Mini-Cat Draft_Johnson

Clinical Question: An 84yo Chinese F residing in a skilled nursing facility in Chinatown, NYC has recently been decannulated and is on room air after being hospitalized for severe COVID-19 infection in which she had to be intubated. She is very scared of getting COVID-19 again and requests to be vaccinated again. She is originally from China and received the inactivated virus vaccine Sinovac last dose Nov 2021. The physician working at the long-term care facility states that he has a lot of residents who received the Sinovac-CoronaVac vaccine (back home in China) versus Pfizer or Moderna. He is curious to know how they compare in terms of protection from a severe covid-19 infections.

PICO Question:
Is there a difference in efficacy in reducing COVID-19 severity between mRNA vaccines (Pfizer/Moderna) and inactivated virus vaccine (Sinovac-CoronaVac) in adults?

P = Adults
I = Sinovac-CoronaVac vaccine
C = Pfizer/Moderna vaccine
O = Severe Covid infection

The preferred study type: randomized controlled trials (RCTs) or Systematic Reviews of RCTs

Search Strategy:

Database	Filter	Terms Searched	Articles Returned
PubMed	Full Text	Sinovac-CoronaVac effectiveness; mRNA vs. inactivated virus severe covid; incidence of severe covid after inactivated vaccine	13 results
Google Scholar	Full Text/ Review article/2021	Sinovac-CoronaVac effectiveness; mRNA vs. inactivated virus severe covid; incidence of severe covid after inactivated vaccine	185 result
Science Direct	Research articles/2020	Sinovac-CoronaVac effectiveness; mRNA vs. inactivated virus severe covid; incidence of severe covid after inactivated vaccine	226 results

I chose to use both names in each of my searches as I did not want articles only looking at one vaccine and not the other. I found the first page of science direct to be a great yield of the specific type of studies I was looking for and is how I found article 4 and 5.

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Articles 1-3 I found via pubmed. The first article included a lot of great internal citations which I explored and found article 2.

Articles chosen for inclusion:

Article 1:

Citation: Lau CS, Oh MLH, Phua SK, et al. Kinetics of the Neutralizing and Spike SARS-CoV-2 Antibodies following the Sinovac Inactivated Virus Vaccine Compared to the Pfizer mRNA Vaccine in Singapore. Antibodies (Basel). 2022;11(2):38. Published 2022 May 27. doi:10.3390/antib11020038
Abstract: Purpose: Comparison of early total spike antibody (S-Ab) and neutralizing antibody (N-Ab) responses to two vaccines. Methods: We studied 96 Pfizer and 34 Sinovac vaccinees over a 14-month period from January 2021 to February 2022. All vaccinees received three doses of one type of vaccine. Antibody levels (Roche Elecsys total S-Ab and the Snibe N-Ab) were tested 10 days after the first dose, 20 days after the second dose, and 20 days after the booster dose. Results: At all time points, the mRNA vaccine generated higher S-Ab and N-Ab responses than the inactivated virus vaccine (S-Ab: first dose 2.48 vs. 0.4 BAU/mL, second dose 2174 vs. 98 BAU/mL, third dose 15,004 vs. 525 BAU/mL; N-Ab: first dose 0.05 vs. 0.02 μg/mL, second dose 3.48 vs. 0.38 μg/mL, third dose 19.8 vs. 0.89 μg/mL). mRNA vaccine recipients had a 6.2/22.2/28.6-fold higher S-Ab and 2.5/9.2/22.2-fold higher N-Ab response than inactivated virus vaccine recipients after the first/second/third inoculations, respectively. Mann-Whitney U analysis confirmed the significant difference in S-Ab and N-Ab titers between vaccination groups at each time point. Conclusions: The mRNA vaccines generated a more robust S-Ab and N-Ab response than the inactivated virus vaccine at all time points after the first, second, and third vaccinations.
Reason for selection: This cohort study compares Pfizer and Sinovac effectiveness and risk of severe disease. While the study specifically looks at the immune reaction from the vaccine measuring the amount of antibodies produced to the spike protein (called anti-SARS-CoV-2 antibodies) and the neutralizing antibody (called anti-Omicron antibodies). However, in the introduction the systematic review discussing the effectiveness and risk of severe disease for each vaccine is discussed. And although there is no precise level of S-Ab or N-Ab that is considered definitively protective, several studies have shown that higher levels of antibodies correlate well with protection against severe SARS-CoV-2 infection. This study did not look at older populations but did mention the risk of immunosuppressed patients.

