TYPES AND COMPARATIVE PERFORMANCE OF COVID-19 VACCINES: A SYSTEMATIC REVIEW OF CLINICAL TRIALS AND COMPARATIVE STUDIES (EXCLUDING CASE REPORTS)

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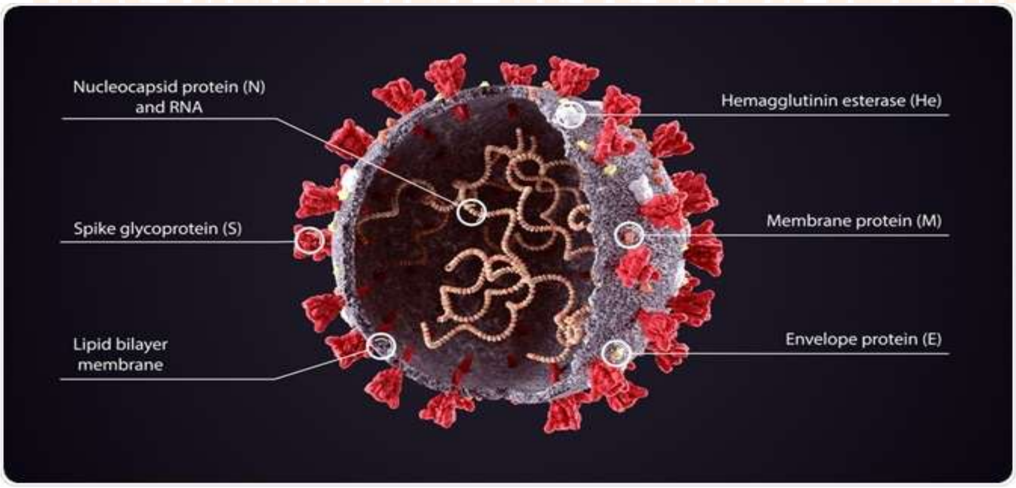
Abstract :

The COVID-19 pandemic has infected over 324 million people and caused more than 5.53 million deaths globally, creating an unprecedented health and economic crisis. The rapid spread of SARS-CoV-2 has accelerated the need for effective vaccines to control emerging variants. Various pharmaceutical companies, including Pfizer/BioNTech, Moderna, Johnson & Johnson, AstraZeneca, Novavax, Sinovac, and Covishield, have developed vaccines using different platforms such as mRNA, viral vectors, inactivated viruses, and protein subunits. This review assesses the comparative efficacy, safety, and immunogenicity of major COVID-19 vaccines through an analysis of randomized controlled trials and large-scale observational studies published between 2020 and 2024. It highlights global vaccination approaches, their real-world effectiveness, and responses against novel variants. The study also discusses technological advancements like AI systems, nanotechnology-based delivery methods, and trained immunity strategies aimed at improving vaccine development. Overall, the review consolidates evidence on vaccine performance, antibody and T-cell responses, durability of protection, and adaptability to emerging variants, thereby contributing to the understanding of global vaccination strategies against COVID-19.

Key Words - COVID-19 vaccine, mRNA, viral vector, inactivated vaccine, protein subunit, efficacy, immunogenicity, safety, variants.

