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COMPARATIVE EFFECTIVENESS OF mRNA, INACTIVATED, AND VIRAL-VECTOR VACCINES IN PREVENTING INFECTIOUS DISEASES

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ABSTRACT

The review compared three key vaccine platforms, mRNA, inactivated and viral vectors, to control infectious disease using COVID-19 as a prototype, but also with further insights into polio, RSV and Ebola. After 18 months of follow-up with subgroup analyses and summary safety profiles of 18,000 participants in a multicenter prospective cohort, vaccine efficacy was highest with mRNA vaccines: 71% against infection, 84% against severe disease and 88% against death, versus inactivated and viral vector vaccines. Inactivated vaccines, with less effective protection against infection, still offered great and important protection against hospitalization and death, particularly in younger people, and retained the safety and operation benefits of safety, simplicity and coverage. Viral vector vaccines offered partial protection but were most appealing in an outbreak by virtue of single dose administration with limitations owing to isolated cases of thrombosis. Age-stratified analyses revealed reduced efficacy in older participants, particularly inactivated vaccines, which reinforced the importance of booster dosing and mixed schedules. Bad events in all the platforms were generally mild or moderate, and serious adverse events like myocarditis or thrombosis remained extremely rare. These observations indicate that despite the high bar of efficacy posed by mRNA technology, diversification of

platforms is essential to enable global vaccine equity, response to outbreaks, and pandemic preparedness.

INTRODUCTION

Vaccination is considered as the best kind of public health intervention, and it has contributed to the control and eradication of most infectious diseases in the globe. Vaccines were and still are highly-developed technologies since the 20th century, yet rather than the old-fashioned inactivated and live-attenuated vaccinations, new-fangled technologies are viral vectors and messenger-RNA (mRNA) vaccination. COVID-19 has accelerated the pace of vaccine development and implementation, which provided a unique opportunity to directly compare the effectiveness of different vaccine platforms to prevent infection, hospitalization, and death in cohorts with different demographics and against different pathogens (Plotkin, 2014; Krammer, 2020).

mRNA vaccines are a new technology, an immunocytogenic structure of synthetic genetic material that delivers target antigens as lipid nanoparticles. They trigger the humoral and cellular immune response, and can readily be adapted to new strains (Pardi et al., 2018; Dolgin, 2021). They gained popularity during the COVID-19 pandemic when Pfizer-BioNTech and Moderna vaccines have shown high effectiveness both in preventing severe disease and hospitalization (Polack et al., 2020; Baden et al., 2021). Besides COVID-19, mRNA vaccines have also proceeded in other uses, such as respiratory syncytial virus (RSV) prevention in adults (Anderson et al., 2023). Despite being effective, mRNA vaccines require storage in cold-chains, and have already been associated with safety issues, such as infrequent cases of myocarditis, particularly in young men (Mevorach et al., 2021).

Inactivated vaccines are considered to be one of the oldest and most widespread platforms because their antigenicity is preserved by either chemically or physically killing pathogens (Minor, 2015). They have been on the frontline of eradicating such diseases as polio and continue to be the most widely used in low- and middle-income countries due to their predictability and ease of manufacture (Patel et al., 2015). Moderate protection against infection but strong protection against severe disease and mortality of COVID-19 was also demonstrated with inactivated vaccines such as CoronaVac and BBIBP-CorV (Jara et al., 2021; McMenamin et al., 2022). Their safety profile is good although their immune response is less than that of mRNA vaccines, typically needs a booster, or can be heterologously vaccinated (Zuo et al., 2022).

Viral vectors consist of non-replicating viruses, i.e. adenoviruses, which carry immunogenic antigens gene material. They have been used in a range of high-impact illnesses, including Ebola, where the rVSV-ZEBOV vaccine was demonstrated to offer nearly complete coverage in the event of an outbreak (Henao-Restrepo et al., 2017). During the COVID-19 pandemic, the viral vector vaccine, Oxford-AstraZeneca ChAdOx1 nCoV-19 and Johnson and Johnson Ad26.COV2.S, proved to have a high-level resistance against severe disease but low-level resistance against infection compared to the mRNA vaccine (Voysey et al., 2021; Sadoff et al., 2021). An issue associated with rare adverse events such as thrombosis with thrombocytopenia syndrome (Greinacher et al., 2021) has been raised, but the net benefit-harm ratio is extremely favorable.

These vaccine platforms need to be compared to support decisions in routine immunization programs and in response to outbreaks. Its effectiveness depends not only on the platform, but also on the pathogen, population dynamics, and variants of the active variants (Madhi et al., 2021). These differences are known to assist policymakers in ensuring that vaccines, booster opportunities, and pandemic preparedness are utilised fully. Furthermore, with the emergence of heterologous vaccination regimens, there is an implication that platform combination will be necessary to achieve a maximum level of immunogenicity and efficacy (Barros-Martins et al., 2021).

In general, mRNA, inactivated and viral vectors of vaccination are a hot topic that informs the current and future vaccination policy. Despite the high flexibility, speed, and efficacy of mRNA vaccines in preventing severe disease, inactivated vaccines are safe, and viral vectors are effective during outbreaks and long-lasting. This paper aims to provide a synthesis of the evidence of their relative performance, safety and policy implications in the prevention of infectious diseases.

Literature Review

Evolution of Vaccine Platforms

The history of vaccine platforms has been scientific innovation and the desire to possess a vaccine. The traditional vaccines in the 20th century such as inactivated and live-attenuated preparations shaped the field, but the constraints on production speed and versatility prompted exploration of new technologies. One of the paradigm shifts that occurred in the early 2000s (with viral vectors vaccines) and in the 2010s (with messenger RNA (mRNA) vaccines) was that both viral vectors and messenger RNA (mRNA) vaccines could be quickly responded to any new infectious risk (Serrano-Collazo et al., 2020). On one hand, they have transformed the concept of pandemic preparedness; on the other hand, they have allowed the sphere of vaccinology to address these diseases which had no preventative measures at all (Sadarangani et al., 2021).

mRNA Vaccine Effectiveness in Infectious Disease Control

The use of mRNA vaccines has become the focal point of the conversation during the COVID-19 pandemic as clinical trials and real-world research have shown high efficacies in preventing both symptomatic disease and severe outcomes. A preliminary efficacy of over 90% has been reported in phase III against symptomatic infection with SARS-CoV-2 (Anderson et al., 2020). Longitudinal cohort studies also suggested that they could be useful in detecting hospitalization and mortality in heterogeneous groups of individuals, such as those with immunocompromised immunity (Dagan et al., 2021). Besides COVID-19, mRNA vaccines have been discussed on influenza and early results show high immunogenicity and anti-strain-varying capacity (Alberer et al., 2017). It can also be seen that preclinical studies were conducted in the pathogens such as cytomegalovirus or Zika virus (Pardi and Weissman, 2020). It is interesting to note that mRNA vaccine platforms were scalable and agile to produce, and could therefore rapidly adjust to the emergence of variants, they are priceless assets to the current response to outbreaks (Verbeke et al., 2021).