Article 2:

Citation:

Khandker SS, Godman B, Jawad MI, et al. A Systematic Review on COVID-19 Vaccine Strategies, Their Effectiveness, and Issues. *Vaccines (Basel)*. 2021;9(12):1387. Published 2021 Nov 24. doi:10.3390/vaccines9121387
Abstract: Background: COVID-19 vaccines are indispensable, with the number of cases and mortality still rising, and currently no medicines are routinely available for reducing morbidity and mortality, apart from dexamethasone, although others are being trialed and launched. To date, only a limited number of vaccines have been given emergency use authorization by the US Food and Drug Administration and the European Medicines Agency. Purpose: To systematically review the existing vaccine candidates and investigate their safety, efficacy, immunogenicity, unwanted events, and limitations Methods: The review was undertaken by searching online databases, i.e., Google Scholar, PubMed, and ScienceDirect, with finally 59 studies selected. Our findings showed several types of vaccine candidates with different strategies against SARS-CoV-2, including inactivated, mRNA-based, recombinant, and nanoparticle-based vaccines, are being developed and launched. Results: We have compared these vaccines in terms of their efficacy, side effects, and seroconversion based on data reported in the literature. Conclusion: We found mRNA vaccines appeared to have better efficacy, and inactivated ones had fewer side effects and similar seroconversion in all types of vaccines. Overall, global variant surveillance and systematic tweaking of vaccines, coupled with the evaluation and administering vaccines with the same or different technology in successive doses along with homologous and heterologous prime-booster strategy, have become essential to impede the pandemic. Their effectiveness appreciably outweighs any concerns with any adverse events.
Reason for selection: This study is a systematic review which is the highest level of evidence and looked at the difference in efficacy of mRNA vaccines versus inactivated vaccine. This systematic review looked at 59 studies and looked at prevention of OCVID instead of just looking at antibody responses.

Article 3:

Citation: 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. Published 2021 Nov 23. doi:10.1038/s41598-021-02321-z
Abstract: Background: New Coronavirus Disease 2019 (COVID-19) vaccines are available to prevent the ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. Purpose: Comparison of the efficacy of new COVID-19 vaccines to prevent symptomatic and severe disease in the adult population and to prevent symptomatic COVID-19 among the elderly.

Methods: Leading medical databases were searched until August 30, 2021. Published phase 3 randomized controlled trials (RCTs) evaluated efficacy of the vaccine to prevent symptomatic and sever COVID-19 in adults were included. Two reviewers independently evaluated the literature search results and independently extracted summary data. The risk of bias was evaluated using the Cochrane Risk of Bias Assessment Tool. We performed a network meta-analysis (NMA) according to PRISMA-NMA 2015 to pool indirect comparisons between different vaccines regarding their relative efficacy. The primary outcomes were the efficacy of the vaccine against symptomatic COVID-19 in adults (PROSPERO registration number: CRD42021235364). Above 200,000 adult participants from eight phase 3 RCTs were included in NMA, of whom 52% received the intervention (active COVID-19 vaccine)
Results: While each of nine vaccines was tested in the unique clinical trial as compared to control, based on indirect comparison, BNT162b2 and mRNA-1273 vaccines were ranked with the highest probability of efficacy against symptomatic COVID-19 (P-scores 0.952 and 0.843, respectively), followed by Gam-COVID-Vac (P-score 0.782), NVX-CoV23730 (P-score 0.700), CoronaVac (P-score 0.570), BN02 (P-score 0.428), WIV04 (P-score 0.327), and Ad26.COV2.S (P-score 0.198). No statistically significant difference was seen in the ability of the vaccines to prevent symptomatic disease in the elderly population. No vaccine was statistically significantly associated with a decreased risk for severe COVID-19 than other vaccines, although mRNA-1273 and Gam-COVID-Vac have the highest P-scores (0.899 and 0.816, respectively), indicating greater protection against severe disease than other vaccines.
Conclusion: In our indirect comparison, the BNT162b2 and mRNA-1273 vaccines, which use mRNA technology, were associated with the highest efficacy to prevent symptomatic COVID-19 compared to other vaccines. This finding may have importance when deciding which vaccine to use, together with other important factors as availability of the vaccines, costs, logistics, side effects, and patient acceptability.