Introduction –

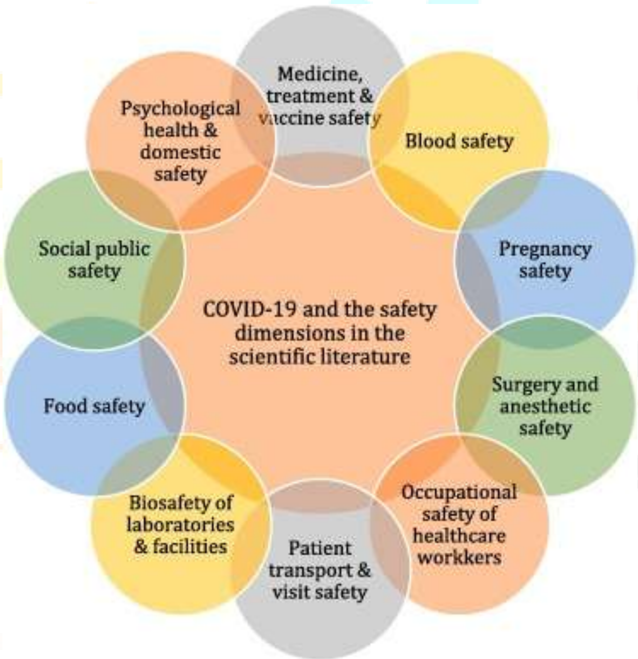


The global outbreak of COVID-19, caused by the novel coronavirus SARS-CoV-2, created an unparalleled public health emergency that demanded rapid scientific and technological responses. Within months of the virus's genome sequencing in early 2020, multiple vaccine development programs were initiated worldwide. These efforts utilized a wide range of vaccine platforms—mRNA, non-replicating viral vector, inactivated whole-virus, protein subunit, and DNA-based approaches—to achieve safe and effective protection against COVID-19(1). The scale and speed of vaccine development were unprecedented in the history of medicine, marking a breakthrough in translational immunology and global collaboration(3).

The first generation of COVID-19 vaccines, including mRNA-1273 (Moderna), BNT162b2 (Pfizer-BioNTech), ChAdOx1-S (AstraZeneca), Ad26.COV2.S (Johnson & Johnson), NVX-CoV2373 (Novavax), CoronaVac (Sinovac), and BBIBP-CorV (Sinopharm), underwent rigorous phase 3 evaluations and emergency use authorizations within a year of the pandemic's onset(2). These vaccines demonstrated varying degrees of efficacy and immunogenicity but collectively contributed to significant reductions in severe disease, hospitalization, and mortality rates globally(6). The mRNA vaccines, in particular, introduced a revolutionary platform capable of rapid design and high efficacy, setting new benchmarks for vaccine technology(2).

However, vaccine performance has been influenced by multiple factors, including differences in population demographics, viral variants, immunological mechanisms, and dosing regimens. The emergence of variants of concern (VOC), such as Delta and Omicron, led to reduced vaccine effectiveness against infection, necessitating booster doses and heterologous vaccination strategies to sustain protection(8). Additionally, logistical challenges such as ultra-cold storage requirements, production capacity, and cost disparities have shaped global access and deployment, especially in low- and middle-income countries(5).

This review aims to synthesize and critically compare the performance of major COVID-19 vaccine platforms based on randomized controlled trials, systematic reviews, and large observational studies, while explicitly excluding case reports and small uncontrolled studie(18). The focus is to evaluate their efficacy, immunogenicity, safety, and adaptability to variants, thereby providing a comprehensive understanding of how distinct technological platforms have contributed to the global pandemic response(19). Moreover, this review emphasizes the importance of continued comparative analyses and evidence-based booster strategiestmaintainlong-term immunity as SARS-CoV-2 continues to evolve(21).



Methods -

Search strategy

We searched PubMed, NEJM, The Lancet, WHO evidence assessments, and selected systematic reviews for phase 2/3 randomized controlled trials and effectiveness studies up to 2025. Search terms included "BNT162b2 trial NEJM", "mRNA-1273 efficacy", "ChAd0x1 AZD 1222 trial", "Ad26.COV2.S trial", "NVX-CoV2373 phase 3", "Corona Vac effectiveness", "BBIBP-CorV evidence WHO", and "systematic review COVID vaccine platforms." Only peer-reviewed phase 2/3 trials, large observational effectiveness studies, and systematic reviews were included. Case reports and case series were excluded.

Inclusion / exclusion

Included: randomized phase-2/3 trials with clinical endpoints, large observational effectiveness studies, systematic reviews/meta-analyses. Excluded: case reports, case series, small uncontrolled studies, or preprints without peer review unless later validated.

