Challenges to COVID-19 vaccination: variants, side effects and public concern

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Abstract: At present, the global epidemic of COVID-19 situation continues to be serious. Vaccines are an important step in controlling the COVID-19 pandemic, but as vaccinations move forward, there are challenges. First of all, the article mainly introduces the basic situation of several major new virus variants that appear with the continuous development of the epidemic and whether existing vaccines remain effective against these variants. Specific examples and characteristic analyses are made for the two main types of variants, variant of interest and variant of concern. Second, it explores whether vaccines should be used in some special populations or whether other negative effects will emerge. The impact of the vaccine on these people is still unclear, and these people do not recommend vaccination at present. Then, the side effects of the vaccine are listed in more detail. In addition, Take the research surveys in the United States and China as examples to analyze different people's attitudes towards vaccination and the trend that more and more people are willing to vaccinate. Finally, to improve the ability of future vaccination to control the epidemic situation and the effectiveness of vaccines to the diverse variants, some suggestions for the next generation vaccine were put forward.

1. Introduction

Covid-19, which may be one of the most hazardous global health crises, has been raised since December 2019. The virus that causes the Covid-19 is called SARS-CoV-2. The development of the vaccine and the policies across the globe make its severity better than before. Yet, as the virus continues to mutate, the fight against Covid-19 is still too early to say human beings find the ultimate solution to it. Vaccination is by far the most effective means of preventing and controlling the spread of COVID-19, and vaccines play an essential role in controlling mortality and morbidity [1]. However, with the spread of the epidemic, variants of the virus have successively emerged in different regions, such as the widely known alpha and delta variants. Several new variants emerging have been identified as superior transmission potential. They are more susceptible to infection than the first-generation virus, and these variants can also lead to more severe clinical responses and even higher fatality rates. Not only variants, vaccines still face many other challenges in controlling the epidemic. Since vaccines are not used clinically for very long, there are still many problems that remain undetermined. Not everyone is suitable for vaccination, and many specific populations are unsure of their suitability for vaccination because of their own immune system problems. There have been many confirmed side effects after vaccination, to some extent, can also give people certain psychological expectations, which is the most important concern of most people before vaccination. However, there are still rare side effects that occur as accidents, depending on the specific physical condition of different people, and even cause a strong immune response leading to serious illness. These side effects are still difficult to control. Attitudes to vaccines vary, but so far, most people have completed vaccinations and are willing to do so in the future. As the vaccine is further vaccinated, its safety and effectiveness are further proven. Attitudes toward vaccines have also changed from being more resistant at the beginning to being accepted.

2. Major variants of SARS-CoV-2 and their features

With the continuous spread of the global COVID-19 pandemic, several SARS-CoV-2 variants have emerged. There are three categories of subdivided variants: variant of interest (VOI), variant of concern (VOC) and variant that has significant implications for transmission, disease severity, diagnostics, vaccines and therapeutics. The major variants of these categories are shown in Table 1.

Some of these variants may alter the neutralizing activities of vaccine antibodies and monoclonal antibodies, leading to mild-to-substantial efficacy loss, which will reduce some COVID-19 vaccines' effectiveness and have a direct impact on the immunotherapeutic. To be clear, current vaccines' efficiency and coverage are not sufficient to deal with the newly and rapidly spreading variants. Only a few clinical trials have investigated the effects of COVID-19 vaccines on variants.

Table 1. the main variants of SARS-CoV-2

Categories	Name	First detected	Spike protein mutations
VOI	B.1.525 (eta)	United States	A67V, Δ69/70, Δ144, E484K, D614G, Q677H, F888L
	B.1.526 (lota)	United States	T95I, D253G, D614G, A701V*, S477N*, E484K*, L5F*
	P.2 (zeta)	Brazil	E484K, D614G, V1176F
VOC	B.1.1.7 (alpha)	United Kingdom	Δ69/70, Δ144Y, N501Y, A570D, D614G, P681H, E484K*, S494P*
	B.1.351 (beta)	South Africa	K417N, E484K, N501Y, D614G
	B.1.617.2 (delta)	India	T19R, Δ157-158, L452R, T478K, D614G, P681R, D950N
	B.1.427/B.1.429 (epsilon)	United States	L452R, D614G or S13I, W152C, L452R, D614G
	P.1 (gamma)	Japan/Brazil	K417N, E484K, N501Y, D614G
Variant of High Consequence (To date, there are no SARS-CoV-2 variants that has the potential to attain the level of high consequence)			

2.1 Variant of Concern

B.1.525 is now designated as the variant under investigation and will be the subject of risk assessment studies. It may be re-designated as Variant of Concern (VOC). B.1.526 is a variant with multiple mutations that could facilitate the spread of SARS-CoV-2 infection. Recent results suggest that existing vaccines will remain protected against the B.1.526 variant. P.2 is a potential reduction in neutralisation through convalescence and post-vaccination serums.

