

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

171,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Chapter

Advances in Diagnosis and Treatment for SARS-CoV-2 Variants

Naheed Akhter, Sadia Sana, Muhammad Adnan Ahsan, Zafaar Siddique, Abu Huraira and Somara Sana

Abstract

The COVID-19 pandemic's epidemiological and clinical characteristics have been affected in recent months by the introduction of SARS-CoV-2 variants with unique spikes of protein alterations. These variations can lessen the protection provided by suppressing monoclonal antibodies and vaccines, as well as enhance the frequencies of transmission of the virus and/or the risk of contracting the disease. Due to these mutations, SARS-CoV-2 may be able to proliferate despite increasing levels of vaccination coverage while preserving and enhancing its reproduction efficiency. This is one of the main strategies in tackling the COVID-19 epidemics, the accessibility of precise and trustworthy biomarkers for the SARS-CoV-2 genetic material and also its nucleic acids is important to investigate the disease in suspect communities, start making diagnoses and management in symptomatic or asymptomatic persons, and evaluate authorization of the pathogen after infection. Quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) for virus nucleic acid identification is still the most effective method for such uses due to its sensitivity, quickness, high-throughput sequencing capacity, and trustworthiness. It is essential to update the primer and probe sequences to maintain the recognition of recently emerging variations. Concerning viral variations could develop that are dangerously resistant to the immunization induced by the present vaccinations in coronavirus disease 2019. Additionally, the significance of effective public health interventions and vaccination programs will grow if some variations of concern exhibit an increased risk of transmission or toxicity. The international reaction must've been immediate and established in science. These results supported ongoing efforts to prevent and identify infection, as well as to describe mutations in vaccine recipients, and they suggest a potential risk of illness following effective immunization and transmission of pathogens with a mutant viral.

Keywords: coronavirus 2 (SARS-CoV-2), DNA testing, RT-PCR test, diagnosis, treatment, ADAR enzyme

1. Introduction

According to the World Health Organization (WHO), incidences of pneumonia with an unknown cause were reported in many locations in late 2019 and early 2020 [1]. This pneumonia's pathogen was recognized as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2] and was given the label coronavirus infectious disease (COVID-19).

SARS-CoV-2 infections affected more than 83 million known COVID-19 patients by the end of 2020, but significant progress had been achieved with the approval and implementation of vaccines and antibody treatments. These treatments target the infectious spike protein, although the advent of vigorous variations puts their effectiveness in danger (**Figure 1**) [3].

These fears have prompted an increase in viral DNA testing and sequencing in infected patients in terms of understanding the risk of transmission, virulence, and potential of variants to avoid modern vaccinations. The number of viral variants in New York City has risen alarmingly. As of March 30, 2021, the B.1.1.7 variant, first discovered in Great Britain (UK) for 26.2% of all the cases of coronavirus disease, and the B.1.526 variant, initially discovered in New York City, contributed to even more than 72% of cases, which were newly admitted (in 42.9%) [3]. The ability of variations to circumvent vaccine-induced immunity and cause asymptomatic infection (and thus viral transmission) or disease is of particular concern. Both repercussions are significant and must be evaluated separately.

Reliable laboratory testing is one of the top priorities for facilitating public actions. A reliable test is now the most efficient method for detecting patients in a large community, especially asymptomatic illnesses, identifying transmission pathways and hosts, evaluating the success of therapeutic options, and determining infection's eradication. As one of the most important instruments for monitoring, isolating, as well as diagnosing COVID-19 pandemics, each country should priorities investing in cutting-edge techniques and offering economic incentives for the implementation and verification of accurate COVID-19 diagnostics. To

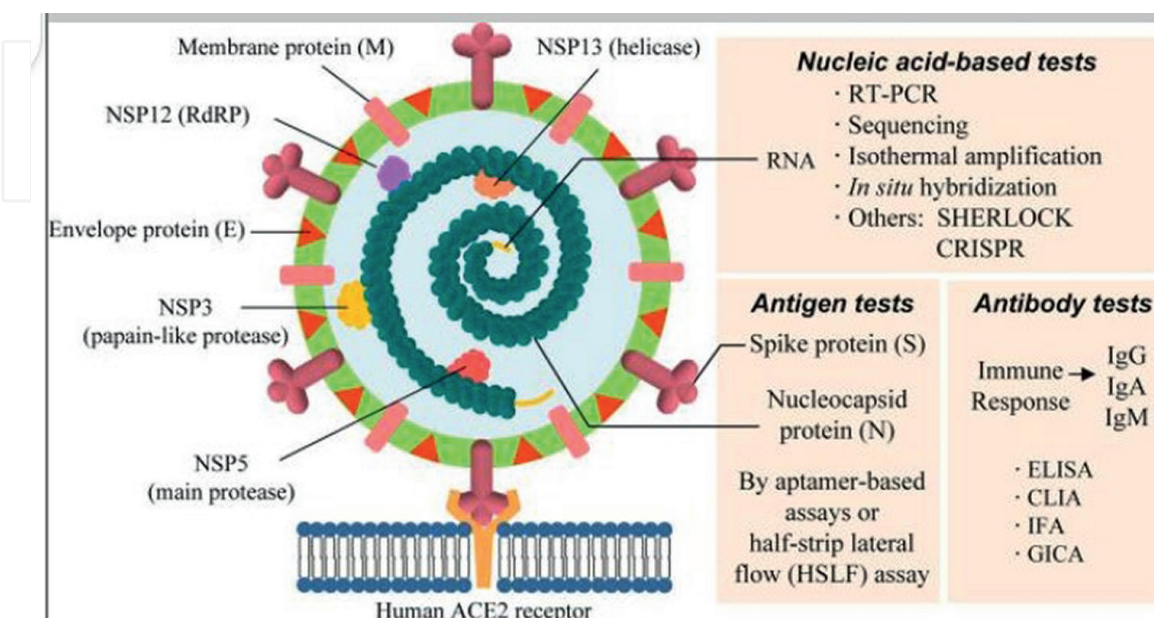


Figure 1.
Structure of the SARS-CoV-19 variants.

present, most existing examinations typically meet the expectations of mass testing examination, personal diagnosis, or variation detection; however, capability varies significantly between countries, regions, and races, mainly to socioeconomic inequalities. Because the pathogen of COVID-19 is recognized, as well as the genome, transmission channels, and host antigen for viral attachment, there are two types of tests presently offered: For the identification of viral antigens or host antibodies, there are two types of diagnostics: (1) nucleic-acid-based tests and (2) serology-based tests. Serological techniques identify antibodies found within blood serum and infectious antigens within tissues, discharge fluids, or eliminations by persons who have current or previous infections, whereas nucleic acid tests immediately investigate for viruses RNA via the throat and nose swabs taken from patients [4].