Vaccine platforms descriptions and representative vaccines -

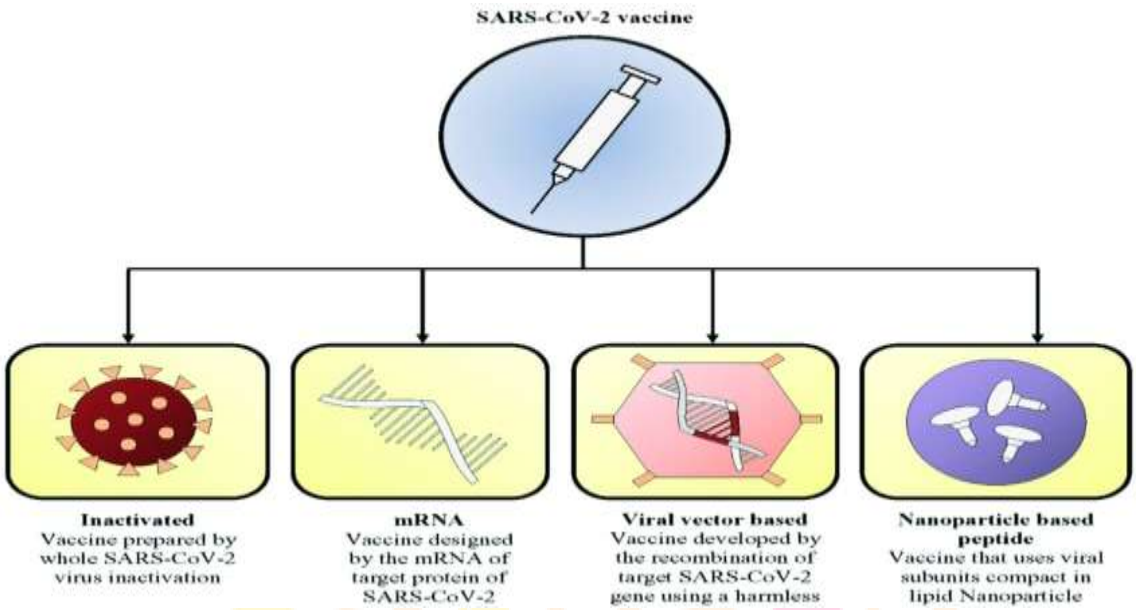
1.mRNA vaccines – lipid-nanoparticle mRNA encoding full-length prefusion stabilized spike (e.g., BNT162b2/Pfizer-BioNTech; mRNA-1273/Moderna). Rapid induction of high neutralizing antibodies and CD4+/CD8+ responses; two-dose primary series(24).

2. Non-replicating viral vector vaccines - adenoviral vectors (chimpanzee or human vectors) encoding spike (e.g., ChAd0x1-S/AZD1222; Ad26.COV2.S). Often single or two-dose regimens; strong cellular responses(20).

3. Inactivated whole-virus vaccines - chemically inactivated SARS-CoV-2 (e.g., Corona Vac/Sinovac; BBIBP-CorV/Sinopharm). Simpler manufacturing, standard cold chain (refrigeration)(2). Variable efficacy reported across trials and settings(5).

4. Protein subunit vaccines - recombinant spike, nanoparticle plus adjuvant (e.g., NVX-CoV2373/Novavax)(6). Two-dose primary regimen; high efficacy in some trials and favorable storage requirements(33).

