	Booster Vaccination Against SARS-CoV-2	Recruiting	18 Years to 60 Years Â (Adult)	Phase 2	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Triple (Participant, Care Provider, Investigator)|Primary Purpose: Prevention	12-Jul-22	https://ClinicalTrials.gov/show/NCT04979949
NCT04651790	Efficacy, Safety, and Immunogenicity of Two Vaccination Schedules of an Inactivated Vaccine Against COVID-19 in Adults	Recruiting	18 Years and older Â (Adult, Older Adult)	Phase 3	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	Mar-22	https://ClinicalTrials.gov/show/NCT04651790
NCT04800133	Covid-19 Vaccination in Adolescents	Recruiting	11 Years to 100 Years Â (Child, Adult, Older Adult)	Phase 2	Interventional	Allocation: Non-Randomized|Intervention Model: Parallel Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	31-Mar-25	https://ClinicalTrials.gov/show/NCT04800133
NCT04898946	Serological Response to mRNA and Inactivated COVID-19 Vaccine in Health Care Workers in Hong Kong	Recruiting	18 Years and older Â (Adult, Older Adult)		Observational	Observational Model: Cohort|Time Perspective: Prospective	8-Mar-22	https://ClinicalTrials.gov/show/NCT04898946
NCT04611243	Lung Function, Exercise Capacity, and Serology Responses in Patients With COVID-19	Recruiting	18 Years and older Â (Adult, Older Adult)		Observational	Observational Model: Cohort|Time Perspective: Prospective	17-Feb-25	https://ClinicalTrials.gov/show/NCT04611243
NCT04953325	Immunogenicity and Safety of an Inactivated COVID-19 Vaccine	Recruiting	18 Years and older Â (Adult, Older Adult)	Phase 4	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	31-Jan-22	https://ClinicalTrials.gov/show/NCT04953325

NCT Number	Title	Status	Age	Phases	Study Type	Study Designs	Completion Date	URL
NCT04888793	Immune Response to Anti COVID-19 Vaccine in Immunocompromised Patients: a Cohort Study	Recruiting	18 Years and older Â (Adult, Older Adult)		Observational	Observational Model: Cohort|Time Perspective: Prospective	20-Dec-21	https://ClinicalTrials.gov/show/NCT04888793
NCT04992208	Safety of an Inactivated SARS-CoV-2 Vaccine for Prevention of COVID-19 in Children and Adolescents	Not yet recruiting	3 Years to 17 Years Â (Child)	Phase 4	Interventional	Allocation: N/A|Intervention Model: Single Group Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	25-Dec-22	https://ClinicalTrials.gov/show/NCT04992208
NCT04911790	Safety of an Inactivated SARS-CoV-2 Vaccine for Prevention of COVID-19 in Adults	Recruiting	18 Years and older Â (Adult, Older Adult)	Phase 4	Interventional	Allocation: N/A|Intervention Model: Single Group Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	31-Dec-22	https://ClinicalTrials.gov/show/NCT04911790
NCT04962308	Clinical Trial of Inactivated SARS-CoV-2 Vaccine for Prevention of COVID-19 in Healthy Adults	Recruiting	18 Years to 59 Years Â (Adult)	Phase 4	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	19-Dec-21	https://ClinicalTrials.gov/show/NCT04962308
NCT04751721	Oxidative Stress Parameters, Trace Element and Quality of Life in Women Before and After Covid-19 Vaccines	Not yet recruiting	35 Years to 65 Years Â (Adult, Older Adult)	Not Applicable	Interventional	Allocation: N/A|Intervention Model: Single Group Assignment|Masking: None (Open Label)|Primary Purpose: Screening	Apr-21	https://ClinicalTrials.gov/show/NCT04751721
NCT04992260	Efficacy, Immunogenicity and Safety of COVID-19 Vaccine , Inactivated in Children and Adolescents	Not yet recruiting	6 Months to 17 Years Â (Child)	Phase 3	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Double (Participant, Investigator)|Primary Purpose: Prevention	1-Apr-23	https://ClinicalTrials.gov/show/NCT04992260
NCT04747821	An Effectiveness Study of the Sinovac's Adsorbed COVID-19 (Inactivated) Vaccine	Active, not recruiting	18 Years and older Â (Adult, Older Adult)	Phase 4	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	Feb-22	https://ClinicalTrials.gov/show/NCT04747821