Many common areas in the SARS-CoV-2 genomes were selected as effective objectives for sample preparation in several PCR techniques, and they are used in the majority of COVID-19 molecular diagnoses around the world. According to the WHO [5], at least two targets should be used in clinical practice to avoid SARS-CoV-2 genetic mutation and cross-multiplication with the other COVID-19 viruses. For the construction of primers and probes, three portions that have been preserved (the E, N, and ORF1ab genes) are commonly chosen as standard objectives. Furthermore, sequencing the viral DNA aids in the detection of novel coronavirus variants that emerge over time. Newly developed portable or quantitative sequence alignment techniques, as opposed to classical sequence alignment methods, which are typically highly expensive, may offer accurate elevated diagnostics throughout pandemics.

1.1 Epidemiology of SARS-CoV-2 variants

Coronaviruses have a nuclease enzyme that reduces the likelihood of replication failure in vitro by 15–20 times, resulting in a 10-fold reduced risk of virus mutation in vivo than influenza [6]. When variations with mutated genes infected the same victim [7], however, they gather alterations and produce greater variety through the recombination mechanism. SARS-CoV-2 [8] is considered to have formed as a result of recombination between different SARS-related coronaviruses, and recombination is still occurring among propagating SARS-CoV-2 variants [9], showing the challenges in detecting it based on the similarities among most sequences. As evidenced by the prevalence of C to U changes in specific dinucleotide situations, SARS-CoV-2 diversity is further supported by host-mediated transcriptional control by APOBEC and ADAR enzymes [10, 11].

Although that was initially thought that decreasing immunity would have been the reason for people's frequent reinfection with symptomatic widely accepted COVID-19 viruses [12], recent research suggests that genetic variation could also play a significant role in the absence of lengthy resistance after COVID-19 virus outbreaks [13]. HCoV-229E and HCoV-OC43 sequence data demonstrate a ladder-like phylogenetic evaluation topology over a 30-year period, which has been maintained with the incidence of novel variants going to spread through the global population at a slower rate than seasonal influenza, with pathogens separated from one point and time frequently evading neutralization by blood plasma from individuals infected numerous decades prior [14].

SARS-CoV-2 is thought to evolve at a rate between about 4×10^{-4} and 2×10^{-3} variations per codon per annum [15–17]. Even though the probability of synonymous variations influencing SARS-CoV-2 morphologic features must be discounted, zero

reviews of this concept happening inside the SARS-CoV-2 spikes genotype have been found. As a result, we refer to an NH₂ mutation from the Wuhan-Hu-1 known sequences (GenBank accession: NC 045512.2) as a mutation in this Review.

Because new lineages are sometimes separated from some nucleotides, the classification of emerging SARS-CoV-2 genotypes based on organic evolution has proven difficult [18]. Because the majority of mutations have been identified in a variety of countries, and the number of viruses undergoing sequencing varies substantially between countries, geographical classification has proven difficult. The NextStrain and Phylogenetic Assignment of Named Global Outbreak (PANGO) genealogy [19] systems have been developed for control and prevention. The Phylogenetic Assignment of Named Global Outbreak genealogy approach is more popular and provides greater specificity. Sub-lineages are indicated by an alphabetical beginning as well as termination containing two to three digits interspersed with periods (such as B.1.1.7). However, because the method only supports three levels of hierarchy, the variant's parental relationship cannot be established by adding a new genealogy ending. The linkage of a virus may not always correlate to the changes in its components. For example, a virus may acquire new genetic alterations related to its physiological function without ever being associated with a recent linkage.

The very first evidence of SARS-CoV-2 genetic development evolutionary changes appeared in early 2020 when a unique viral variant with the spike variant D614G arose and spread rapidly to a prevalence of over 100% by June 2020 [20, 21]. By the end of 2020 and early 2021, plenty of variants with long-term mutations (most notably D614G) had been discovered, mostly but not exclusively in the spikes protein. B.1.1.7, a fast-growing species in England connected with an extremely large number of genetic changes, was reported on the virological.org conversation forum²⁷ in December 2020. The first therapeutic specimen of this kind was obtained in late September 2020 in England, according to retrospective analysis.

Two further fast expanding links with significant amounts of genetic variations were found in South Africa within a month [16] and Brazil [22]. The frequency of the B.1.351 variant jumped from 11percentage points in October to 87% in December [23] in South Africa. The P.1 variety was detected in Manaus, Brazil, a town with a 75% infection rate in October 2020, but a spike in new cases began in November 2020 [24, 25]. Following that, the prevalence of a novel variant (B.1.617.2) increased from 2 percentage points around February 2021 to 87% in May 2021 in Maharashtra, India, which, like the rest of the country, experienced a significant increase in the number of cases [26]. Since then, the B.1.617.2 variety has expanded over a number of countries [27] and has shown to be much greater spreadable than that of the B.1.1.7 variant. It has a higher risk of causing disease than prior viral variation (**Figure 2**) [28].

Variants of concern (VOCs) are those that have spread widely and shown evidence of being more transmissible, causing more severe disease, and/or reducing neutralization by immunoglobulin produced during prior infection or vaccination, according to the World Health Organization (WHO), the US Centers for Disease Control and Prevention (CDC), and the COVID-19 Genome sequencing UK Consortium (COG-UK) [29]. Those that have not quite expanded as broadly include alterations comparable to those found in VOCs are of particular relevance (VOIs). On May 31, 2021, the WHO began using the Greek alphabet to classify VOCs and VOIs, with the current VOC classifications being Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (D.1) (B.1.617.2).