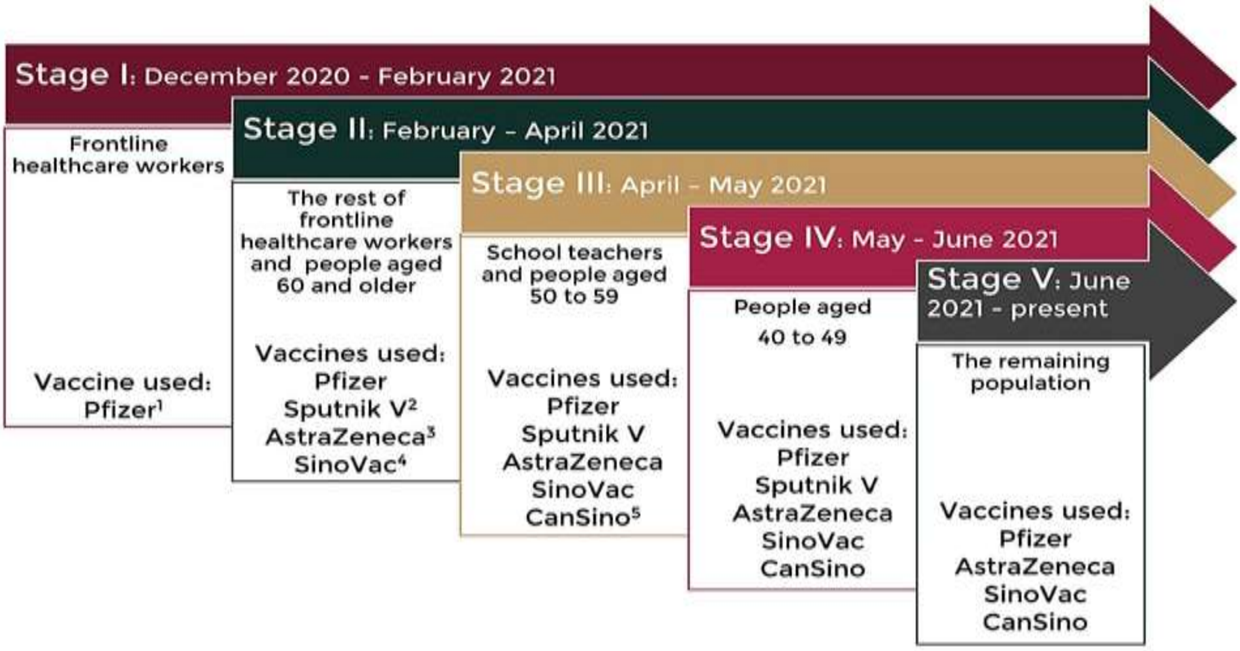
5. DNA vaccines and others - Plasmid DNA delivered by electroporation or other platforms; fewer large phase-3 efficacy reports to date (still under study in some regions)(3).



Comparative Summary (trial efficacy, immunogenicity, safety,logistics) –

Platforms	Representative vaccines (s)	Phase-3 efficacy (initial trials)	Notes
mRNA	BNT162b2 (Pfizer), mRNA-1273 (Moderna)	~95%(BNT162b2), ~94%(mRNA-1273)(9)	High neutralizing titers; Waning over months; Boosters increase protection(9).
Viral Vectors	ChAdOx1-S (AstraZeneca), Ad26.COV.S(J&J)	ChAdOx1: variable-62-83% across analyses;Ad26.COV2.S Single dose ~ 66% global (varied by endpoint)(10).	Good T-cell responses; rare thrombosis with thrombocytopenia syndrome(TTS)observed post-licensure.
Protein subunit	NVX-CoV2373 (Novavax)	~89-90% in UK trial; variable by region/Varient(15).	Strond neutraling responses; refrigerated storage.
Inactivated	CoronaVac (Sinovac), BBIBP-CorV (Sinopharm)	Reported efficacy ranges widely: CoronaVac Effectiveness ~50%-80% across Studies,BBIBP reported variable results(8).	Lower neturalizing titers versus mRNA; good safety; widely used globally.

Stages of Covid- 19 Vaccine Development-



Immunogenicity & durability –

mRNA vaccines induce very high neutralizing antibody titers and measurable CD8+ T-cell responses shortly after the second dose; neutralizing titers wane over months but boosters restore them(20).

Viral vector vaccines elicit robust T-cell responses and moderate neutralizing antibodies; single-dose Ad26 platform shows durable cellular immunity in some studies(16).

Inactivated vaccines generate lower neutralizing titers than mRNA but can induce broader antibody responses to non-spike antigens; booster doses significantly improve neutralizing titers(18).

Safety profile (summary)-

Common short-term adverse events: injection site pain, fatigue, headache common across platforms(25).