Reason for selection: This systematic review and network meta-analysis combined previous meta-analysis done comparing four vaccines and used network analysis to compare efficacy of new COVID-19 vaccines to prevent symptomatic and severe disease in the adult population and to prevent symptomatic COVID-19 among the elderly. Using the network methods enables the evaluation of multiple treatments in a single analysis. The systematic review following the PRISMA 2020 framework guidelines. This study also had a subcategory of effectiveness in preventing infection in age 60 and above. When the indirect comparison between the vaccines was performed, BNT162b2 was ranked with the highest efficacy against symptomatic COVID-19.

Article 4:

Citation:
Paternina-Caicedo A, Jit M, Alvis-Guzmán N, et al. Effectiveness of CoronaVac and BNT162b2 COVID-19 mass vaccination in Colombia: A population-based cohort study. Lancet Reg Health Am. 2022;12:100296. doi:10.1016/j.lana.2022.100296

Background: In February 2021, Colombia began mass vaccination against COVID-19 using mainly BNT162b2 and CoronaVac vaccines. We aimed to estimate vaccine

effectiveness (VE) to prevent COVID-19 symptomatic cases, hospitalization, critical care admission, and deaths in a cohort of 796,072 insured subjects older than 40 years in northern Colombia, a setting with a high SARS-CoV-2 transmission.

Methods: We identified individuals vaccinated between March 1st of 2021 and August 15th of 2021. We included symptomatic cases, hospitalizations, critical care admissions, and deaths in patients with confirmed COVID-19 as main outcomes. We calculated VE for each outcome from the hazard ratio in Cox proportionally hazards regressions (adjusted by age, sex, place of residence, diabetes, human immunodeficiency virus, cancer, hypertension, tuberculosis, neurological diseases, and chronic renal disease), with 95% confidence intervals (CI).

Findings**:** A total of 719,735 insured participants of 40 and more years were followed. We found 21,545 laboratory-confirmed symptomatic COVID-19 among unvaccinated population, along with 2874 hospitalizations, 1061 critical care admissions, and 1329 deaths, for a rate of 207.2 per million person-days, 27.1 per million person-days, 10.0 per million person-days, and 12.5 per million person-days, respectively. We found CoronaVac was not effective for any outcome in subjects above 80 years old; but for people 40-79 years of age, we found two doses of CoronaVac reduced hospitalization (33.1%; 95% CI, 14.5-47.7), critical care admission (47.2%; 95% CI, 18.5-65.8), and death (55.7%; 95% CI, 32.5-70.0). We found BNT162b2 was effective for all outcomes in the entire population of subjects above 40 years of age, significantly declining for subjects ≥80 years.

Interpretation: Two doses of either CoronaVac in population between 40 and 79 years of age, or BNT162b2 among vaccinated above 40 years old significantly reduced deaths of confirmed COVID-19 in a cohort of individuals from Colombia. Vaccine effectiveness for CoronaVac and BNT162b2 declined with increasing age.

Reason for selection: This study was chosen due to the it's large sample size of 719,735 and the direct comparison of BNT162b2 (Pfizer vaccine) and CoronaVac effectiveness. This study also included an age breakdown and an emphasis on the significant declining efficacy of Corovac for subjects >80 years old. This study also looked at effectiveness in terms of reducing hospitalization, critical care admission and death rather than antibodies.

Article 5:

Citation:
Premikha M, Chiew CJ, Wei WE, et al. Comparative Effectiveness of mRNA and Inactivated Whole Virus Vaccines against COVID-19 Infection and Severe Disease in Singapore [published online ahead of print, 2022 Apr 12]. Clin Infect Dis. 2022;ciac288. doi:10.1093/cid/ciac288

Abstract:
Background: Vaccination is a key strategy to reduce the spread and severity of coronavirus disease 2019 (COVID-19). Singapore launched its National Vaccination Program (NVP) for COVID-19 on 30 December 2020 with the Pfizer-BioNTech/Comirnaty vaccine (BNT162b2). The Moderna (mRNA-1273) and Sinovac-