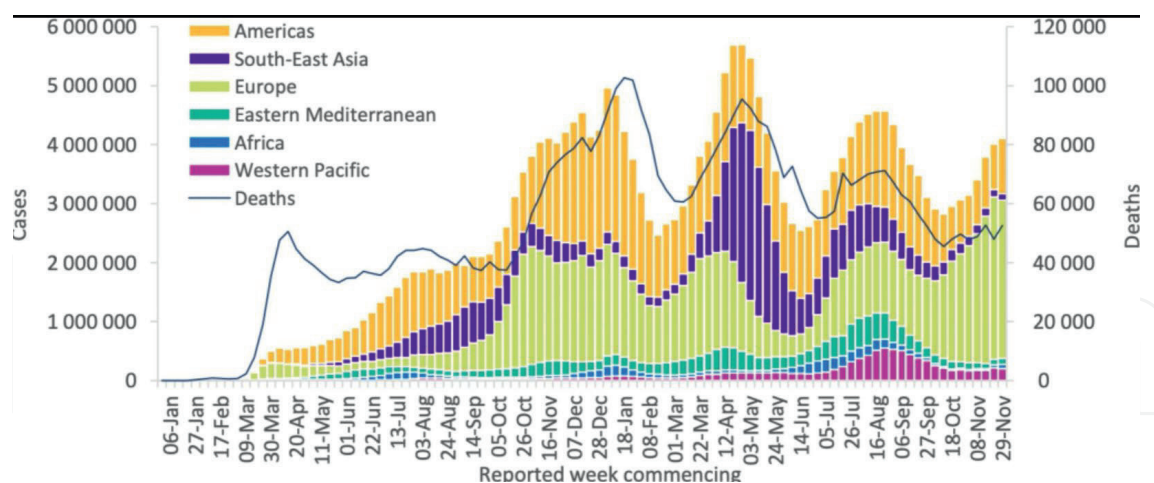


Figure 2.
Epidemiology of COVID-19 variants cases.

1.2 Diagnostic capability

1. Nuclear-acid-based testing of SARS-CoV-2 variants
2. Protein-based testing of SARS-CoV-2 variants

1.2.1 Nuclear acid based testing of SARS-CoV-2 variants

1.2.1.1 Detection of mutated variants with standard RT-PCR

As it multiplies, the virus's genome is continually changing. New SARS-CoV-2 pandemic events could be triggered by new variants containing genetic mutations. Because most PCR primers were built using solitary virions in their early stages [30], notably the standard genetic material (SARS-CoV-2, NC 045512.2) [31], just a genetic variation during a first evolution sequence could result in reduced RT-PCR test amplification efficiency and false-negative detection results [32]. Studies of genotyping samples reported to GenBank and GISAID indicated that variations in the ORF1ab region were most common in Germany and China [33].

Another analysis relies on 31,421 SARS-CoV-2 genomic specimens and discovered that the majority of alterations were with the objective of several N genome primers and probes [34], which could alter the accuracy of PCR amplification in RT-PCR tests that probe the N genome. Variations in the N genome have been observed to interfere with detection in some cases [35]. All objectives of the US CDC-recommended COVID-19 diagnosis primers had mutations, while the targets of N genome primers and probes used throughout Japan, Thailand, and China had various mutations in distinct clusters, suggesting that the N gene may not have been a reliable target for RT-PCR kits and that these N gene-based kits should be reported periodically for a rising alpha, beta, gamma, delta variants [35].

1.2.1.2 Sequencing for diagnosis of SARA-CoV-2 variants

When compared with real time-PCR, virus genotype had the limitations of being more expensive, requiring more analysis of given information, and having

lesser medical efficiency, making it inappropriate for massive population detection. However, utilizing metagenomics RNA sequencing techniques [31], the first genetic arrangement of SARS-CoV-2 was obtained. A study by the WHO and China found that during the beginning of December 2019 to the middle of February 2020, Illumina and Nanopore technologies were used to identify and sequence 104 SARS-CoV-2 variants [36]. More than 1000 comparable variants have since been published in the GISAID and GenBank databases, and the genomic and proteomics of SARS-CoV-2 have also been found [37]. The benefit of homologous recombination identification is that it allows for the tracking of viral changes by gathering data on recent variants. The viral genome is sequenced for the detection and classification of novel coronavirus variants throughout time [36]. Random changes in the genetic coding accrue with the speed of about 2/month when the virus multiplies and expands, according to data from closely watching viral development [38]. The latest mutant (changed) coronaviruses had been discovered, such as alpha (B.1.1.7), beta (B.1.351), gamma (P.1), and delta (B.1.617.2), which could result in the virus spreading considerably faster [39].

High-throughput approaches or portable fast sequence arrangement technologies had already been designed as distinguishing equipment for COVID-19 due to increased demand. Nanopore target sequencing (NTS) is appealing for clinical testing since it is fast, accessible, and efficient. In 1 h of sequencing [40], an NTS technique sequencing viral areas can identify very few as 10 viral copies/mL. These recently developed portable or quantifiable technologies, in comparison to classic sequencing techniques, which are typically expensive, may give accurate elevated diagnostics during epidemics. In the United Kingdom, NTS is being used in a projected genetic monitoring effort to create real-time genetic monitoring of SARS-CoV-2 [41], allowing sample-to-report in less than 24 hours. The use of genetic and epidemiologic analyses together speeds up the detection of possible transmission events and aids in the implementation of prompt control and prevention measures. When NTS is utilized to examine for reductions and different mutations in the SARS-CoV-2 gene in patients who have been infected with the virus, a putative pathogenic mechanism may be uncovered [42]. Furthermore, a novel molecular testing method relying on Sanger sequence techniques was capable to identify SARS-CoV-2 Genetic code (RNA) from viruses suspended components in the transmissible channel, RNA extraction could be skipped altogether without sacrificing performance at a testing flow rate of more than 1,000,000 tests per day [43], meaning that RNA extraction may be omitted fully without sacrificing performance. Natural variations in large populations could be tracked at general genomic ranges or specific regions over time or within a geographic location with this capability, allowing the locations and provenance of mutations to be identified once the quantitative capability is in place (**Figure 3**).

1.2.2 Protein-based testing of SARS-CoV-2 variants

1. Antibody testing
2. Antigen testing

1.2.2.1 Antibody testing

As a growing number of people around the world prefer to keep a maximum distance from every person and remain at their houses, the concentration of pandemic protection and management has moved to comprehensive serological antibody