2.2 Variant of Interest

B.1.1.7 is characterized by 17 mutations. Three mutations of the transitory protein, in particular, are considered the most important [2]. N501Y is in the binding domain of the advanced protein receptor. It has been demonstrated to increase its binding affinity with the human angiotensin 2 concertation enzyme2, the first mode of viral penetration into human cells. It is believed that Δ69/70 causes an increase in communicability in combination with N501Y. P681H is adjacent to the site of furin cleavage, which has the potential to affect membrane fusion. While variant B.1.1.7 showed increased transmissibility, it did not exhibit a higher clinical severity [3]. B.1.1.7 is related to a transmission increase of approximately 50%. The reproduction number of the variant exceeds that of the pre-existing variants. The variant binds to ACE2 with twice as much affinity as the original receiving link domain. There is a higher risk of death than that associated with previous variants in circulation. The presence of the E484K mutation in variant B.1.1.7 results in a significant loss of neutralizing activity of vaccine-induced antibodies (BNT162b2). This variant was still susceptible (albeit at moderately reduced concentrations) to the neutralization by serum samples from NVX-CoV2373 (Novavax) and mRNA-1273 (Moderna) recipients. The effectiveness of the COVID-19

vaccine AZD1222 (Oxford-AstraZeneca) because of variant B.1.1.7 was 74.6% (non-B1.1.7, 84%). Antibodies inactivated by COVID-19 vaccine BBV152 (Bharat Biotech) maintained neutralizing activity against the variant B 1.1.7.

B.1.351 has been reported from over 40 countries. Variant B.1.351 is resistant to neutralization by a number of monoclonal antibodies directed towards the apex of the RBD, several of which have been granted emergency use permission [4]. Data from some laboratories indicate that the B.1.351 variant decreased neutralization based on analysis of serum samples obtained from vaccinated individuals. B.1.351 binds to ACE2 with an affinity five times greater than the original receptor bind field. This variation is associated with a transmission increase of approximately 50%. Reduced neutralization of mRNA-1273 sera has been observed in vaccinated individuals. Neutralizing serum activity was significantly reduced in subjects vaccinated with mRNA-1273 and BNT162b2. A decrease in the titre of antibodies neutralizing the virus was observed in hamster serum AZD1222 (Oxford-AstraZeneca) vaccinated against B.1.351 compared with B.1.1.7. The effectiveness of the AZD1222 mild to moderate COVID-19 vaccine because of variant B.1.351 was only 10.4%. NVX-CoV2373 was tested to be 51.0% effective against variant B.1.351.A trial was contemporaneous, with 95% of subjects being infected with the B.1.351 variant, but no vaccine is reported to be effective against the B.1.351 variant. Overall efficacy was only 22%, and efficacy against the B.1.351 variant was only 10%.

The B.1.617.2 (delta) variant was initially detected in India in December 2020. And then, the variant had been successively detected in 43 countries as of May 19, 2021. Several of these B.1.617.2 mutations can change the immune responses directed toward the key antigenic regions of the binding protein to the receptor (452 and 478) and suppress a portion of the N-terminal field. P681R is located in the S1–S2 split site, and it seems that mutation-carrying strains at the site may have enhanced replication, resulting in higher viral load and enhanced transmission. However, evidence regarding the effectiveness of COVID-19 vaccines in relation to the clinical outcomes of this variant has been limited. The absolute discrepancy in the effectiveness of the vaccine against symptomatic disease with the first dose of vaccine with the B.1.617.2 variant as compared with the B.1.1.7 variant was around 12% to 19%. However, the differences in vaccine effectiveness after both two doses were smaller. This occurred with the BNT162b2 and ChAdOx1 nCoV-19 vaccines [5].