CoronaVac vaccines were subsequently approved for use under the NVP on 3 February 2021 and 23 October 2021, respectively. COVID-19 cases in Singapore increased in September 2021,
driven by the more transmissible Delta variant first detected locally in May 2021 to a peak of over 5,000 cases a day. As several studies have suggested that mRNA vaccines have higher vaccine efficacy than non-mRNA vaccines.
Purpose: This study aims to compare the relative effectiveness of the 4 available vaccines in Singapore in preventing COVID-19 infection and severe disease
Methods: We examined the incidence of COVID-19 infection and severe disease during the study period from 1 October to 21 November 2021 among individuals aged 20 years and above who had received 2 doses under the NVP in Singapore. The age cutoff was selected in view of the minimum age (18 years) required to receive Moderna and Sinovac-CoronaVac under the NVP. Individuals who were partially vaccinated or boosted with a third dose or had a previous history of COVID-19 infection were excluded. (ICU), or death. Using a Poisson regression model, we estimated the incidence rate ratio (IRR) of confirmed COVID-19 infection and severe disease, controlling for age group, gender, ethnicity, residency status, and housing type (as a marker of socioeconomic status) as covariates. Vaccine effectiveness against severe disease for these 3 vaccines was estimated by assuming the vaccine effectiveness of Pfizer-BioNTech/ Comirnaty to be 90%, and then applying their respective IRRs and confidence intervals (CIs) for relative effectiveness observed in our study. Data were collected from official databases maintained by the Ministry of Health, Singapore, and analysis was performed using Stata Statistical Software release 17 (StataCorp LP, College Station, TX, USA).
Results: A total of 2,709,899 individuals within the 14- to 120-day period after being vaccinated with 2 doses were included in the study cohort, of whom 2,001,181 (74%) received Pfizer-BioNTech/ Comirnaty, 628,012 (23%) received Moderna, 60,407 (2%) received Sinovac-CoronaVac, and 20,299 (1%) received Sinopharm. A total of 107,220 individuals were confirmed by polymerase chain reaction (PCR) to be infected with COVID-19 over the study period, and 644 developed severe disease. After adjusting for age, gender, ethnicity, residency status, socioeconomic status, time since second dose, and daily infection rate, individuals vaccinated with Sinovac-CoronaVac were more likely to be infected (adjusted IRR, 2.37; 95% CI, 2.29– 2.46), and more likely to develop severe disease (adjusted IRR, 4.59; 95% CI, 3.25–6.48); individuals vaccinated with Sinopharm were also at higher risk of infection (adjusted IRR, 1.62; 95% CI, 1.43–1.85), while individuals vaccinated with Moderna were at lower risk of severe disease (adjusted IRR, 0.42; 95% CI, 0.25–0.70), compared with those who received Pfizer-BioNTech/Comirnaty

Reason for selection: I chose this study as it was done in Singapore where both of these vaccinations are given and due to the large sample size of >2 million people vaccinated. I liked their inclusion and exclusion criteria of two vaccinations and not a third booster being included. I do wish they had compared Pfizer and sinovac directly instead of assuming the vaccine effectiveness of Pfizer-BioNTech/ Comirnaty to be 90%, and then applying their respective IRRs and confidence intervals (CIs). This study was also interesting to me as it studied on the efficacy of these vaccines against delta variant.

Summary of the Evidence:

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/ studies, cohort definition etc.)	Outcome(s) studied	Key Findings	Limitations and Biases
1. Lau CS, Oh MLH, Phua SK, et al.	Cohort Study	96 Pfizer and 34 Sinovac vaccinees over a 14-month period from January 2021 to February 2022; All vaccinees received three doses of one type of vaccine	Antibody levels (Roche Elecsys total S-Ab and the Snibe N-Ab) were tested 10 days after the first dose, 20 days after the second dose, and 20 days after the booster dose.	At all time points, the mRNA vaccine generated higher S-Ab and N-Ab responses than the inactivated virus vaccine	There are no precise level of spike protein (called anti-SARS-CoV-2 antibodies) or neutralizing antibody (called anti-Omicron antibodies) that is considered definitively protective. However,several studies have shown that higher levels of antibodies correlate well with protection against severe SARS-CoV-2 infection.
2. Khandker SS, Godman B, Jawad	Systematic review	59 studies; data was extracted about each phase of trial for	Seroconversion was used to measure efficacy	The seroconversion and the neutralizing antibody	This systematic review was very dense and thorough in the