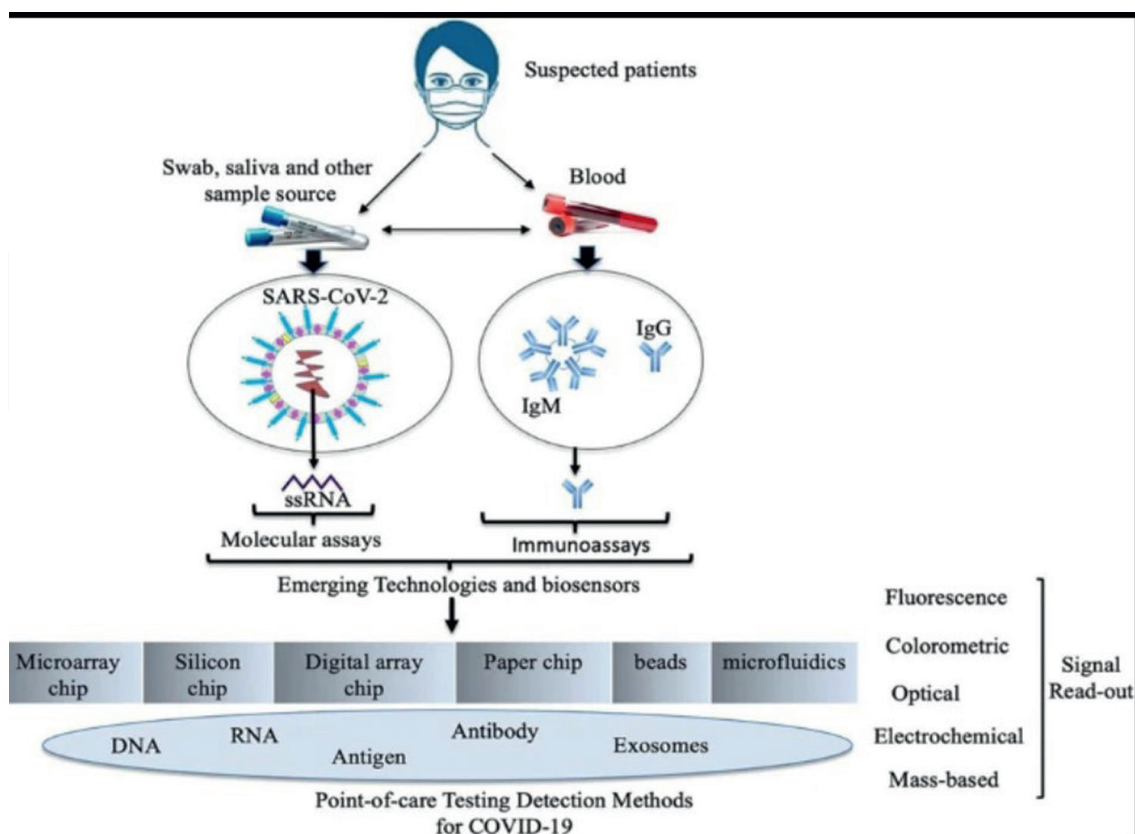


Figure 3.
 Type of diagnostic method.

diagnostics of community to supervise infectious disease condition, vaccine effectiveness, immune defense perseverance, and high-titer neutralizing antibody monitoring and selection. These diagnostics, including the enzyme-linked immunochromatographic analysis (ELISA), chemiluminescent immunoassay (CLIA), immunofluorescent test (IFA), and colloidal gold immune chromatographic test (GICA), are lying on the detection of SARS-CoV-2 via IgM and/or IgG antibodies in blood plasma or biological fluids specimen. Several months before the first case was identified, one study looked for SARS-CoV-2 special antibody in 959 patients taken acquired from a prospective lung cancerous tumor testing between healthy people [44]. According to tests, SARS-CoV-2 disorders were found in about 11.6% of a native community before COVID-19 was discovered. Antibody tests are useful in community exposure research to determine the speed of exposure during a special pandemic episode in an area, as well as to determine regardless of where neutralizable antibodies are progressing in people who were attacked by the COVID-19 virus, as well as the period and titer modified into neutralizing antibodies with the time. Since many types of vaccinations preventing SARS-CoV-2 disease are provided to the public, it is crucial to monitor neutralizing antibody production after immunization.

1.2.2.2 Antigen testing

N protein and S protein are now primary immunogens in SARS-CoV 2, and antibodies to such two proteins can survive up to 30 weeks in SARS patients' serum [45]. A new antigen-based ensures quick diagnostic test had high specificity and sensitivity during the first week between many patients diagnosed and specimens

with greater primary infection [46], whereas a quick procedure relies upon a fluorescence immunologic chromatography screening test detecting N protein had effectiveness just in the first stage of the disease. N protein was identified in a gargle liquid specimen from a COVID-19-effective person [47], according to mass spectrometry analysis. In 73.6% of COVID-19 patients, a fluorescence immunological chromatography analysis identified N protein in a urine specimen. S protein is more useful for monitoring during the recovery phase because of its late development [48], and a supersensitive antigen screening for S protein is easily done with a microplate reader [49].

With popular approaches, the SARS-CoV-2 coronavirus nucleocapsid antigen-identifying half-strip lateral flow (HSLF) analysis has been created, which has higher therapeutic effectiveness than classic serology techniques, with an LOD of 3.03 ng/mL [50] for publically present Genscript N protein. With an LOD of 0.1 ng/mL for synthesized spikes antigen of SARS-CoV-2 [51], a unique nanozyme-based chemiluminescent paper test may be performed by using a lens of a standard mobile.

A particular nucleotide gene encoding opposite to N protein seems to have identical features to recognize the objective as an antibody for antigen detection; however, it may have superior effectiveness and best choices for the creation of tests for other purposes. A particular ssDNA transcription factor linked with N protein had been recommended as a reliable and efficient probe for the identification of SARS-CoV-2 using a SELEX screening strategy [52]. Another investigation found four DNA microarrays with a sensitivity of less than 5 nM that form a sandwich-type interaction with the N protein with an LOD of 1 ng/mL [78]. When compared with using simply antibodies in ELISA with LODs ranging from 50 to 100 ng/mL [53], the LOD of aptamer-based approaches was significantly lesser than that of standard immune screening inside a short turn-around time (TAT) having remarkable consistency and renewability [54]. As a result, in terms of diagnostic accuracy and biosensor conjugation flexibility, aptamer-based antigen recognition might well be superior to antibody-based detection of antibodies [52].

Finally, fast antigen detection has a sensitivity 1000 times lower than virus incubation and 10^3 times smaller than RT-PCR [55]. According to previous studies, the effectiveness of the rapid diagnostic test is only around 30% of that of nucleic acid screening [56], implying this antigen screening is not a fast technique but could be utilized as verification or analysis for a special patient specimen.

1.3 Vaccination and its effectiveness

1.3.1 Examining the efficacy of existing vaccines against variants

While current immunizations are being administered, therapeutic information can be collected not just from preplanned controlled research [57], but also through clinical experiments comparing immunizations versus placebo, one vaccination against the other, or various immunization schedules (e.g., various doses, different counts of doses, and time duration between doses).

In areas where vaccine supply or delivery capacity is limited, trying to make the first vaccine dosage accessible to several of the test group on just a randomly selected basis can give valuable important knowledge about effectiveness against significant variants rather than enabling management plans to evaluate the sequence wherein individuals are fully immunized. This is particularly true if the number of individuals

who are randomly assigned is high enough to support the measurement of “hard” endpoints like hospitalization or serious disease.