B.1.427/B.1.429 exhibited an additional 18.6 to 24 per cent increase in communicability compared with wild strains. B.1.427/B.1.429 also experienced an increase in viral excretion in vivo [6]. And the antibody neutralization assays indicated a decrease in the neutralizing titers from vaccine recipients (BNT162b2 and mRNA-1273).

P.1 has been detected in up to 20 countries. P.1 was resistant to neutralization with recovery plasma and vaccinated serums. The emergence of lineage P.1 has been associated with a swift increase in COVID-19 cases and associated hospitalizations. P.1 demonstrated increased resistance to neutralization by vaccine serums in subjects vaccinated against mRNA-1273 and BNT162b2. P.1 is considerably less resistant to antibody reactions acquired or induced by the vaccine than B.1.351 [7].

3. The safety of vaccines for special populations (such as cancer patients)

Although many vaccines' effectiveness and safety have been confirmed, there is no clinical trial that shows that it is the same for patients with cancer [8]. The patients with malignancy are at high risk of becoming infected with COVID-19 and have a higher mortality rate. During this pandemic, it is essential to reconsider how to treat and protect these individuals. It is important to minimize the risk of infection for cancer patients. An important reason for the higher incidence of those people is the immunosuppression status. To date, there is no guidance on whether cancer patients should be vaccinated or whether only certain sub-groups should be vaccinated. Immune checkpoint inhibitors (ICIs) are a novel anticancer strategy. ICI treatment after COVID-19 vaccination has improved in virus protection and little impact on the toxicity associated with COVID-19 vaccination during ICI treatment [9]. Because of the lack of clinical data, it is impossible to accurately assess post-vaccination cancer patients' adverse reactions. Consequently, patients who have malignant tumors are

not advised to get certain vaccines before both the safety and the effectiveness of the vaccine can be ensured. To deal with these problems, Clinical trials of COVID-19 vaccines for cancer patients and recoveries are essential to ascertain the dosage, safety, reactogenicity and immunogenicity of the vaccine in this group.

Vaccination resembles a mild, naturally occurring infection. Due to its specific biological activity and pathogenicity, it can reproduce in the organism after injection. If it is impossible to control, it will result in infectious diseases. Until that happens, the vaccine will be responsible for the disease. The immune function of cancer patients is impaired during cancer therapy, which reduces immunity to the virus. If the cancer patients finish the vaccination, due to the unique features of cancer, the side effects of vaccination may be more severe than those of healthy individuals. It is unknown whether possible adverse effects may occur following vaccination if there is an impact between vaccines and cancer therapies and how it affects the long-term clinical outcome of tumors. Based on analysis of reasons for vaccine refusal in the questionnaire, the primary reason cancer patients refuse to be vaccinated is because they are afraid of side effects, followed by doubts as to whether the vaccine is effective. The primary reason that the patients' family members refuse the vaccine is a lack of confidence in its effectiveness. Hence, it is not the appropriate time to recommend vaccines for those cancer patients.

4. Side effects

To point out the side effects of vaccines to remind people, The National Health Service (NHS) and NICE in the United Kingdom originally informed the public of some side effects, including the incidence of fatigue, headache, muscle pain and the general feeling of illness and an aching arm where the needle has entered [10].

An investigation was conducted into certain types of side effects in 803 healthcare workers (HCWs) who were vaccinated with the BNT162b2 mRNA vaccine [11]. The result shows that the main generalized symptoms reported by the recipients were flushing (7.1%, 57/803), dizziness (8.34%), sweating (9.22%), fever (22.04%), chills (35.99%), headache (44.83%) and generalized weakness or fatigue (58.9%) as for musculoskeletal symptoms reported by the recipients, muscle stiffness (9.59%), arthritis or joint pain (16.56%) and muscle pain (45.7%). Localizes symptoms, approximately 88.04% (707/803) of HCWs reported a sore arm or pain at where the needle went in as their primary localized side effect, followed by bleeding (0.37%), residual skin discoloration (1.25%), rash (2.49%), regional or axillary lymphadenopathy (3.36%), itching (5.35%) and localized swelling at the injection site (5.48%).