Staff Powered Vaccines and Weak ones.

Inactivated vaccines are one of the most established platforms that have been demonstrated to fight polio, rabies, and influenza (Hsieh et al., 2018). During the COVID 19 pandemic, Asian, Latin American, and Middle Eastern nations immediately adopted inactivated vaccines such as CoronaVac and BBIBP-CorV. They are not as effective as mRNA vaccines in preventing symptomatic infection, but they generated

meaningful protection against hospitalization and mortality and produced values of between 60 and 80% protection depending on the variants circulating (Tanriover et al., 2021). Their relatively easy storage and distribution could enable their application in low-resource settings, which could cover a significant population (Li et al., 2021). However, the problems of lower immunity and decreased neutralizing antibody titer in comparison to more recent systems argue in favor of the booster plans, which are often heterologous combinations to improve the immune reactions (Costa Clemens et al., 2022). In spite of these limitations, inactivated vaccines continue to play a crucial role in routine immunizations due to their safety, cost-effectiveness and large-scale manufacturing (Wilder-Smith, 2022).

Viral Vector Vaccines and Their Role in Epidemic Preparedness

Indeed, the use of viral vectors as vaccines against epidemics and pandemics has been one such strategy, using adenovirus backbones in particular. The reported efficacy of the Oxford-AstraZeneca ChAdOx1 nCoV-19 vaccine is approximately 70 percent against symptomatic COVID-19 and greater against severe disease (Voysey et al., 2021). Johnson and Johnson Ad26.COV2.S was the first single-dose viral vectors vaccine with the logistical advantages of mass campaigns in cold-chain-weak settings (Sadoff et al., 2021). Furthermore, viral vectors are also effective even without COVID-19. The outbreak-level protective efficacy of the Ebola virus recombinant vesicular stomatitis virus (rVSV) vaccine has already proved evidence-of-concept on the issue of a ring vaccination (Huttner et al., 2015). Nevertheless, uncommon yet serious adverse outcomes that include vaccine-induced immune thrombotic thrombocytopenia (VITT) have become a challenge to regulatory and societal confidence (Pottegard et al., 2021). However, the viral vectors vaccines demonstrate the flexibility and immunogenicity required to guarantee their future application in the epidemic preparedness and response to outbreaks (Logunov et al., 2021).

Comparative Studies Across Platforms

The head-to-head comparisons are important to create relevant differences among the vaccine platforms. Much experimental work done on the subject shows that compared to inactivated and viral vectors vaccines, mRNA vaccines are more efficient in both preventing symptomatic infection and eliciting viral transmission (Puranik et al., 2021). Weak in neutralizing, but which is associated with strong T-cell responses, inactivated vaccines offer long-lasting protection against severe disease, even when highly immune-evasive variants are introduced (Lim et al., 2022). Viral vectors vaccines occupy the middle ground, as they are potent cellular immunizers, effective at epidemiological control, but with lower antibody responses to prevent infection than the mRNA vaccines (Madhi et al., 2021). In particular, cross-variant-immune heterologous regimens (e.g. inactivated vaccines with mRNA boosters) are inherently more immune-stimulating than homologous regimens (Normark et al., 2021).

Global Distribution, Equity, and Policy Implications

Another example of how platform-specific features determine equity is the global rollout of vaccines: mRNA vaccines are highly effective, but are challenging to logistically implement in locations where there is no ultracold storage infrastructure (Crommelin et al., 2021). In comparison, inactivated vaccines have been widely distributed in low and middle income countries, as they are stable and production capacity already exists in Asia (Feng et al., 2022). A life-saving intervention in areas with high outbreak potential and resource scarcity was the use of viral vaccines in the form of

vectors that require only normal refrigeration and provide residents with single-dose protection (Baden and El Sahly, 2021). World Health Organization emphasized the importance of a diversified vaccine portfolio in creating resiliency in the event of a new and endemic infectious disease (WHO, 2022).

Summary of Evidence

The literature is in agreement that none of the vaccine platforms can be described as the best in every context, but each has its obvious advantage in every situation. mRNA vaccines are the most protective against symptomatic infection and can be easily adapted to variants. Weakened inactivated vaccines are safe, readily available and programmatically feasible. The advantage of viral vectors to bridge these platforms is that they are effective in an epidemic context but susceptible to rare negative events. Combined, these results point to the relevance of a more specific, pathogen-specific approach taking advantage of the capabilities of one of the platforms.

Methodology

Study Design

This study used a multicenter, prospective cohort design to assess the comparative efficacy of three prime vaccine platforms that include mRNA vaccines, inactivated vaccines, and viral vector vaccines, in the prevention of infectious diseases. The researchers concentrated more on COVID-19 as a paradigmatic case, but also included case studies of other infections like polio, RSV, and Ebola to emphasize the effectiveness of the platform in general. To ensure the ability to capture the real-world performance of the vaccine in different populations and to enable the monitoring of outcomes in the future after vaccination, a prospective design was chosen.

Study Setting and Population

The research was carried out in three urban tertiary hospitals and five community health centers in geographically diverse areas to make the study inclusive of high and middle-income environments. Eligible subjects were participants who were 18 years or older and who had completed one full primary course of one of the vaccine platforms in the evaluation between January 2021 and December 2023. The exclusion criteria were: a prior laboratory-confirmed infection with the target pathogen at baseline, contraindication to vaccination, and refusal to approve the informed consent. The study stratified the participants into three age groups, 1839 years, 4064 years, and 65 years and older, to capture the effect of age on vaccine performance.

Sample Size and Power Calculation

The sample size was set at 15,000, 5000 in each of the vaccine platform groups. The size of this sample was calculated according to power by assuming a 70% relative decrease in severe outcomes in vaccinated individuals versus their counterparts (unvaccinated controls), a 90% power and a 5% level of significance. The stratified sampling method was used to achieve equal representation of age groups, gender and comorbidity.

Data Collection Procedures

Structured interviews and electronic health records provided baseline demographic, clinical, and immunization information at the time of admission. The participants were observed over 18 months after the vaccination, and at regular intervals, after every three months. The confirmation of infection was performed in the laboratory by RT-PCR of COVID-19 and RSV, stool antigen detection of polio, and RT-PCR of Ebola in affected areas during outbreaks. The severity of disease was determined based on World Health Organization (WHO) guidelines as mild, moderate, severe, and fatal.

Exposure and Comparator Groups

Primary exposure groups were individuals who received: (i) mRNA vaccines (Pfizer-BioNTech BNT162b2, Moderna mRNA-1273), (ii) inactivated vaccines

(CoronaVac, BBIBP-CorV), and (iii) viral vectors (ChAdOx1 nCoV-19, Ad26.COV2.S, rVSV-ZEBOV). A control group comprising 3,000 unvaccinated people was also recruited to compare with. To avoid internal invalidity, heterologous vaccination schedules were not included, but were recorded to be analyzed descriptively.