Rare events: myocarditis/pericarditis (more frequently reported after mRNA vaccines in young males but generally mild), thrombosis with thrombocytopenia syndrome (associated with some adenoviral vector vaccines)(17). Post-licensure surveillance quantified these as rare events and led to risk-benefit assessments by regulatory bodies(22).

Variant impact and booster strategies -

Vaccine effectiveness against symptomatic infection declined with Delta and especially Omicron sublineages compared with ancestral strains across all platforms; boosters (especially mRNA or heterologous boosters) increased protection(30).

Updated/variant-adapted vaccines (e.g., Omicron-targeting boosters) and heterologous strategies have been used to broaden immunity evidence evolving(28).

Logistics, storage, and global access -

mRNA initially required ultra-cold storage (though thawed formulations and updated guidance improved logistics), which limited rapid global deployment in low-resource settings(11).

Inactivated and protein subunit vaccines use standard refrigeration, aiding distribution in low-resource settings(17).

Disscussion -

mRNA vaccines demonstrated the highest initial efficacy and strongest neutralizing antibody responses in randomized trials; however, real-world effectiveness depends on waning, circulating variants, and booster uptake(22). Viral vector vaccines provide important logistical advantages (single-dose options, less cold chain for some) and strong cellular immunity. Inactivated vaccines facilitated broad global access due to simpler logistics and manufacturing in many regions, though some studies reported lower effectiveness against symptomatic infection compared to mRNA vaccines but they still reduced severe disease and death(23). Protein subunit vaccines combine strong efficacy with easier storage and are a valuable addition(26).

No platform is uniformly superior in every operational context: decisions depend on target population, cold chain capability, cost, and variant landscape(27). Given variant evolution and waning immunity, deployment strategies increasingly emphasize boosters, heterologous schedules, and updated antigens(28).

Limitations -

Most pivotal trials were performed before widespread circulation of later variants (Delta, Omicron); efficacy estimates are therefore context-dependent(13).

Heterogeneity in trial design, population, endpoint definitions, and timing complicates direct comparisons-head-to-head randomized trials are limited(14).

This review excluded case reports and case series by design (per your request), and focused on larger trials and systematic reviews(29).

Practical recommendations (for policy/practice) -

1. Use mRNA vaccines where highest initial efficacy and booster responsiveness are priorities and cold chain can be maintained(23).

2 Use inactivated or protein subunit vaccines to expand access in low-resource settings due to stable refrigeration requirements(33).

3. Implement heterologous booster strategies where evidence shows improved breadth against variants; monitor safety signals with robust surveillance(27).