And some gastrointestinal symptoms like constipation (0.37%), heartburn (1.12%), vomiting (1.49%), abdominal pain (3.11%), diarrhoea (4.61%), decreased appetite (5.73%) and nausea (15.94%). Psychological or psychiatric symptoms, behavioural changes (0.12%), manic/hypomanic mood changes (0.37%), depression (0.37%), psychological stress (0.75%), decrease in memory (0.75%), increased sleep (2.12%), anxiety (2.49%), decreased sleep quality (5.35%), feelings of relief/gratitude/joy (6.35%). Neurological symptoms reported by the recipients were seizures (0.12%), facial weakness (0.12%), loss of fainting/consciousness (0.25%), lack of coordination (0.5%), paralysis/extremity weakness (0.62%), vertigo-like symptoms (2.49%), numbness (2.86%), tingling of the extremity at the injection site (4.86%) and brain fogging or reduced mental attention/concentration/clarity (5.85%). Of note, two participants reported reactivation of herpes or shingle-like lesions after receiving the vaccine. Throat/mouth/nose/ears/eyes/heads symptoms reported by the recipients were bleeding gums (0.12%), ear discharge (0.12%), flashing lights (0.25%), changes in hearing (0.37%), hoarseness (0.37%), blurred vision (0.5%), eye pain (0.87%), ringing sensation in the ears (1.99%), runny nose (2.24%), sore throat (2.99%) and Nasal stuffiness (4.61%). Endocrine symptoms reported by recipients have increased urine production (0.25%), increased appetite (0.87%), increased thirst (1.2%), heat or cold intolerance (3.24%) and decreased appetite (5.73%). Cardiovascular symptoms reported by the recipients were changes and syncope (0.87%), chest pain (1.12%) and palpitations/racing heart (4.36%). Respiratory symptoms reported

by the recipients were wheezing (0.25%), coughing (0.87%) and Shortness of breath (1.99%). Allergic/skin symptoms reported by the recipients were swelling of the lips (0.12%), atopic eczema (0.25%), swelling in the throat/mouth (0.37%), hives (0.62%). Urinary symptoms reported by the recipients were dysuria (0.12%), difficulty in urination (0.12%), increased frequency of urination (0.37%), urgent urination (0.75%). The development of skin rashes was a newer side effect reported.

Similarly, less than 2% of Pfizer and Moderna vaccine recipients developed severe fevers between 39°C and 40°C. However, more people are likely to experience other transient side effects.

The independent board that conducted the interim analysis of Moderna's huge trial indicated that severe side effects included headache in 4.5% of participants, joint pain in 5.2%, muscle pain in 8.9%, and fatigue in 9.7%. According to the Pfizer/BioNTech survey, the numbers were lower, with serious side effects, including headache (2%) and fatigue (3.8%).

A case of a 24-year-old man who was diagnosed with myocarditis after his second dose of COVID-19 Moderna vaccine was reported [12]. The patient performed a similar thoracic discomfort after the initial administration of the vaccine, but these symptoms were not as severe. However, the second dose usually has more severe side effects than the first dose. The Israeli Ministry of Health reported 62 cases of myocarditis in COVID-19 vaccinated patients out of 5 million people who were vaccinated. The majority of cases occurred after the second dose of the mRNA vaccine, and only six cases were identified after the first dose.

5. Public concern towards vaccination

COVID-19 vaccine acceptance is statistically significant. An estimated 69% to 80% of adults would be willing to be vaccinated against COVID-19 in countries such as England, Denmark, the United States, Australia and France. [13-18] An investigation shows that people who thought the outbreak seemed to be getting worse were usually already vaccinated, while the intent to be vaccinated was not related to perceptions about the length of the outbreak. In addition, the deemed impact of the epidemic on daily life, confidence in the government's COVID-19 information, or trust in the government’s administration of the epidemic did not link to the intention of whether to get vaccinated or not.

In the United States, participants completed a questionnaire in early May 2020 [19]. Among the 672 participants surveyed, 450, or 67 per cent, said they would be willing to take the initiative to get the vaccine even if they were not recommended. In addition, men (72%) in comparison with women, older adults (78%) versus younger adults, Asians (81%) versus other racial and ethnic groups, and Those with a college or advanced degree (75%) versus those without a college diploma were more likely to accept the vaccine. Comparing the reported use of influenza vaccine with the declared acceptance of the COVID-19 vaccine, the result was that participants who had not graduated from high school had a very low rate of influenza vaccine use (10%), but 60% indicated that they would get the vaccination in the future. Unemployed participants reported less use of influenza and lower acceptance of the COVID-19 vaccine than employed or retirees.