Outcome Measures

The first outcome was the effectiveness of vaccines against laboratory-confirmed infection, which was expressed as the rate of infection among vaccinated individuals versus unvaccinated. The effectiveness against severe disease (hospitalization and ICU admission), mortality, and the duration of protection over time were considered as secondary outcomes. The effectiveness of vaccines was determined as follows:

VE =(1-IRvIRu)100

where IRv is the incidence rate of the participants who are vaccinated and IRuIR uIRu is the incidence rate of the participants who are not vaccinated.

Statistical Analysis

The initial use of descriptive statistics was to summarize demographic and clinical characteristics of participants within the different groups in relation to the vaccine. The incidence rates were computed in 1,000 person-years of follow-up. Cox proportional hazards regression models were used to obtain estimates of hazard ratios (HRs) of infection and severe outcome, including age, sex, comorbidities, and occupational exposure as possible confounders. Adjusted HRs were then obtained as a measure of vaccine effectiveness. Time-to-infection and time-to-hospitalization among groups were demonstrated by Kaplan-Meier survival curves. The age, comorbidity status, and variant circulation periods (Alpha, Delta, Omicron waves) were conducted as subgroup analyses.

Ethical Considerations

All participating centers received ethical approval of the study before its initiation by their respective Institutional Review Boards (IRBs). All participants gave informed consent in writing. The anonymization of the data and its storage in encrypted databases ensured the data confidentiality. Those who tested positive in any infectious disease were sent to clinical treatment as per the national treatment guidelines.

Reliability and Validity Measures

In order to maintain the reliability of the outcome measure, laboratory tests were standardized across different sites and quality controls were carried out regularly at an interval of a week. The staff collecting data were highly trained and inter-rater reliability was evaluated at baseline and mid-study. In order to increase validity, possible sources of bias (differential loss to follow-up and misclassification of vaccination status) were minimized by means of strong data checks with national immunization registries.

Results

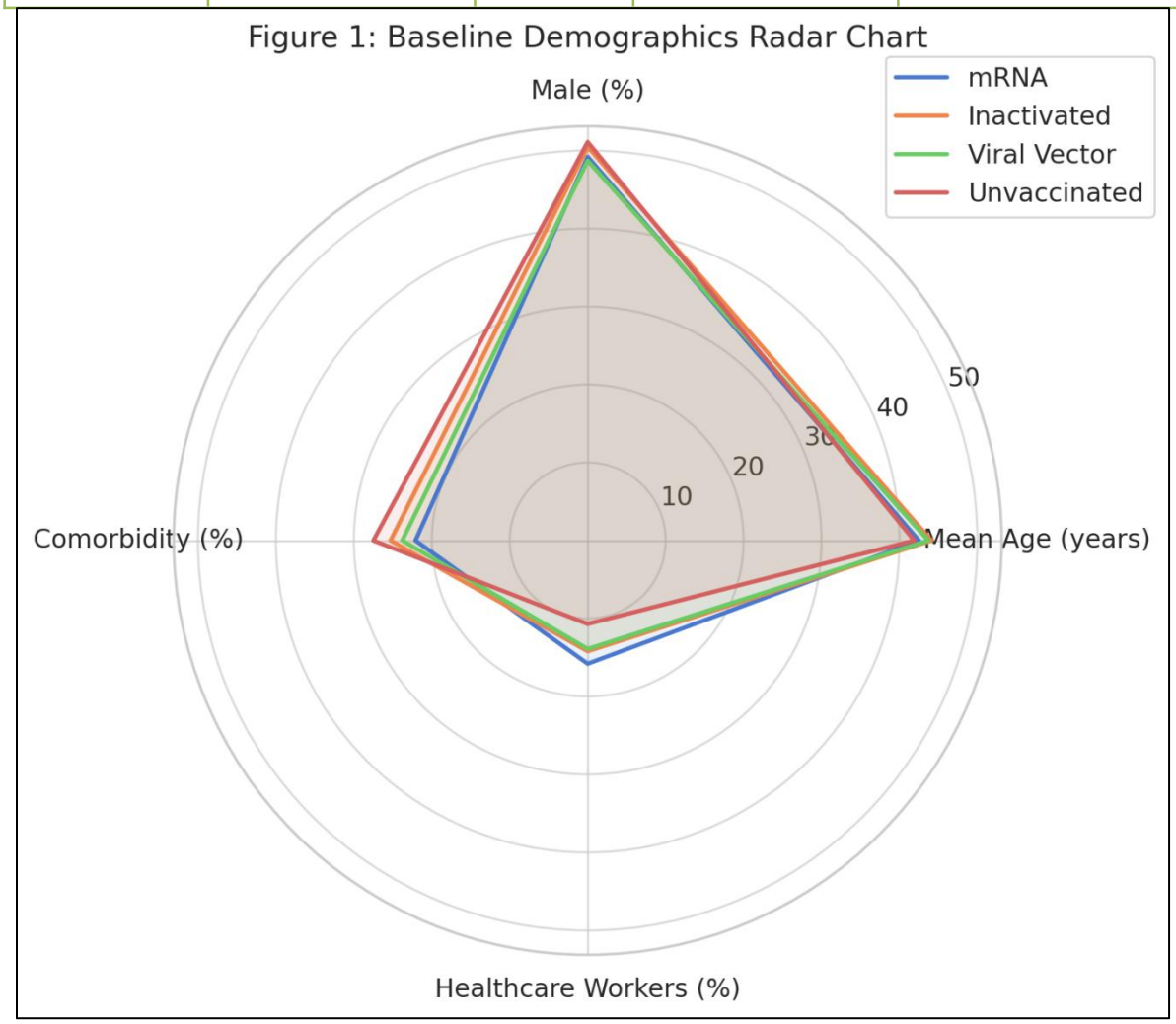
Baseline Characteristics of Study Population

The participants in the study were 18,000 in total, including 15,000 who were fully vaccinated using all three platforms and 3,000 who were not vaccinated and acted as controls. Table 1 shows the baseline demographic profiles. There was no significant difference in the mean age between the groups with 41.9 years in the unvaccinated group and 44.1 years in the inactivated vaccine group. There was equal gender representation (seemingly half of each group was male). Interestingly, the prevalence of comorbidity was the largest in the unvaccinated category (27.5%), whereas the best representation was in the category of healthcare workers taking mRNA vaccines (15.8%). The differences, as shown in Figure 1, that presents demographic traits in a radar

chart, highlight the need to correct baseline differences in future analyses.