In simple controlled studies conducted during vaccine deployment, the roles of scientists, vaccines, and vaccinators are deployed.

If a huge randomized was used during vaccination installation to compare the impact of parental secondary doses with that of postponed secondary shots, any changes in efficacy may be accurately measured not just too generally but possibly concerning such genetic variation. In some populations, public health programs may include random assignment of vaccination dates or locations, and those who become suitable for vaccination may be assigned randomly to appointments with a longer or shorter gap between vaccinations. This technique could permit hundreds of thousands of people to be randomly assigned vaccines at little or no expense to the immunization program and with little or no disruption to current vaccination capability. Whether any immunizations had been discovered to be capable of preventing COVID-19 even after an encounter with SARS-CoV-2, modest, controlled trials of post-exposure prophylaxis might provide crucial insights into vaccination effectiveness (or comparative efficiency) versus different strains.

Bias exists throughout all nonrandomized epidemiological research seeking to establish vaccine efficiency. In regions where differences are co-circulating, including several but hardly all of the community members have received vaccinations, epidemiological data specifically planned to show the dispersion of highly contagious genetic variants between instances in immunized and unvaccinated people may generate reasonably effective forecasts of comparative vaccine efficacy against various variations. If the level of vaccines is related to the relative frequency of alterations between sites, such research must take prospective interference into account. Recent disease patients’ epidemiological investigations may show a lack of defense against problematic variations.

To examine the effects of concern variants on vaccination effectiveness and duration, new methodologic methods are still needed. Almost complete genotyping of isolates from specified sentinel areas could eliminate bias in the sample chosen for sequencing in vaccination sensitivity studies against variations of concern. Samples from unassigned vaccination receptors with emerging diseases and identical non-vaccinated subjects can be utilized to evaluate the impact of specific genomic characteristics on vaccine effectiveness. Important insights regarding the importance of particular viral properties could be gained using such methodologies in trials or research published after vaccine deployment, and these insights could propagate to an enhanced selection of the variants in the development of a mutated vaccine.

It’s unclear how reliable any immunological sign could be like a “correlate of protection.” The impact of vaccines on these biomarkers could enable regulatory action for novel candidate vaccines if such biomarkers proved to be a reliable assumption of vaccine effects on frequency of outbreak infections. However, there are some drawbacks, such as the possibility that immunological correlates of prevention are dependent on vaccine-specific variables, virus variants, and COVID-19 research exit points.

1.3.2 Examining the efficacy of new and modified vaccines for variants

Although there will be an unwillingness to dispatch vaccination lies on recent sequence data until there is perfect proof that earliest vaccination having failed [57], there would also an unwillingness to permit a sustained flow of vaccine-resistant variant while fresh immunizations or adapted vaccination are now established if that could be avoided. Because vaccine-resistant variations are certain to occur, now is necessary to schedule the

creation of modified vaccinations that can defend against them. The impact of vaccine alteration on vaccine production and rollout timelines should be considered during planning.

Adapted vaccines (i.e., vaccines that deliver a fresh pathogen through with a vaccine, which have proven for being extremely effective against traditionally circulatory highly contagious variations) must be tested for their ability to evoke immune function in both people who have never had an immune reaction to SARS-CoV-2 and people who have already been vaccinated. Variations in the in vitro eradication of systemic pathogens by immunization antibodies do not always imply decreased efficiency. Even neutralization reactions should not be used to indicate vaccination effectiveness, large variations may be sufficient to justify regulatory decisions. For example, after receiving a customized vaccination, testing size of the immune reaction between greater than one mutation of concern might be evaluated to the immunological response against the prototypes virus after receiving the initial, confirmed vaccine. Analyzing neutralizing reactions to multiple different variations of concern as well as the prototype virus may assist in deciding whether more than one vaccine (or, eventually, a powerful and versatile vaccine) is required.

In regulatory changes discussions and WHO recommendations, it has been agreed that large, traditional clinical terminal trials are unlikely to be required to launch modified vaccinations against variations of concern. Because discrepancies in immune response analyses can make direct comparisons difficult, According to the FDA, animal specimen should be utilized to provide additional proof of the efficacy of customized vaccinations against variations of concern (**Figure 4**) [58].

Even if some vaccines are administered that are medically beneficial, greater would be required to combat the global epidemic. Latest vaccines against new viral variations may be more beneficial than prior vaccinations, and they may be given in a standard injection, be non-injectable, circumvent cold-chain restrictions, or have enhanced manufacturing scalability. International antigenic composition recommendations should be used in the development of modified or entirely new vaccines.

By using randomization, analyzing impacts not just on immunologic as well as on clinical endpoints and using placebo controls when ethically appropriate [59], such as in communities where vaccine supply is limited or subpopulations where the possibility of advancement to dangerous infections is very low [60], new vaccine trials can still give accurate and easily understandable results in an efficient manner.

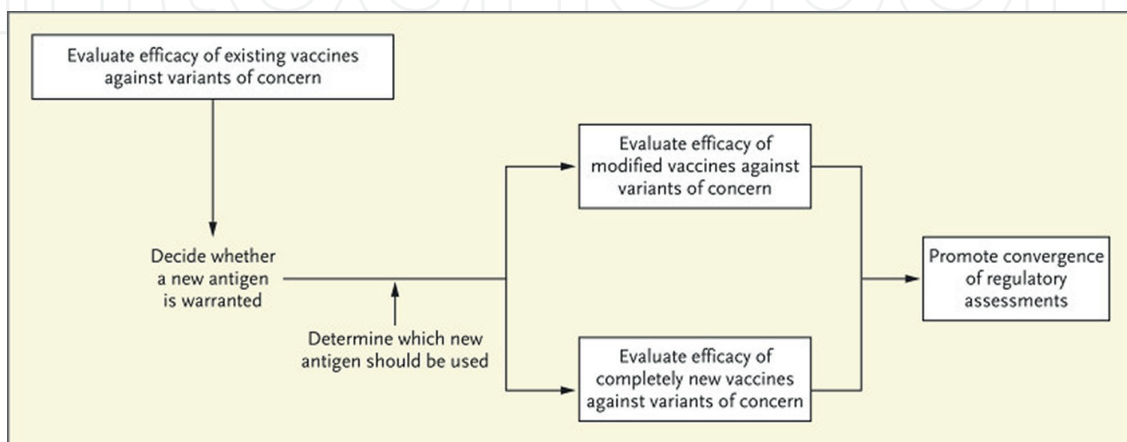


Figure 4.
A framework for evaluating vaccines against variants of concern.