NCT04456595	Clinical Trial of Efficacy and Safety of Sinovac's Adsorbed COVID-19 (Inactivated) Vaccine in Healthcare Professionals	Active, not recruiting	18 Years and older Â (Adult, Older Adult)	Phase 3	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)|Primary Purpose: Prevention	Feb-22	https://ClinicalTrials.gov/show/NCT04456595
NCT04751695	Oxidative Stress Parameters, Trace Element and Quality of Life in Men Before and After Covid-19 Vaccines	Not yet recruiting	35 Years to 65 Years Â (Adult, Older Adult)	Not Applicable	Interventional	Allocation: N/A|Intervention Model: Single Group Assignment|Masking: None (Open Label)|Primary Purpose: Screening	Apr-21	https://ClinicalTrials.gov/show/NCT04751695

NCT Number	Title	Status	Age	Phases	Study Type	Study Designs	Completion Date	URL
NCT05026879	Adverse Events Report of Inactivated COVID-19 Vaccine	Completed	18 Years and older Â (Adult, Older Adult)		Observational	Observational Model: Cohort|Time Perspective: Cross-Sectional	14-Mar-21	https://ClinicalTrials.gov/show/NCT05026879
NCT04582344	Clinical Trial For SARS-CoV-2 Vaccine (COVID-19)	Active, not recruiting	18 Years to 59 Years Â (Adult)	Phase 3	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Triple (Participant, Care Provider, Investigator)|Primary Purpose: Prevention	15-Apr-22	https://ClinicalTrials.gov/show/NCT04582344
NCT04952727	Study on Sequential Immunization of Inactivated COVID-19 Vaccine and Recombinant COVID-19 Vaccine (Ad5 Vector)	Not yet recruiting	60 Years and older Â (Adult, Older Adult)	Phase 4	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Triple (Participant, Investigator, Outcomes Assessor)|Primary Purpose: Prevention	2-Mar-22	https://ClinicalTrials.gov/show/NCT04952727
NCT04892459	Study on Sequential Immunization of Inactivated SARS-CoV-2 Vaccine and Recombinant SARS-CoV-2 Vaccine (Ad5 Vector)	Active, not recruiting	18 Years to 59 Years Â (Adult)	Phase 4	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Triple (Participant, Investigator, Outcomes Assessor)|Primary Purpose: Prevention	25-Dec-21	https://ClinicalTrials.gov/show/NCT04892459
NCT04992182	Reactogenicity, Safety, and Immunogenicity of Covid-19 Vaccine Booster	Active, not recruiting	18 Years and older Â (Adult, Older Adult)	Phase 2	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Double (Participant, Investigator)|Primary Purpose: Treatment	30-Jun-22	https://ClinicalTrials.gov/show/NCT04992182
NCT04845048	Active Pharmacovigilance Study of Adsorbed COVID-19 (Inactivated) Vaccine	Not yet recruiting	18 Years and older Â (Adult, Older Adult)		Observational	Observational Model: Cohort|Time Perspective: Prospective	Nov-21	https://ClinicalTrials.gov/show/NCT04845048
NCT04775069	Antibody Response to COVID-19 Vaccines in Liver Disease Patients	Recruiting	18 Years and older Â (Adult, Older Adult)	Phase 4	Interventional	Allocation: Non-Randomized|Intervention Model: Parallel Assignment|Masking: None (Open Label)|Primary Purpose: Prevention	31-Mar-22	https://ClinicalTrials.gov/show/NCT04775069
NCT05033834	Covid-19 Infection in After Vaccination	Not yet recruiting	18 Years to 80 Years Â (Adult, Older Adult)		Observational	Observational Model: Cohort|Time Perspective: Prospective	31-Dec-22	https://ClinicalTrials.gov/show/NCT05033834
NCT04834869	COVID-19 Vaccines Safety Tracking (CoVaST)	Recruiting	18 Years and older Â (Adult, Older Adult)		Observational	Observational Model: Other|Time Perspective: Prospective	31-Jan-22	https://ClinicalTrials.gov/show/NCT04834869
NCT05029245	IntraDermal Versus Intramuscular ComirnatyÂ® Efficacy Study	Not yet recruiting	18 Years and older Â (Adult, Older Adult)	Phase 3	Interventional	Allocation: Randomized|Intervention Model: Parallel Assignment|Masking: Single (Participant)|Primary Purpose: Prevention	31-Oct-22	https://ClinicalTrials.gov/show/NCT05029245