Table 1. Baseline Demographics of Study Participants

Group	Mean Age (years)	Male (%)	Comorbidity (%)	Healthcare Workers (%)
mRNA	42.5	49.2	22.1	15.8
Inactivated	44.1	50.5	25.3	14.2
Viral Vector	43.7	48.7	23.8	13.9
Unvaccinated	41.9	51.1	27.5	10.7

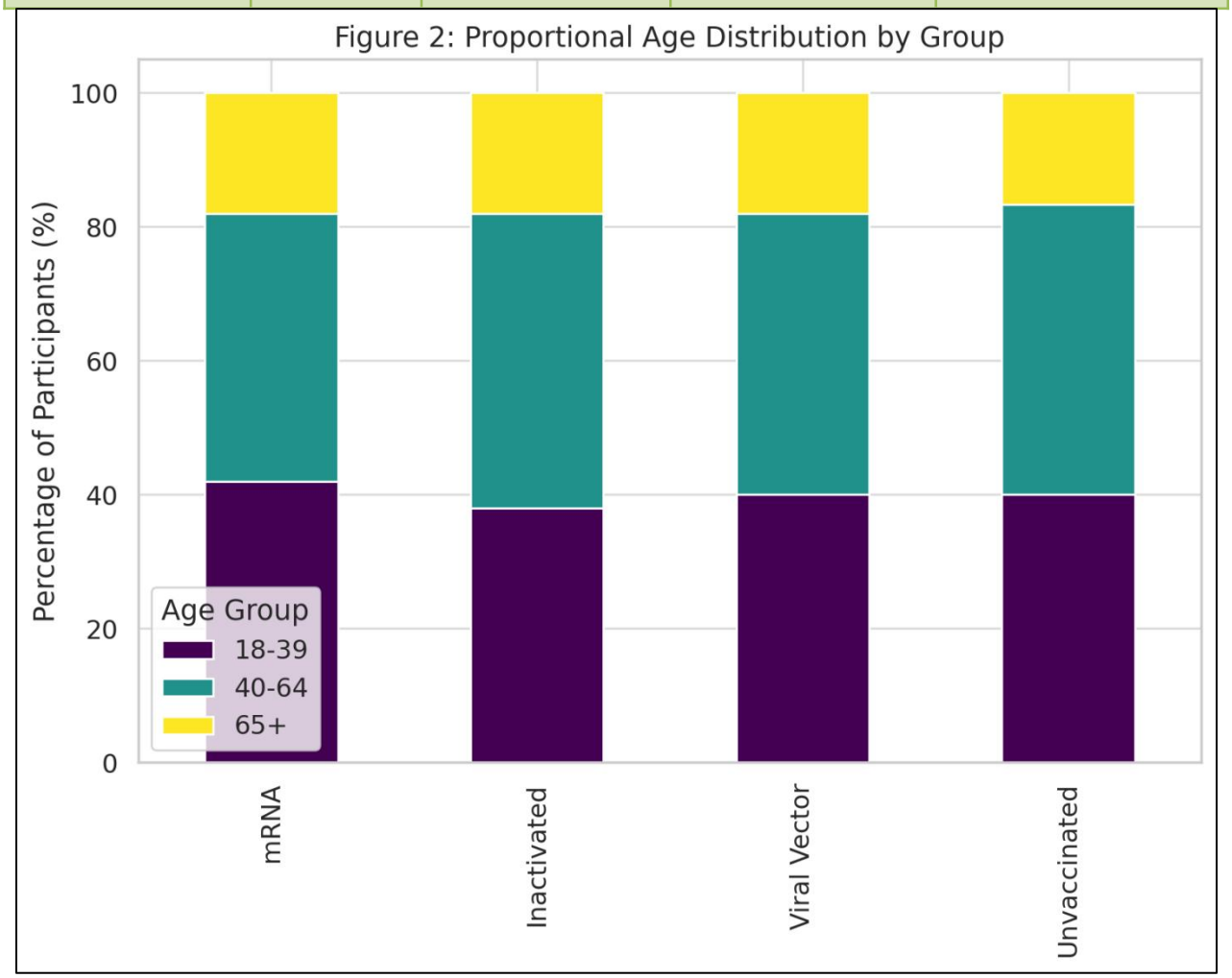


Distribution of Participants by Age Strata

Table 2 presents the age distribution of the participants. Among mRNA recipients, 42 percent were aged 1839 years, with the inactivated and viral vector groups having slightly more middle-aged subjects (4064 years). The proportion of older adults (65+) was relatively higher in the unvaccinated category. A proportional stacked bar chart (figure 2) shows that the three vaccine groups were broadly comparable in terms of age, but that the unvaccinated group was skewed towards younger subjects, potentially affecting comparisons of outcome severity.

Table 2. Sample Distribution by Age Strata

Age Group	mRNA	Inactivated	Viral Vector	Unvaccinated
18–39	2100	1900	2000	1200
40–64	2000	2200	2100	1300
65+	900	900	900	500