Randomized trials involve more planning, but they avoid undiscovered research strategy differences from affecting research results when possible [61]. Multiple analyses, along with the evaluation of the impact of viral variation on vaccination effectiveness, and virus sequencing in persons having an outbreak infectious disease may support this theory (during or after trials). In randomized, controlled research, such sequencing likewise provides neutral details regarding variant-specific efficiency. Countries that take part in this kind of study can evaluate vaccine efficacy against regionally predominant virus strains and should have immediate access to investigational vaccinations if they have been proved to be safe and effective. In regions in which placebo-controlled experiments of novel vaccines aren't acceptable, the inclusion of an effective comparison could nevertheless yield important results [62]. The authenticity of a nonrandomized experiment wherein an effective comparator vaccination is used like the supervision depends upon the ability of prior active comparator vaccine research providing researchers with recognition accuracy into the effective comparator vaccine's effectiveness against virion variants that are currently present in the trial's communities.

Following the introduction of modified or entirely new vaccines to resolve new variants, the process could be restarted by screening for even more variants that may demand additional modifications in the vaccine antigen sequencing. Multiple varieties may propagate in the same area, therefore development and deployment plans should accommodate for this possibility. It would also be beneficial to do research in which one vaccine is supplemented with a subsequent dose of another.

2. Conclusion

The worldwide COVID-19 epidemic has been the greatest catastrophic infectious disorder into human historical life in the form of disease rates and death rates and strongly affected regions facing the high hospitalization rate and death rates still now, despite continued immunization for large populations. The appearance and outbreak of novel variants in more than 20 nations have resulted in a large increase in the number of infections and faster transmission in the affected areas. Mutated variants provide some new issues in diagnosing nucleic acid identification and the efficiency of presently offered mRNA-based, recombinant, or neutralized vaccines, such as false negativity. Due to the reemergence of community-acquired transmission in China as a result of people traveling abroad or commodities being imported, large-scale population screening has been implemented. As a result, society and small-scale pandemics have been effectively controlled. Detecting pathogenic factors, such as non-symptomatic people, infectious people with this virus, or infectious commodities, has thus become a useful tool for limiting population spread.

As previously discussed, RT-PCR seems to be the most precise as well as a rapid method for inspection and diagnosing in a huge population, whereas viral genotyping has been the most successful way for tracking contagious causes, tracking genetic changes, and defining genomic different kinds with reduced capability for particular people. The use of RT-PCR to determine infection rate is useful for tracking illness progression, therapy effectiveness, and diagnosis.

New variants of significance can originate and propagate swiftly in any area of the world, and recurrent alterations have been observed in variants of significance reported in different regions of the globe. Modifications of vaccination sequence patterns to satisfy the requirements of one state could have consequences in other

countries. As a result, vaccine research, vaccine development, and vaccine deployment should be considered global endeavors, with organizations that are facing the WHO assisting in the global distribution of benefits.

Coordination is necessary in order to determine the need for the latest or improved vaccinations and advance research knowledge about the risks presented by emerging variations and the linkages between genetic differences and immunological escape. To determine which variants of significance warrant attention, a clear and timely scientific discussion is required. Criteria are performed to evaluate the compatibility of existing vaccinations and the potential effect of developing variants on vaccinations and to support guidelines for the improvement and development of changed and new vaccines, as well as the scheduling of their implementation. This technique can expand on the global platform that the WHO utilizes on a regular basis to coordinate antigen selection in influenza vaccinations.

Author details

Naheed Akhter¹, Sadia Sana^{1*}, Muhammad Adnan Ahsan¹, Zafaar Siddique²,
Abu Huraira¹ and Somara Sana³


1 College of Allied Health Professionals Government College University Faisalabad, Pakistan

2 Faculty of Allied Health Sciences, University Institute of Radiological Sciences and Medical Imaging Technology, The University of Lahore, Pakistan

3 Saleema Siddique Maternity Home Kalar Khar Chowk, District Chakwal, Pakistan

*Address all correspondence to: sadiasana203@gmail.com

IntechOpen

© 2022 The Author(s). Licensee IntechOpen. Distributed under the terms of the Creative Commons Attribution - NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits use, distribution and reproduction for non-commercial purposes, provided the original is properly cited. 

References

- [1] Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;**579**(7798):270-273
- [2] Han GZ. Pangolins harbor SARS-CoV-2-related coronaviruses. *Trends in Microbiology*. 1 Jul 2020;**28**(7):515-517
- [3] Hacısuleyman E, Hale C, Saito Y, Blachere NE, Bergh M, Conlon EG, et al. Vaccine breakthrough infections with SARS-CoV-2 variants. *New England Journal of Medicine*. 2021;**384**(23):2212-2218
- [4] Esbin MN, Whitney ON, Chong S, Maurer A, Darzacq X, Tjian R. Overcoming the bottleneck to widespread testing: A rapid review of nucleic acid testing approaches for COVID-19 detection. *RNA*. 2020;**26**(7):771-783
- [5] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *New England Journal of Medicine*. 30 Apr 2020;**382**(18):1708-1720
- [6] Eckerle LD, Becker MM, Halpin RA, Li K, Venter E, Lu X, et al. Infidelity of SARS-CoV Nsp14-exonuclease mutant virus replication is revealed by complete genome sequencing. *PLoS Pathogens*. 2010;**6**(5):e1000896
- [7] Gribble J, Stevens LJ, Agostini ML, Anderson-Daniels J, Chappell JD, Lu X, et al. The coronavirus proofreading exoribonuclease mediates extensive viral recombination. *PLoS Pathogens*. 2021;**17**(1):e1009226
- [8] Boni MF, Lemey P, Jiang X, Lam TTY, Perry BW, Castoe TA, et al. Evolutionary origins of the SARS-CoV-2 arbovirus lineage responsible for the COVID-19 pandemic. *Nature Microbiology*. 2020;**5**(11):1408-1417
- [9] Korber B, Fischer WM, Gnanakaran S, Yoon H, Theiler J, Abfalterer W, et al. Tracking changes in SARS-CoV-2 spike: Evidence that D614G increases infectivity of the COVID-19 virus. *Cell*. 2020;**182**(4):812-27.e19
- [10] Simmonds P. Rampant C→U hypermutation in the genomes of SARS-CoV-2 and other coronaviruses: Causes and consequences for their short- and long-term evolutionary trajectories. *MSphere*. 2020;**5**(3):e00408-e00420
- [11] van Dorp L, Richard D, Tan C, Shaw LP, Acman M, Balloux F. No evidence for increased transmissibility from recurrent mutations in SARS-CoV-2. *Nature Communications*. 2020;**11**(1):1-8
- [12] Edridge AW, Kaczorowska J, Hoste AC, Bakker M, Klein M, Loans K, et al. Seasonal coronavirus protective immunity is short-lasting. *Nature Medicine*. 2020;**26**(11):1691-1693
- [13] Kistler KE, Bedford T. Evidence for adaptive evolution in the receptor-binding domain of seasonal coronaviruses OC43 and 229e. *eLife*. 2021;**10**:e64509
- [14] Eguia RT, Crawford KH, Stevens-Ayers T, Kelnhofer-Millevolte L, Greninger AL, Englund JA, et al. A human coronavirus evolves antigenically to escape antibody immunity. *PLoS Pathogens*. 2021;**17**(4):e1009453
- [15] Candido DS, Claro IM, De Jesus JG, Souza WM, Moreira FR, Dellicour S,