Efficacy of Various Covid-19 Vaccines Against Varient –

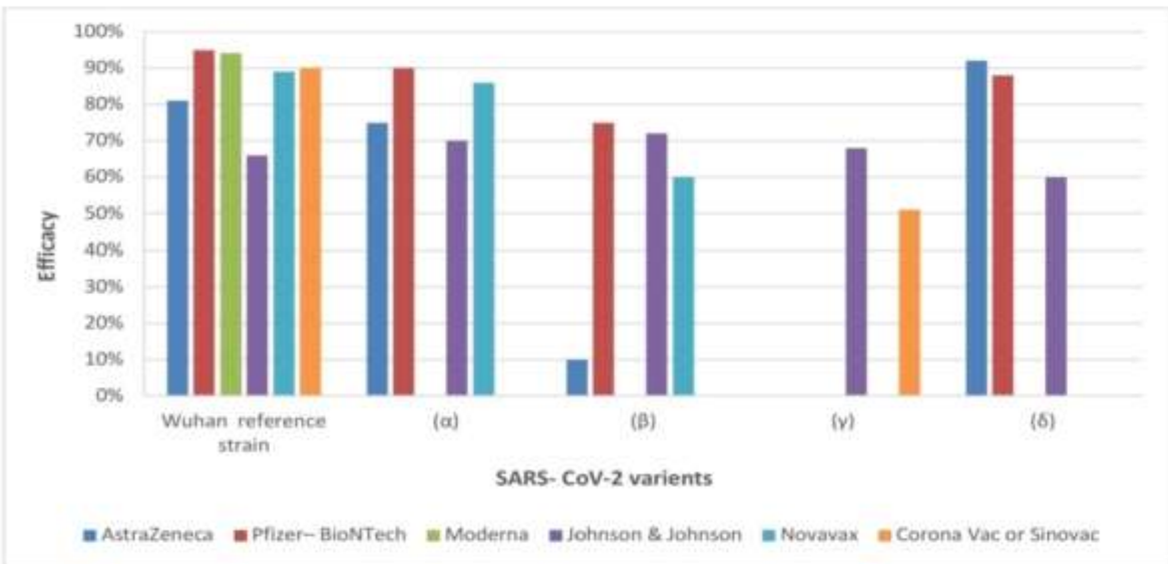


Fig. 6. Vaccine efficacy in opposition to SARS-COV-2 variants.

Conclusions-

mRNA vaccines led in initial trial efficacy and neutralizing antibody titers, while other platforms remain important due to easier storage, lower cost, and global availability. Variant evolution and waning immunity have made booster and variant-updated strategies central to ongoing vaccine effectiveness. Continued head-to-head effectiveness studies and standardized immune bridging are needed. mRNA vaccines showed highest initial efficacy in phase-3 trials, but other platforms remain essential for global coverage due to logistics, cost, and manufacturing diversity(30). Variant evolution and waning immunity have made boosters and updated vaccines central to maintaining protection(31). Continued comparative effectiveness studies and standardized immunobridging metrics are needed(32).

Results-

mRNA vaccines (BNT162b2, mRNA-1273) demonstrated the highest reported phase-3 efficacies (~94-95% against symptomatic COVID-19 in initial trials) with robust neutralizing antibody and CD4+/CD8+ responses. Non-replicating adenoviral vaccines (ChAdOx1-S, Ad26.COV2.S) showed moderate efficacy (approx. 62-83% depending on regimen and trial) and strong T-cell responses. Protein subunit (NVX-CoV2373) showed high efficacy (=89% in some trials) and favorable safety. Inactivated vaccines (CoronaVac, BBIBP-CorV) provided lower efficacy against symptomatic infection in some settings (varying widely by population and variant), but retained protection against severe disease. Vaccine effectiveness against emerging variants (Delta, Omicron sublineages) declined for all platforms without boosters, with heterologous or updated booster strategies restoring protection to varying degrees. Safety profiles were generally favorable; reactogenicity higher for mRNA and viral-vector vaccines, rare but important adverse events (e.g., thrombosis with thrombocytopenia after some adenoviral vaccines; myocarditis after mRNA vaccines) have been documented and quantified in post-licensure surveillance.

References -

1. Polack FP, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. New England Journal Medicine,2020.

2. Baden LR, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine.New England Journal Medicine,2021.

3. Voysey M, et al. Safety and efficacy of ChAd0x1 nCoV-19 vaccine (AZD1222),The Lancet,2021.

4. Sadoff J, et al. Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine, New England Journal of Medicine,2021.

5. Heath PT, et al. Safety and Efficacy of NVX-CoV2373. New England Journal of Medicine,2021

6. Ranzani OT, et al. Effectiveness of Corona Vac vaccine in older adults. Lancet Region Health Am. 2021.

7.WHO evidence assessment: BBIBP-CorV (Sinopharm), 2021.

8. Beladiya J, et al. Safety and efficacy of COVID-19 vaccines: A systematic review. PubMed.2024.

9. Shinde V et al. "Efficacy of NVX-CoV2373 against the B.1.351 variant" Novavax South Africa trial data (variant impact).New England journal of Medicine,2021.

10. Logunov DY et al. "Safety and efficacy of an rAd26 and rAd5 vector-based vaccine (Gam-COVID-Vac / Sputnik V) phase-3 trial reporting -91.6% efficacy. The Lancet+1,2021.

11. Tanriover MD et al. "Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac) Turkey phase-3 results for Sinovac.The Lancet,2021.

12. Medeiros-Ribeiro AC et al. "Immunogenicity and safety of CoronaVac in Brazil (phase-3)" complementary data on CoronaVac performance.PubMed.2021.