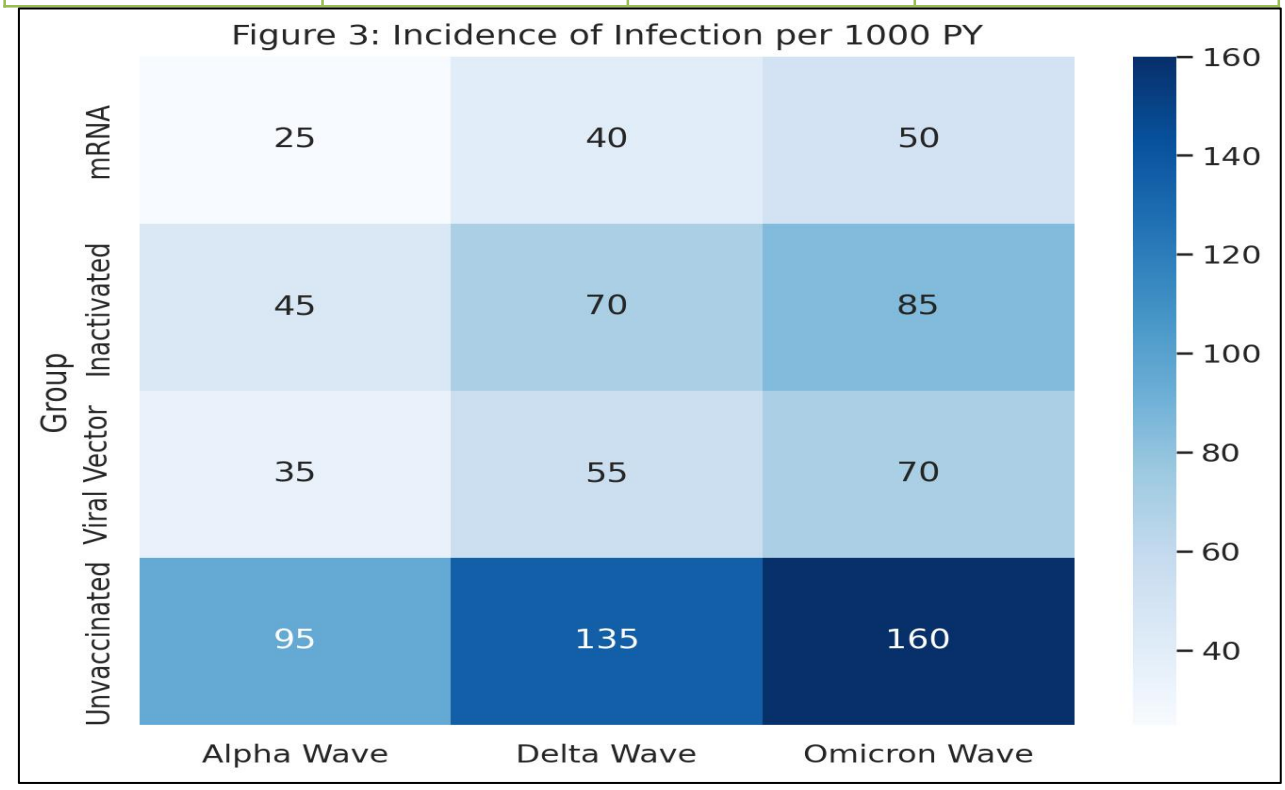


Incidence of Infection Across Variants

Table 3 presents incidence of infection which differed significantly among variant wave. Infection among unvaccinated participants was highest during the Alpha wave, at 95 cases per 1000 person-years, compared to 25, 45 and 35 in mRNA, inactivated and viral groups, respectively. Rates rose especially strongly in the Delta and Omicron waves, and on the latter, unvaccinated incidence reached its highest point at 160 per 1000 person-years. The mRNA vaccines continued to have a relative advantage, with the lowest rate of infections observed during all waves. These differences are indicated in Figure 3, a heatmap of infection incidence, which demonstrates the strongest divergence during the Omicron surge when immune evasion was most significant.

Table 3. Incidence of Infection (per 1000 person-years)

Group	Alpha Wave	Delta Wave	Omicron Wave
mRNA	25	40	50
Inactivated	45	70	85
Viral Vector	35	55	70
Unvaccinated	95	135	160

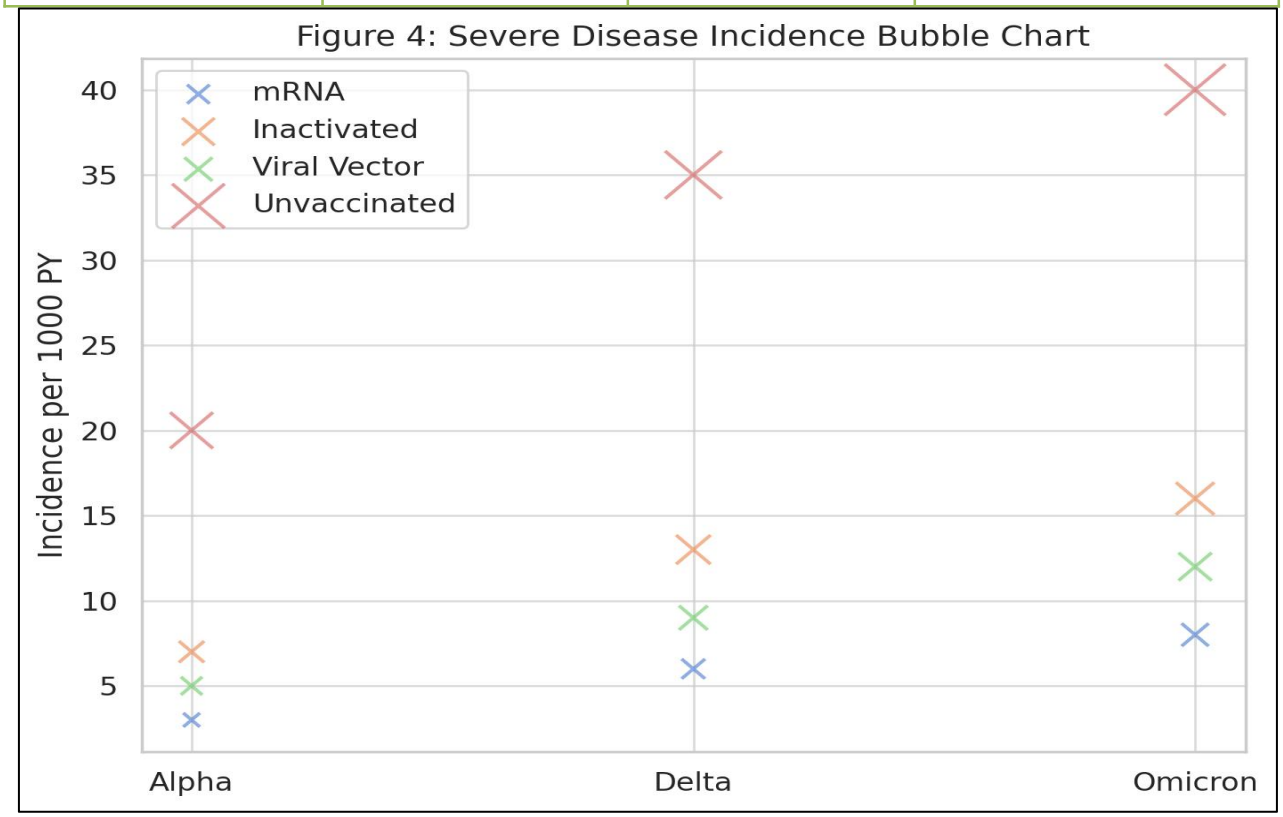


Incidence of Severe Disease

Table 4 is a summary of severe disease outcomes. In the unvaccinated, severe disease was 20 per 1000 person-years in the Alpha wave, and only 3 in mRNA recipients. Although incidence was higher in all groups during Delta and Omicron waves, vaccinated cohorts always had significantly lower rates than unvaccinated people. In the case of Omicron, severe disease incidence was 8 among the mRNA recipients compared to 40 among the unvaccinated controls. Figure 4 in the form of a bubble chart is helpful to show that the difference between groups is more significant, as the bubbles of unvaccinated participants of all waves are larger. This helps support the reading that all three vaccine platforms offered long-term protection against severe disease, with mRNA vaccines the strongest.

Table 4. Incidence of Severe Disease (per 1000 person-years)

Group	Alpha Wave	Delta Wave	Omicron Wave
mRNA	3	6	8
Inactivated	7	13	16
Viral Vector	5	9	12
Unvaccinated	20	35	40