In China, 1,057 teens took part in a survey that showed that 799 (75.59%) of them would agree to receive COVID-19 vaccination in the future [20]. Most teens who had already heard about COVID-19 vaccines were more willing to accept a future COVID-19 vaccine, indicating a greater recognition of the effectiveness of vaccines in the pandemic response. To cope with the deep impacts of the episodic, China has taken strong public health actions to limit the spread of COVID-19 since the outbreak. Chinese residents frequently believe strongly in the effectiveness of COVID-19 vaccination, and this positive attitude can explain why teens who had heard of COVID-19 vaccines before were more willing to accept COVID-19 vaccination. To conclude, Chinese teens seemed to have a positive attitude towards COVID-19 vaccines. Increasing public confidence and awareness about the effectiveness and safety of COVID-19 vaccines plays a significant role to make the success of vaccination programs to be maximised.

6. Conclusion

In general, the vaccine still can protect most variants, but the effectiveness will be reduced to a certain extent. The efficiency and the coverage of current vaccines are insufficient to deal with the new severe variants. And there is no evidence proved that current vaccines have the same safety and effectiveness for some special individuals. Common side effects of the vaccine include but are not limited to the incidence of fatigue, headache, muscle pain and a general feeling of illness and an aching arm where the needle has entered. In addition, there are still some rare and undiscovered side effects. COVID-19 vaccine acceptance is significant to future vaccination. So far, most people have completed vaccinations and are willing to do so in the future.

As for the next-generation vaccines, the design and clinical trials of next-generation vaccines have to take emerging variants into account. Second, countries where vaccines are lacking should adopt a more flexible vaccination strategy. Third, further evidence is needed to verify which types of vaccines can be mixed and which vaccines have sufficient safety and efficacy to cope with a temporary shortage of a given vaccine. Finally, special populations, including the elderly, infants, and immunocompromised patients, such as those with AIDS or cancer, are not yet fully covered in clinical trials on COVID-19 vaccines and should be considered in the future.

Next-generation vaccines, like multi-valent vaccines, would be effective tools for controlling the spread of SARS-CoV-2 variants. Many labs around the world are planning to develop next-generation vaccines. Johnson & Johnson is in the process of developing variant vaccines and plans to add the original vaccine to form a bi-valent vaccine. In addition, Moderna has developed a recall vaccine (mRNA-1273.351) for the newly emergent variant B.1.351.

References

[1] Rezaei, S., Sefidbakht, Y., Uskoković, V. (2021) Tracking the pipeline: immunoinformatic and the COVID-19 vaccine design. Briefings in Bioinformatics., bbab241.

[2] Williams, G.H., Llewelyn, A., Brandao, R., Chowdhary, K., Hardisty, K.M., Loddo, M. (2021) SARS-CoV-2 testing and sequencing for international arrivals reveals significant cross border transmission of high-risk variants into the United Kingdom. EClinicalMedicine., 8.

[3] Public Health England. Investigation of novel SARS-CoV-2 variant -technical briefing 2 [Internet]. 2020.

[4] Bian L., Gao F., Zhang J., He Q., Mao Q., Xu M., Liang Z. (2021) Effects of SARS-CoV-2 variants on vaccine efficacy and response strategies. Expert Rev Vaccines., 20 (4): 365 – 373.

[5] Jamie, J. B., Nick, A., Charlotte, G., Eileen, T., Ruth, S., Simon, T., Julia, S., Elise, T., Natalie, G., Gavin, D., Richard, M., Gayatri, A., Matt, E., Maria, Z., Brown, K. E., Susan, H., Meera, C., Mary, R. (2021) Effectiveness of Covid-19 Vaccines against the B. 1.617.2 (Delta) Variant. New England Journal of Medicine., 385 (7).

[6] Sharun, K., Tiwari, R., Dhama, K., Rabaan, A.A., Alhumaid, S. (2021) Emerging SARS-CoV-2 variants: impact on vaccine efficacy and neutralizing antibodies. Human Vaccines & Immunotherapeutic., 17 (10): 3491 – 3494.