- et al. Evolution and epidemic spread of SARS-CoV-2 in Brazil. *Science*. 2020;**369**(6508):1255-1260
- [16] Tegally H, Wilkinson E, Giovanetti M, Iranzadeh A, Fonseca V, Giandhari J, et al. Detection of a SARS-CoV-2 variant of concern in South Africa. *Nature*. 2021;**592**(7854):438-443
- [17] Pereson MJ, Mojsiejczuk L, Martínez AP, Flichman DM, Garcia GH, Di Lello FA. Phylogenetic analysis of SARS-CoV-2 in the first few months since its emergence. *Journal of Medical Virology*. 2021;**93**(3):1722-1731
- [18] Moravian C, Pond SK, Marini S, Magalis BR, Vandamme A-M, Dellicour S, et al. Sampling bias and incorrect rooting make phylogenetic network tracing of SARS-COV-2 infections unreliable. *Proceedings of the National Academy of Sciences*. 2020;**117**(23):12522-12523
- [19] Rambaut A, Holmes EC, O'Toole Á, Hill V, McCrone JT, Ruis C, et al. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. *Nature Microbiology*. 2020;**5**(11):1403-1407
- [20] Dearlove B, Lewitus E, Bai H, Li Y, Reeves DB, Joyce MG, et al. A SARS-CoV-2 vaccine candidate would likely match all currently circulating variants. *Proceedings of the National Academy of Sciences*. 2020;**117**(38):23652-23662
- [21] Martin DP, Weaver S, Tegally H, San JE, Shank SD, Wilkinson E, et al. The emergence and ongoing convergent evolution of the SARS-CoV-2 N501Y lineages. *Cell*. 30 Sep 2021;**184**(20):5189-5200
- [22] Faria NR, Mellan TA, Whittaker C, Claro IM, Candido DDS, Mishra S, et al. Genomics and epidemiology of the P. 1 SARS-CoV-2 lineage in Manaus, Brazil. *Science*. 2021;**372**(6544):815-821
- [23] Abdool Karim SS, de Oliveira T. New SARS-CoV-2 variants—Clinical, public health, and vaccine implications. *New England Journal of Medicine*. 2021;**384**(19):1866-1868
- [24] Buss LF, Prete CA Jr, Abraham CM, Mendrone A Jr, Salomon T, de Almeida-Neto C, et al. Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic. *Science*. 2021;**371**(6526):288-292
- [25] Sabino EC, Buss LF, Carvalho MP, Prete CA, Crispim MA, Fraiji NA, et al. Resurgence of COVID-19 in Manaus, Brazil, despite high seroprevalence. *The Lancet*. 2021;**397**(10273):452-455
- [26] Gupta N, Kaur H, Yadav PD, Mukhopadhyay L, Sahay RR, Kumar A, et al. Clinical characterization and genomic analysis of samples from COVID-19 breakthrough infections during the second wave among the various states of India. *Viruses*. 7 Sep 2021;**13**(9):1782
- [27] Lucas C, Vogels CB, Yildirim I, Rothman JE, Lu P, Monteiro V, et al. Impact of circulating SARS-CoV-2 variants on mRNA vaccine-induced immunity. *Nature*. Dec 2021;**600**(7889):523-529
- [28] Challen R, Dyson L, Overton CE, Guzman-Rincon LM, Hill EM, Stage HB, et al. Early epidemiological signatures of novel SARS-CoV-2 variants: establishment of B. 1.617. 2 in England. *Medrxiv*. 2021
- [29] COVID T. An integrated national scale SARS-CoV-2 genomic surveillance network. *The Lancet Microbe*. 2020;**1**(3):e99

- [30] Chan JF-W, Yip CC-Y, To KK-W, Tang TH-C, Wong SC-Y, Leung K-H, et al. Improved molecular diagnosis of COVID-19 by the novel, highly sensitive, and specific COVID-19-RdRp/Hel real-time reverse transcription-PCR assay validated in vitro and with clinical specimens. *Journal of Clinical Microbiology*. 2020;**58**(5):e00310-e00320
- [31] Wu F, Zhao S, Yu B, Chen Y-M, Wang W, Song Z-G, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020;**579**(7798):265-269
- [32] Bru D, Martin-Laurent F, Philippot L. Quantification of the detrimental effect of a single primer-template mismatch by real-time PCR using the 16S rRNA gene as an example. *Applied and Environmental Microbiology*. 2008;**74**(5):1660-1663
- [33] Koyama T, Platt D, Parida L. Variant analysis of SARS-CoV-2 genomes. *Bulletin of the World Health Organization*. 2020;**98**(7):495
- [34] Wang R, Hozumi Y, Yin C, Wei G-W. Mutations on COVID-19 diagnostic targets. *Genomics*. 2020;**112**(6):5204-5213
- [35] Kaden R. Early phylogenetic diversification of SARS-CoV-2: Determination of variants and the effect on epidemiology, immunology, and diagnostics. *Journal of Clinical Medicine*. 2020;**9**(6):1615
- [36] Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterization and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. *The Lancet*. 2020;**395**(10224):565-574
- [37] Udugama B, Kadhiresan P, Kozlowski HN, Malekjahani A, Osborne M, Li VY, et al. Diagnosing COVID-19: The disease and tools for detection. *ACS Nano*. 2020;**14**(4):3822-3835
- [38] Hadfield J, Megill C, Bell SM, Huddleston J, Potter B, Callender C, et al. Nextstrain: Real-time tracking of pathogen evolution. *Bioinformatics (Oxford, England)*. 2018;**34**(23):4121-4123
- [39] Tang JW, Tambyah PA, Hui DS. The emergence of a new SARS-CoV-2 variant in the UK. *The Journal of Infection*. 2021;**82**(4):e27-ee8
- [40] Wang M, Fu A, Hu B, Tong Y, Liu R, Liu Z, et al. Nanopore targeted sequencing for the accurate and comprehensive detection of SARS-CoV-2 and other respiratory viruses. *Small (Weinheim an der Bergstrasse, Germany)*. 2020;**16**(32):e2002169
- [41] Meredith LW, Hamilton WL, Warne B, Houldcroft CJ, Hosmillo M, Jahun AS, et al. Rapid implementation of SARS-CoV-2 sequencing to investigate cases of health-care associated COVID-19: A prospective genomic surveillance study. *The Lancet Infectious Diseases*. 2020;**20**(11):1263-1272
- [42] Moore SC, Penrice-Randal R, Alruwaili M, Randle N, Armstrong S, Hartley C, et al. Amplicon-based detection and sequencing of SARS-CoV-2 in nasopharyngeal swabs from patients with COVID-19 and identification of deletions in the viral genome that encode proteins involved in interferon antagonism. *Viruses*. 14 Oct 2020;**12**(10):1164
- [43] Dinnes J, Deeks JJ, Berhane S, Taylor M, Adriano A, Davenport C, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database of Systematic Reviews*. 2021;(3)