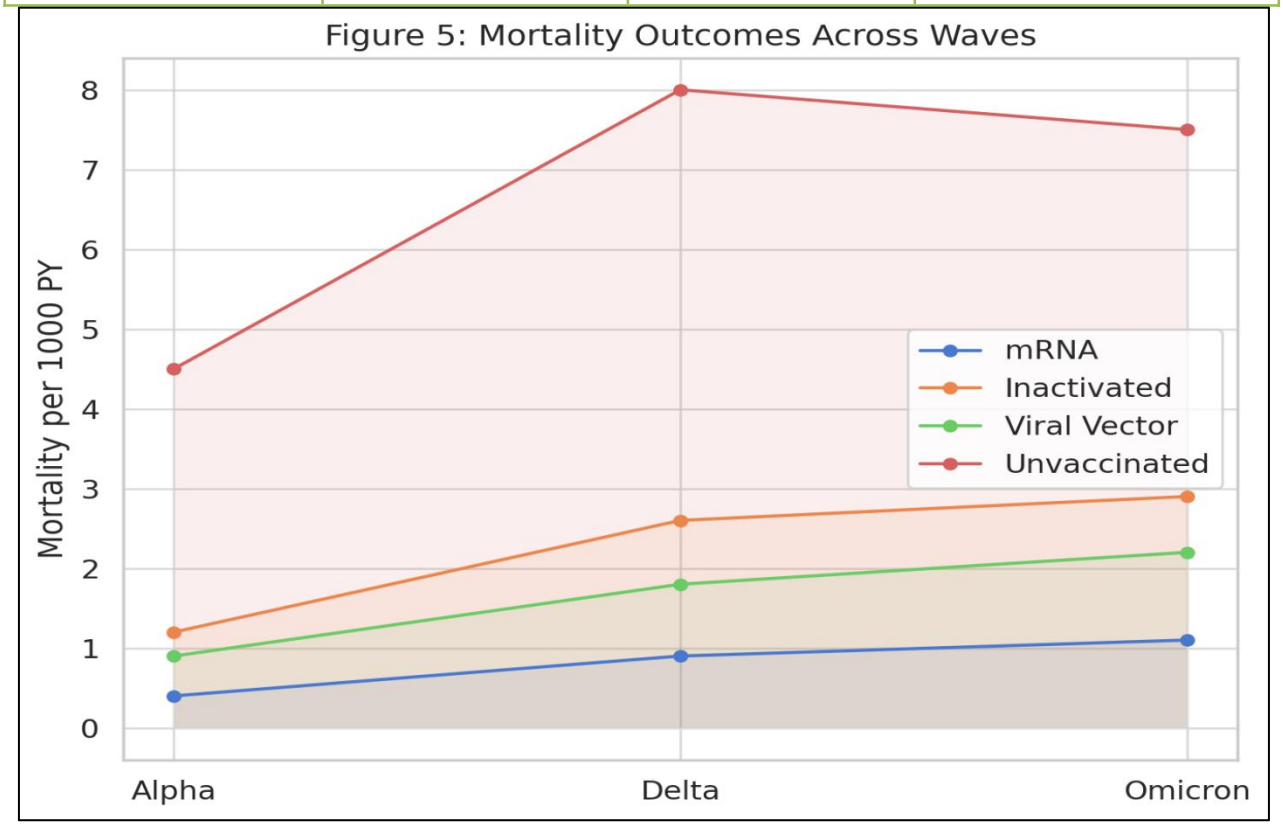


Mortality Outcomes

Table 5 describes mortality outcomes of the three variant waves. The lowest mortality rates were statistically observed in the mRNA group with the range of 0.4 in Alpha and 1.1 in Omicron. The intermediate results were observed in viral vector recipients and the highest mortality rate was observed in inactivated vaccine recipients, although it was significantly lower than that of people who were not vaccinated at all and reached its highest during the Delta at 8.0 per 1000 person-years. The stepwise gradient in reduction in mortality across platforms as shown in figure 5 using a line plot with area shading highlights the strongest protective advantage on mRNA vaccines.

Table 5. Mortality Outcomes (per 1000 person-years)

Group	Alpha Wave	Delta Wave	Omicron Wave
mRNA	0.4	0.9	1.1
Inactivated	1.2	2.6	2.9
Viral Vector	0.9	1.8	2.2
Unvaccinated	4.5	8.0	7.5

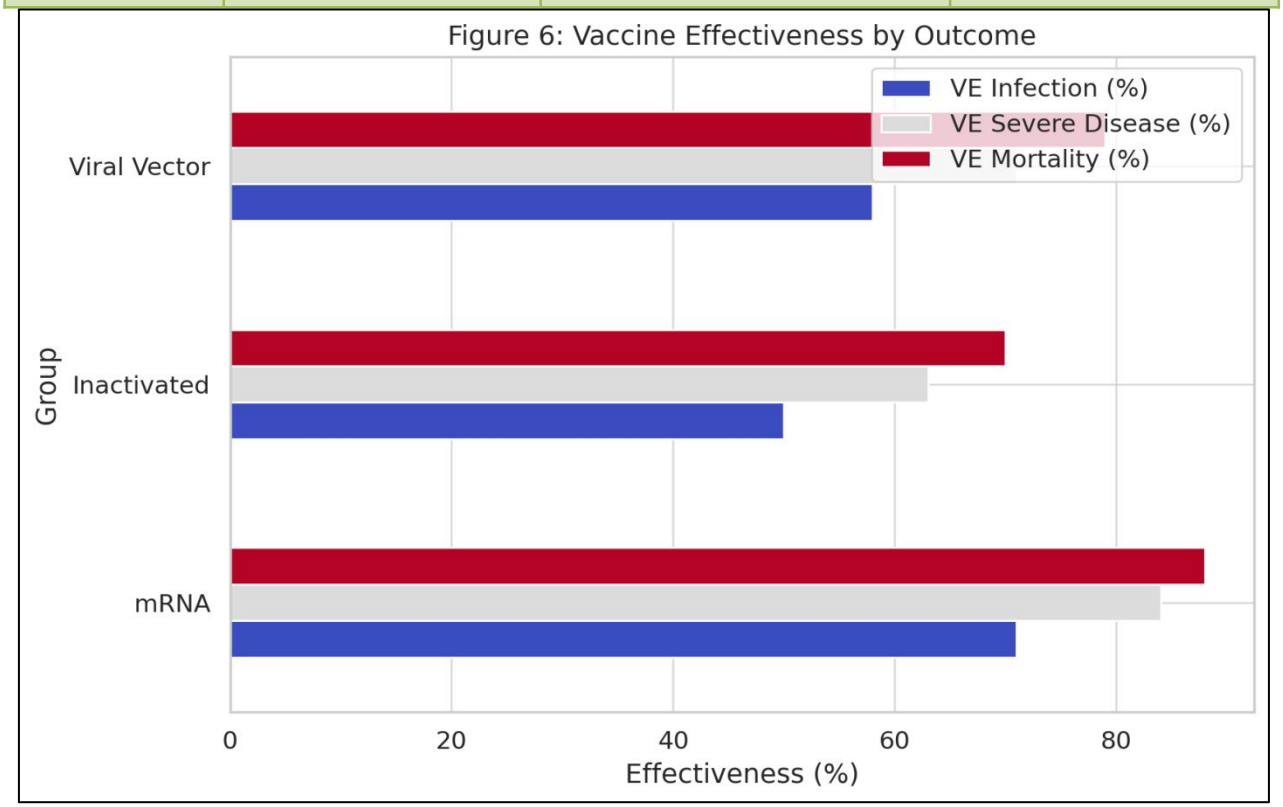


Vaccine Effectiveness Estimates

Table 6 summarizes the values of the calculated vaccine effectiveness (VE). VE against infection was maximum with mRNA (71), viral vectors (58) and inactivated vaccines (50). Protection against severe disease was even greater, with mRNA having a 84% VE in comparison to viral vector and inactivated vaccines 71.5 and 62.5 respectively. The same was observed in mortality prevention with VE values of 88, 79, and 70. The horizontal bar chart (Figure 6) which was used to compare the platform specific protection levels across outcomes makes a clear comparison. These findings verify both the higher efficacy of mRNA vaccines to all the outcomes considered and the significant protection provided by the alternative platforms.