[7] Dejnirattisai, W., Zhou, D., Supasa, P., Liu, C., Mentzer, A. J., Ginn, H.M., Zhao, Y., Duyvesteyn, H. M. E., Tuekprakhon, A., Nutalai, R., Wang, B., López-Camacho, C., Slon-Campos, J., Walter, T. S., Skelly, D., Costaclemens, S. A., Naveca, F. G., Nascimento, V., Nascimento, F., Fernandes da Costa, C., Resende, P.C., Pauvolid-Correa, A., Siqueira, M.M., Dold, C., Levin, R., Dong. T., Pollard, A.J., Knight, J.C., Crook, D., Lambe, T., Clutterbuck, E., Bibi, S., Flaxman, A., Bittaye, M., Belij-Rammerstorfer, S., Gilbert, S.C., Carroll, M.W., Klenerman, P., Barnes, E., Dunachie, S.J., Paterson, N.G., Williams, M.A., Hall, D.R., Hulswit, R.J.G., Bowden, T.A., Fry, E.E., Mongkolsapaya, J., Ren, J., Stuart, D.I., Screaton, G. R. (2021) Antibody evasion by the P.1 strain of SARS-CoV-2. Cell., 184 (11): 2939 – 2954.

[8] He, Y., Ding, Y., Cao, B., Huang, Y., Wang, X. (2021) COVID-19 vaccine development from the perspective of cancer patients. Hum Vaccin Immunotherapy., 17 (10): 3281 – 3287.

[9] Luo, B., Li, J., Hou, X., Yang, Q., Zhou, Y., Ye, J., Wu, X., Feng, Y., Hu, T., Xu, Z., He, Y., Sun, J. (2021) Indications for and contraindications of immune checkpoint inhibitors in cancer patients with COVID-19 vaccination. Future Oncology., 17 (26): 3477 – 3484.

[10] Zafar, M., Ewnetu, B., Ahmed, S., Iqbal, U., Whitehead, M. (2021) COVID-19 Vaccination-Induced Rash: Does the Choice of Vaccine Matter? Cures., 13 (6).

[11] Kadali, R.A.K., Janagama, R., Peruru, S., Malayala, S.V. (2021) Side effects of BNT162b2 mRNA COVID-19 vaccine: A randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers. International Journal of Infectious Diseases., 106: 376–381.

[12] Albert, E., Aurigemma, G., Saucedo, J., Gerson, D.S. (2021) Myocarditis following COVID-19 vaccination. Radiology Case Reports., 16 (8): 2142 – 2145.

[13] Reiter, P. L., Pennell, M. L., Katz, M. L. (2020) Acceptability of a COVID-19 vaccine among adults in the United States: how many people would get vaccinated? Vaccine., 38: 6500 – 6507.

[14] Wang, J., Jing, R., Lai, X., Zhang, H., Lyu, Y., Knoll, M.D. (2020) Acceptance of COVID-19 Vaccination during the COVID-19 pandemic in China. Vaccines., 8 (3).

[15] Bell, S., Clarke, R., Mounier-Jack, S., Walker, J.L., Paterson, P. (2020) Parents' and guardians' views on the acceptability of a future COVID-19 vaccine: a multi-methods study in England. Vaccine., 38: 7789 – 7798.

[16] Dodd, R. H., Cvejic, E., Bonner, C., Pickles, K., McCaffery, K. J. (2021) Willingness to vaccinate against COVID-19 in Australia. Lancet Infect Dis., 21: 318 – 319.

[17] Eumann-Bohme, S.V., Sabat, N.E., Barros, I., Brouwer, P.P., Van-Exel, W., Schreyogg, J. (2020) Once we have it, will we use it A European survey on willingness to be vaccinated against COVID-19. Eur J Health Econ., 21: 977 – 982.

[18] The COCONEL Group. (2020) A future vaccination campaign against COVID-19 at risk of vaccine hesitancy and politicization. Lancet Infect Dis., 20: 769 – 770.

[19] Malik, A. A., McFadden, S.M., Elharake, J., Omer, S. B. (2020) Determinants of COVID-19 vaccine acceptance in the US. EClinicalMedicine., 26.

[20] Cai, H., Bai, W., Liu, S., Liu, H., Chen, X., Qi, H., Liu, R., Cheung, T., Su, Z., Ng, C., Xiang, Y. (2021) Attitudes Toward COVID-19 Vaccines in Chinese Adolescents. Frontiers in Medicine., 8: 994.