- [44] Apolone G, Montomoli E, Manenti A, Boeri M, Sabia F, Hyseni I, et al. Unexpected detection of SARS-CoV-2 antibodies in the pre-pandemic period in Italy. *Tumori Journal*. 2021;**107**(5):446-451
- [45] Qiu M, Shi Y, Guo Z, Chen Z, He R, Chen R, et al. Antibody responses to individual proteins of SARS coronavirus and their neutralization activities. *Microbes and Infection*. 2005;**7**(5-6):882-889
- [46] Porte L, Legarraga P, Vollrath V, Aguilera X, Munita JM, Araos R, et al. Evaluation of a novel antigen-based rapid detection test for the diagnosis of SARS-CoV-2 in respiratory samples. *International Journal of Infectious Diseases: IJID: Official Publication of the International Society for Infectious Diseases*. 2020;**99**:328-333
- [47] Ihling C, Tänzler D, Hagemann S, Kehlen A, Hüttelmaier S, Arlt C, et al. Mass spectrometric identification of SARS-CoV-2 proteins from gargle solution samples of COVID-19 patients. *Journal of Proteome Research*. 2020;**19**(11):4389-4392
- [48] Tan YJ, Goh PY, Fielding BC, Shen S, Chou CF, Fu JL, et al. Profiles of antibody responses against severe acute respiratory syndrome coronavirus recombinant proteins and their potential use as diagnostic markers. *Clinical and Diagnostic Laboratory Immunology*. 2004;**11**(2):362-371
- [49] Kyosei Y, Namba M, Yamura S, Takeuchi R, Aoki N, Nakaishi K, et al. Proposal of de novo antigen test for COVID-19: ultrasensitive detection of spike proteins of SARS-CoV-2. *Diagnostics*. 14 Aug 2020;**10**(8):594
- [50] Grant BD, Anderson CE, Williford JR, Alonzo LF, Glukhova VA, Boyle DS, et al. SARS-CoV-2 coronavirus Nucleocapsid antigen-detecting half-strip lateral flow assay toward the development of point of care tests using commercially available reagents. *Analytical Chemistry*. 2020;**92**(16):11305-11309
- [51] Liu D, Ju C, Han C, Shi R, Chen X, Duan D, et al. Nanozyme chemiluminescence paper test for rapid and sensitive detection of SARS-CoV-2 antigen. *Biosensors & Bioelectronics*. 2020;**173**:112817
- [52] Li HY, Jia WN, Li XY, Zhang L, Liu C, Wu J. Advances in detection of infectious agents by aptamer-based technologies. *Emerging Microbes & Infections*. 2020;**9**(1):1671-1681
- [53] Mak GCK, Lau SSY, Wong KKY, Chow NLS, Lau CS, Lam ETK, et al. Evaluation of rapid antigen detection kit from the WHO emergency use list for detecting SARS-CoV-2. *Journal of clinical Virology: The Official Publication of the Pan American Society for Clinical Virology*. 2021;**134**:104712
- [54] Li HY, Yin FF, Li XY, Jia WN, Ding J, Zhang L, et al. Novel aptasensor-based assay of sonic hedgehog ligand for detection of portal vein invasion of hepatocellular carcinoma. *Biosensors & Bioelectronics*. 2021;**174**:112738
- [55] Mak GC, Cheng PK, Lau SS, Wong KK, Lau CS, Lam ET, et al. Evaluation of rapid antigen test for detection of SARS-CoV-2 virus. *Journal of Clinical Virology: The Official Publication of the Pan American Society for Clinical Virology*. 2020;**129**:104500
- [56] Scohy A, Anantharajah A, Bodéus M, Kabamba-Mukadi B, Verroken A, Rodriguez-Villalobos H. Low performance of rapid antigen detection test as frontline testing for COVID-19 diagnosis. *Journal of clinical virology*:

the official publication of the Pan
American Society for Clinical Virology.
2020;**129**:104455

[57] Krause PR, Fleming TR, Longini IM,
Peto R, Briand S, Heymann DL, et al.
SARS-CoV-2 variants and vaccines.
New England Journal of Medicine.
2021;**385**(2):179-186

[58] Muñoz-Fontela C, Dowling WE,
Funnell SGP, Gsell PS, Riveros-
Balta AX, Albrecht RA, et al. Animal
models for COVID-19. *Nature*.
2020;**586**(7830):509-515

[59] Singh JA, Kochhar S, Wolff J. Placebo
use and unblinding in COVID-19 vaccine
trials: Recommendations of a WHO
expert working group. *Nature Medicine*.
2021;**27**(4):569-570

[60] Krause PR, Fleming TR,
Longini IM, Peto R, Beral V, Bhargava B,
et al. Placebo-controlled trials of Covid-
19 vaccines - why we still need them.
The New England Journal of Medicine.
2021;**384**(2):e2

[61] Collins R, Bowman L, Landray M,
Peto R. The magic of randomization
versus the myth of real-world evidence.
The New England Journal of Medicine.
2020;**382**(7):674-678

[62] Fleming TR, Krause PR,
Nason M, Longini IM, Henao-
Restrepo AM. COVID-19 vaccine
trials: The use of active controls and
non-inferiority studies. *Clinical Trials*
(London, England). 2021;**18**(3):335-342