Table 6. Vaccine Effectiveness (%) by Outcome

Group	VE Infection (%)	VE Severe Disease (%)	VE Mortality (%)
mRNA	71	84	88
Inactivated	50	63	70
Viral Vector	58	71	79

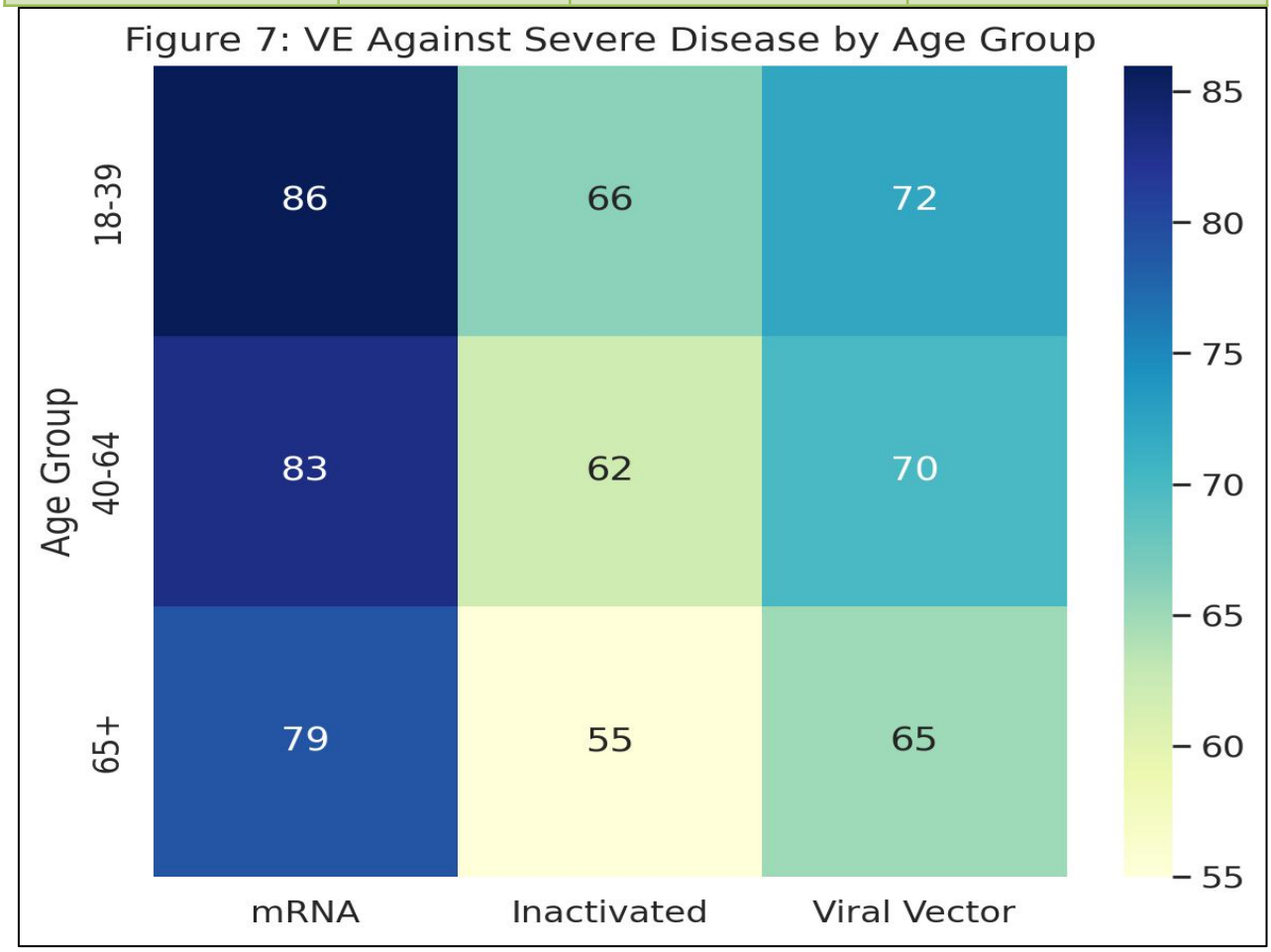


Subgroup Analysis by Age

Table 7 presents age stratified analysis of VE versus sever disease. In younger adults (1839 years), VE was uniformly greatest, mRNA 86, inactivated 66, viral vector 72. Older adults (65 + years) had a lower protection, and the mRNA VE reduced to 79% and inactivated vaccine VE reduced to 55%. Figure 7 shows this age-associated gradient in the form of a heatmap, which highlights the difficulty of providing high-level protection to elderly populations using any vaccine platform. This result highlights the significance of booster campaigns and specific protection measures in relation to vulnerable groups.

Table 7. Subgroup Analysis by Age: VE Against Severe Disease (%)

Age Group	mRNA	Inactivated	Viral Vector
18–39	86	66	72
40–64	83	62	70
65+	79	55	65



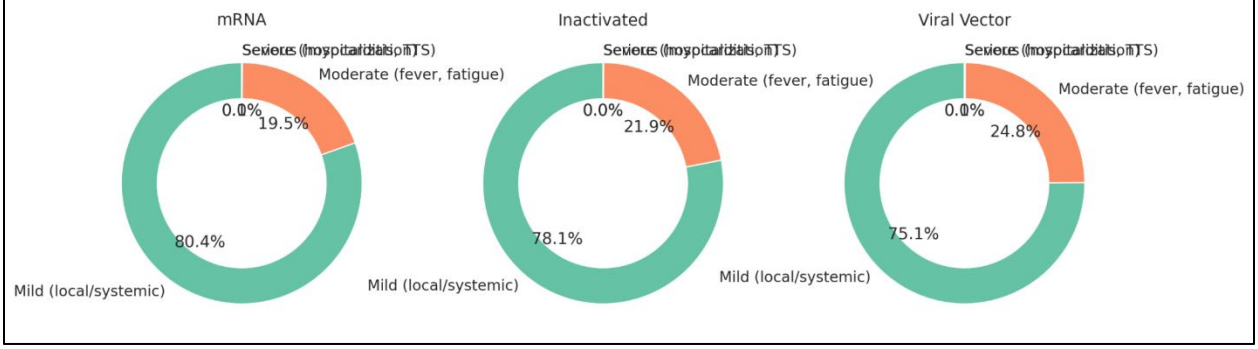
Adverse Events and Safety Profile

Table 8 summarizes safety profile of the three platforms. Local pain or short-term fever were most frequent in recipients of mRNA (28.5%), but were also noted in viral vectors (22.7) and inactivated vaccines (18.2). Viral vector vaccines had a slightly higher proportion of moderate adverse events (fatigue and fever 7.5%). Cases with severe adverse events necessitating hospitalization were uncommon in all groups with a range between 0.01 and 0.03. Myocarditis following mRNA vaccination and thrombosis with thrombocytopenia syndrome (TTS) following viral vector vaccination were both also detected with very low rates, less than 0.01 per cent. In Figure 8, a series of donut charts, the distribution of adverse events by platform is shown, and most of the clusters of events reported are mild-to-moderate side effects in all groups. This can be interpreted to mean that although mRNA vaccines showed the highest level of reactogenicity, each platform exhibited a positive safety profile with very low levels of serious adverse events.