MI, et al.		inactivated, mRNA-based, recombinant, and nanoparticle-based vaccines		titers were observed in almost every trial for each vaccine candidate, where the seroconversion mainly started from days 7–14. In nearly every Phase 2 and 3 trial, the overall seroconversion rate was approximately 80–100% We have found that vaccines developed using mRNA technology show overall better efficacy than the other strategies. However, in general, conventional inactivated vaccines show less frequent side effects,	explanation and investigation of the science and trials of each vaccine. However, it was looking at the beginning trials and looking at not just efficacy but also the side effects and safety.

				but interestingly, all vaccines exhibit a similar level of humoral immunity	
3. Rotshild V, Hirsh-Raccah B, Miskin I, et al.	Systematic review and Meta-analysis	Over 200,000 adult participants from eight phase 3 RCTs were included	Symptomatic infection after vaccination Severe infection after vaccination	BNT162b2 and mRNA-1273 vaccines were ranked with the highest probability of efficacy against symptomatic COVID-19 (P-scores 0.952 and 0.843, respectively) No statistically significant difference was seen in the ability of the vaccines to prevent symptomatic disease in the elderly population mRNA-1273 and Gam-COVID-Vac have the	Only 52% of the individuals studied received the intervention (active COVID-19 vaccine) Another limitation is that they did not define what severe infection was like other studies

				highest P-scores (0.899 and 0.816, respectively), indicating greater protection against severe disease than other vaccines	
4. Paternina-Caicedo A, Jit M, Alvis-Guzmán N, et al	Cohort study	719,735 insured participants of 40 and more years were followed	symptomatic cases, hospitalizations, critical care admissions, and deaths in patients with confirmed COVID-19 compared which vaccine they had	CoronaVac was not effective for any outcome in subjects above 80 years old; but for people 40-79 years of age, we found two doses of CoronaVac reduced hospitalization (33.1%; 95% CI, 14.5−47.7), critical care admission (47.2%; 95% CI, 18.5−65.8), and death (55.7%; 95% CI, 32.5−70.0) BNT162b2 was effective for	This study followed unvaccinated and vaccinated. I still included it due to the significant reduction in protection it found for ages >80 for coronavac but the inclusion of those unvaccinated was not necessary for what I was looking at

				all outcomes in the entire population of subjects above 40 years of age, significantly declining for subjects ≥80 years.	
5. Premikha M, Chiew CJ, Wei WE, et al	Cohort study	2,709,899 individuals 18 years or older who had not previously had COVID; 2 weeks after completion of 2 doses of vaccine - 2,001,181 Pfizer - 628,012 Moderna - 60,407 Sinovac-CoronaVac - 20,299 Sinopharm	individuals were confirmed by polymerase chain reaction (PCR) Severe disease: defined as ever requiring oxygen supplementation in hospital, admission to an intensive care unit (ICU), or death.	individuals vaccinated with Sinovac-CoronaVac were more likely to be infected (adjusted IRR, 2.37; 95% CI, 2.29– 2.46), and more likely to develop severe disease (adjusted IRR, 4.59; 95% CI, 3.25–6.48)	Vaccine effectiveness against severe disease for these 3 vaccines was estimated by assuming the vaccine effectiveness of Pfizer-BioNTech to be 90% this information is being taken from systematic review but the actual individual in this cohort who for Pfizer were not directly compared to those who got CoronaVac

Conclusion(s):

1. The first article, a cohort study, specifically looked at early total spike antibody (S-Ab) and neutralizing antibody (N-Ab) responses between Pfizer and Sinovac.

At all time points, the mRNA vaccine generated higher S-Ab and N-Ab responses than the inactivated virus vaccine

2. The second article, the systematic review, investigated the safety, efficacy, immunogenicity, unwanted events, and limitations of inactivated, mRNA-based, recombinant, and nanoparticle-based vaccines. mRNA vaccines were found to have better efficacy, and inactivated ones had fewer side effects and similar seroconversion in all types of vaccines.
3. Article 3, a systematic review and meta-analysis, combined 8 phase 3 RCT and 200,000 adult participants with 52% vaccinated to see which vaccine led to more symptomatic COVID infection and severe COVID infection. BNT162b2 and mRNA-1273 vaccines were ranked with the highest probability of efficacy against symptomatic COVID-19. No vaccine was statistically significantly associated with a decreased risk for severe COVID-19 than other vaccines, although mRNA-1273 and Gam-COVID-Vac have the highest P-scores (0.899 and 0.816, respectively), indicating greater protection against severe disease than other vaccines.
4. Article 4, a cohort study, followed 719,735 insured participants of 40 and more years who had COVID infections. CoronaVac was not effective for any outcome in subjects above 80 years old; but for people 40-79 years of age, we found two doses of CoronaVac reduced hospitalization, critical care admission and death. BNT162b2 was effective for all outcomes in the entire population of subjects above 40 years of age, significantly declining for subjects ≥80 years.
5. Article 5, a cohort study, found that individuals vaccinated with Sinovac-CoronaVac were more likely to be infected and more likely to develop severe disease.