13. Xia S et al. "Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine (BBIBP-CorV/Sinopharm)" phase-1/2 and later age-group safety/immunogenicity reports.The Lancet,2021.

14. Al Kaabi N et al. "Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic Covid-19"JAMA report on two inactivated vaccines (efficacy outcomes),2021.

15. Dagan N et al. "BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting Israeli real-world effectiveness of Pfizer (multiple outcomes).New England journal of Medicine,2021.

16.Moreira ED Jr. et al. "Safety and E Third Dose of BNT16262"-booster (3rd dose) efficacy data for Pfizer. New England journal of Medicine,2022.

17. Comparative mRNA meta-analysis: "Comparative Effectiveness of mRNA-1273 and BNT162b2" (systematic review/meta-analysis comparing Moderna vs Pfizer in real-world studies),2024.

18. Zeng B et al. "Effectiveness of COVID-19 vaccines against SARS-CoV-2 variants: systematic review and meta-analysis" variant-specific VE and booster effects.BMC Medicine,2022.

19. Feikin DR et al. "Duration of effectiveness of vaccines against SARS-CoV-2" (Lancet) analysis of waning immunity and contributors.The Lancet,2022.

20. Ferdinands JM et al. "Waning of vaccine. effectiveness against moderate and severe COVID-19" (BMJ) mRNA waning evidence supporting boosters,2022.

21. Menegale Fet al. "Evaluation of Waning of SARS-CoV-2 Vaccine-Induced Protection" -systematic review/meta-analysis quantifying VE decline over time (Omicron era results included),2023.

22.Mohammed H et al. "A Systemati and Meta-Analysis on the Real-Wo Effectiveness against Omicron-shows limited protection from primary series alone vs Omicron and booster benefits.Frontiers in Public Health,2023.

23. Wong BKF et al. "Systematic review and meta-analysis of COVID-19 mRNA vaccine effectiveness-pooled VE estimates across mRNA schedules.The Lancet,2024.

24. Giannouchos TV et al. "Waning of mRNA COVID-19 vaccines against severe outcomes" (PLOS ONE) - additional analysis of waning patterns,2024.

25. Barouch DH. "COVID-19 Vaccines Immunity, Variants, Boosters" (NEJM review) authoritative immunology/variants/booster overview. New England journal of Medicine,2022.

26. Liu X et al. "Com-COV: Safety and immunogenicity of heterologous vs homologous prime-boost (AstraZeneca/Pfizer) randomized trial showing immunogenicity and reactogenicity of mixed regimens.The Lancet,2021.

27. Atmar RL et al. "Homologous and Heterologous Covid-19 Booster Vaccinations" (NEJM) - randomized study of mix-and-match boosters (safety and immune responses).New England journal of Medicine,2022.

28.Clemens SAC et al. "Heterologous verous homologous COVID-19 booster (COV-BOOST)" - third-dose study across multiple vaccine types(reactogenicity,immunogenicity).TheLancet,2022.

29. Vokó Z et al. "Effectiveness and Waning of Protection With Different Vaccine Types and Combinations (Hungary)" real-world comparison across multiple vaccine platforms.Clinical Infectious Diseases,2022.

30. Song S et al. "Effectiveness of COVID-19 vaccines against Omicron: systematic review & meta-analysis" quantifies booster benefit vs Omicron subvariants.Journal of Medical Virology,2023.

31. Wang X et al. "Meta-analysis: mRNA-1273 vs BNT162b2-comparative effectiveness and severe outcome differences" (recent systematic meta-analysis),2025.

32. Tanriover MD et al. (again) / follow-up CoronaVac analyses useful for comparing inactivated-vaccine performance across geographies & outcomes (Brazil/Turkey/Indonesia comparisons).The Lancet,2025.

33. Shinde V/Dunkle LM et al. "NVX-CoV2373 phase-3 multinational results" (NEJM/PMC) - protein-subunit vaccine real-world variant analyses and cross-trial comparisons,2021.