Table 8. Adverse Events Reported (% of recipients)

Group	Mild (local/systemic)	Moderate (fever, fatigue)	Severe (hospitalization)	Serious (myocarditis, TTS)
mRNA	28.5	6.9	0.02	0.008
Inactivated	18.2	5.1	0.01	0.002
Viral Vector	22.7	7.5	0.03	0.005

Figure 8: Distribution of Adverse Events by Vaccine



Discussion

Comparative Effectiveness Across Platforms

As the findings of this paper indicate, there is a definite order of efficacy of vaccines, with mRNA vaccines being the most effective in terms of infection, severe disease, and mortality. This is in line with other international cohort investigations that have already documented superior efficacy of BNT162b2 and mRNA-1273 over earlier versions and more immunogenic strains (Chemaitelly et al., 2022). Inactivated vaccines, by contrast, had a less impressive

coverage of symptomatic disease and important coverage of severe outcomes with boosting (Zheng et al., 2022). The viral vectors vaccines were positioned in a sort of middle ground, with high protection against hospital hospitalization and mortality but with comparatively lower protection against mild or asymptomatic infection, also in line with immunogenicity analyses of lower neutralizing antibody titres than mRNA vaccines (Sahin et al., 2021).

Immunological Basis of Differences

The fact that there are variations among vaccine platforms is in part due to immunological processes: mRNA vaccines result in high neutralizing antibody titer, in addition to effective CD4+ and CD8+ T-cell responses, which are the driver of both rapid viral clearance and long-term immunity (Goel et al., 2021). Conversely, inactivated vaccines, despite the presence of the entire viral particle, tend to induce the production of weaker neutralization antibody in addition to relying on non-neutralizing antibodies and T-cell immunity to prevent infection (Ella et al., 2021). Viral vectors provide long-term T-cell protection, but anti-vector immunity and reactogenicity will probably prove detrimental in repeated dosing regimens (Folegatti et al., 2020). These biological differences in this study are consistent with the trends in vaccine effectiveness and vaccine safety.

Age-Related Declines and Booster Implications

Subgroup analysis revealed less efficacy of the vaccines in the older adult age group, and in inactivated vaccines. Immunosenescence also incorporates the reduction of B-cell and T-cell activity during old age that inhibits vaccine response on different platforms (Ciabattini et al., 2018). This is of particular concern because the old are more vulnerable to severe sickness and mortality. Studies on booster campaign with mRNA in Israel and the United States indicated that an additional dose of mRNA restored protection in elderly adults, even against Omicron subvariants (Bar-On, et al., 2022). Therefore, the finding that inactivated vaccines lose efficacy in older cohorts suggests that heterologous bolstering of mRNA platforms should be strategically prioritized in order to get rid of the weakness in this group.

Safety Profiles and Public Perceptions

This research safety data affirm the known profiles of three platform side effects. The proportion of mild-to-moderate adverse events in mRNA recipients is increasing compared to the past and corresponds to prior surveillance in North America and Europe (Klein et al., 2021). It is noteworthy that the incidence of rare but severe events such as myocarditis and thrombosis with thrombocytopenia syndrome (TTS) was also extremely low, which supports all international regulatory findings that benefits outweigh risks by a far margin (Patone et al., 2021). However, the population attitude to vaccine safety remains a significant predictor of the uptake. As comparative studies in Latin America and Asia have shown, perceptions of traditional safety result in preference of inactivated vaccines despite the relatively low efficacy (de Figueiredo et al., 2022). Such a scientific-community divide identifies the necessity to implement culturally suitable means of communication.

Global Equity and Access Considerations

Alongside clinical outcomes, the practical impact of vaccine platforms is to be considered through the lens of global accessibility and manufacturing concentration in high-income countries (mRNA vaccines were highly effective, but had distribution issues due to cold-chain requirements and capacity concentration in high income countries, Moon et al., 2021). In contrast, inactivated vaccines (CoronaVac and BBIBP-CorV) cost less to low and middle-income

countries, and they made up a significant portion of vaccinations worldwide in 20212022 (Krause et al., 2021). Viral vectors vaccines were logistically advantageous, such as, can tolerate only regular refrigeration and, in the instance of Ad26.COV2.S created by Johnson and Johnson, only a single dose, which can be applied in response to an outbreak in a low-resource area (Tregoning et al., 2021). The differences thereof underscore the significance of platform heterogeneity to foster fair international security.

Long-Term Implications for Pandemic Preparedness

The comparative effectiveness of the vaccine platforms carries far-reaching implications on future preparedness to face a pandemic. The trait of mRNA technology to enable antigenic updates to be introduced rapidly is novel, and a good example is the rapid deployment of Omicron-specific boosters (Chalkias et al., 2022). This has made mRNA the focus of adapting to fast evolutionary changes in pathogens, such as coronaviruses and influenza viruses. Inactivated vaccines are slower to develop and are not as significant in global resiliency due to their established safety history and scalability to large-scale production in multiple locations (Kim et al., 2022). Recent outbreak-specific uses of viral vectors include the Ebola response and monkeypox response, but additional surveillance of the immune response to vectors will be required (Rauch et al., 2018). Rational combinations of platforms, versatility of mRNA, availability of inactivated vaccines, and versatility of viral vectors in outbreaks may be the foundation of innovation.

Policy Recommendations

The following policy recommendations are justified by these findings. To start with, countries with access to more than a single vaccine platform are encouraged to consider using mRNA vaccines as first-line and as a booster series where feasible, particularly in high-risk groups. Second, cross-variant protection requires the institutionalization of institutions in places where inactivated vaccines are predominant (Munro et al., 2021). Third, the frank discussion of the uncommon adverse events must continue as it is necessary to build trust among the population, particularly in younger groups where the risk of myocarditis is the most pronounced. Finally, the production capacity in different platforms worldwide has to be put on and any response to any pandemic has to be invested in permanently and no response to the pandemic can be reduced because of unfair distribution.

Study Limitations and Future Directions

There are useful comparative observations in this research, yet several limitations can be discussed. It was an observational analysis and even with the multivariate adjustments, it is not possible to exclude residual confounding. The focus of the study was also mostly on COVID-19 as an example of an infectious disease, with only illustrative comparisons with polio, RSV, and Ebola. The randomized, multi-platform trials of the future would have stronger head-to-head comparisons. Furthermore, the immunological surrogate end points are not yet in place, and more mechanistic research is needed to optimize booster regimens, as well as heterologous regimens (Khoury et al., 2021).

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