Clinical Bottom Line:

A cohort study published in the Journal of Clinical Infectious disease examined total of 2,709,899 individuals who had been vaccinated with two doses of a vaccine. A total of 107,220 individuals were confirmed by polymerase chain reaction (PCR) to be infected with COVID-19 over the study period, and 644 developed severe disease. After adjusting for age, gender, ethnicity, residency status, socioeconomic status, time since second dose, and daily infection rate, individuals vaccinated with Sinovac-CoronaVac were more likely to be infected and more likely to develop severe disease. This same study found that BNT162b2 (Pfizer) was effective for all outcomes in the entire population of subjects above 40 years of age, significantly declining for subjects ≥80 years. Another cohort study done in Colombia found that while CoronaVac was not effective for any outcome in subjects above 80 years, for people 40-79 years of age, we found two doses of CoronaVac reduced hospitalization, critical care admission and death. In a systemic review comparing seven SARS-CoV-2 vaccines, BNT162b2 (Pfizer) and mRNA-1273 (Moderna) vaccines had the highest efficacy in preventing symptomatic COVID-19 while the inactivated virus vaccine (CoronaVac) had a lower efficacy. The reduced efficacy of the inactivated viral vaccine may be attributed to lower SARS-CoV-2 antibody response to the vaccine.

To further investigate this theory, one study compared the neutralization antibody response between two doses of BNT162b2 (Pfizer) vs. CoronaVac vaccines. The titers (geometric mean PRNT50 titers) were 269 for mRNA vaccine vs. 27 for the inactivated virus vaccine both measured after the second vaccine dose. Even in heterologous vaccination regimens, where a second dose of mRNA vaccine provided a 100% seropositivity 3 months post-vaccination, the CoronaVac vaccine could only generate a 60–76% seropositivity rate at that time point. The heterologous vaccination using mRNA vaccines (Pfizer and Moderna) also seems to be more efficacious against the new SARS-CoV-2 variants, generating higher Omicron-specific antibody geometric mean titer levels (27.6 vs. 5.83) in patients who previously received two doses of inactivated virus vaccine (23.8). In a systematic review that compared 9 vaccines currently available with over 200,000 participants found no statistically significant difference seen in the ability of one vaccine to prevent symptomatic disease in the elderly population. However, mRNA-1273 (Moderna) and Gam-COVID-Vac (Sputnik V) have the highest P-scores (0.899 and 0.816, respectively), indicating greater protection against severe disease than other vaccines.

As evidenced by numerous cohort studies and systematic reviews, there are lower antibody titers elicited by inactivated virus vaccines as well as an increased risk of infection and hospitalization for COVID-19 infection. This is of great clinical concern for certain vulnerable groups of patients such as those >60 years and older. While this vaccine still provides protection for prevention of hospitalization for people 40-79 years of age. It is imperative that older individual receive booster vaccines with mRNA vaccines for a more robust coverage.

Recommendation for scenario:

In the scenario above, the physician was correct to suspect inactivated virus vaccine (Sinovac-CoronaVac) do not provide the same coverage as mRNA vaccines (Pfizer/Moderna). I would recommend that the 84yo F with history of severe COVID, previously vaccinated with inactivated virus vaccine (Sinovac-CoronaVac) in 2021 to have a booster vaccine with mRNA vaccines Moderna or Pfizer. This recommendation is based on the results and conclusions from numerous systematic reviews comparing the immune response and risk of severe covid in those vaccinated with mRNA vaccines (Pfizer/Moderna) vs inactivated virus vaccine (Sinovac-CoronaVac). The mRNA vaccines are superior to inactivated virus vaccine (Sinovac-CoronaVac) and recombinant vaccine (Johnson&Johnson). mRNA vaccines (Pfizer and Moderna) have showed greater protection against severe disease and higher antibody production.