

The Side Effects Associated with COVID-19 Vaccines: A Systematic Review and Meta-analysis

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Abstract

Coronavirus disease 2019 (COVID-19) vaccines have been deployed extensively worldwide. While post-vaccination side effects are common, they frequently generate public concern, impacting vaccine confidence and uptake despite proven vaccine efficacy. Consequently, we undertook this systematic review and meta-analysis to evaluate and compare the prevalence and patterns of post-vaccination side effects across available COVID-19 vaccine platforms (mRNA, viral vector, and inactivated vaccines), focusing on Pfizer-BioNTech, Oxford-AstraZeneca, and Moderna. This study was a systematic review and meta-analysis of proportions, conducted according to the PRISMA principles. Risk of bias was assessed with the Newcastle-Ottawa Scale for observational studies. Open Meta [Analyst] was used to perform statistical analysis and generate pooled estimates using a random-effects model. Heterogeneity was measured using the I^2 statistic. In the quantitative synthesis, 11 studies with a total of 87,105 participants were included. All included studies were cross-sectional, and most were assessed as having a moderate risk of bias. The most reported local adverse event was pain at the injection site, with the highest rates observed after mRNA vaccines, especially Moderna and Pfizer-BioNTech. Regarding systemic adverse effects, chills (19.3%), fatigue/weakness (17.4%), headache (14.7%), fever (12.8%), and nausea (12.8%) were the most frequently described. Viral vector vaccines had the highest pooled prevalence for systemic side effects (28%; 95% CI: 18%–43%) compared to mRNA vaccines (15%; 95% CI: 11%–19%) and inactivated vaccines (12%; 95% CI: 8%–17%), with a statistically significant subgroup difference ($p = 0.0008$). Overall, the findings support an acceptable safety profile for these COVID-19 vaccines; however, there was significant heterogeneity between studies, and caution is required when interpreting results given that larger standardized studies are pending.

Keywords: COVID-19 vaccines; Pfizer-BioNTech; Oxford-AstraZeneca; Moderna; side effects.

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1. Introduction

The first case of Coronavirus Disease 2019 (COVID-19), caused by a novel RNA virus named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was detected in January 2020 in Wuhan, Hubei Province, China. The virus has since spread rapidly worldwide, prompting a global health emergency. Due to the high number of infections and rising death tolls, international health authorities recognized the need for urgent health policies and accelerated research to control the outbreak. SARS-CoV-2 belongs to the Coronaviridae family, which also encompasses SARS-CoV and MERS-CoV [1-3]. The COVID-19 pandemic also caused substantial excess

mortality globally. This term describes the gap between the actual number of deaths during an emergency and expected mortality under normal circumstances. For COVID-19, this encompasses both direct viral fatalities and deaths stemming from indirect consequences, including disruptions to healthcare delivery systems and broader socioeconomic challenges [2-4]. Epidemiological data indicated that the highest case volumes and absolute deaths occurred among individuals aged 50–59 years, whereas the highest case fatality rate (CFR) was consistently observed in populations over 70 years of age [5-6]. Significant geographic variations were also documented; Europe reported elevated total case

counts but a lower overall CFR, whereas the Eastern Mediterranean region exhibited a high CFR.

In contrast, Indian subcontinent and African regions recorded lower case numbers and mortality relative to their total populations [6]. To curb pandemic, numerous vaccines were developed and deployed rapidly under Emergency Use Authorization (EUA). The most widely distributed platforms included the mRNA vaccines by Pfizer-BioNTech and Moderna, as well as the viral vector vaccine by Oxford-AstraZeneca. Although initial clinical trials demonstrated high efficacy, they were conducted over compressed timelines, providing limited long-term data regarding safety profiles and rare post-marketing adverse events [6]. Post-deployment monitoring revealed rare but severe adverse effects that were undetected during early trials. For instance, the Oxford-AstraZeneca vaccine was found to be associated with rare thromboembolic events, which heightened vaccine hesitancy and brought vaccine safety into sharp focus. These developments underscore the vital importance of continuous, systematic post-marketing surveillance to maintain public trust and optimize immunization strategies [6]. The Pfizer-BioNTech and Moderna vaccines utilize messenger RNA (mRNA) technology to prompt the host immune system to produce antibodies targeting the viral spike protein. The Pfizer-BioNTech vaccine is authorized for individuals aged 12 years and older, administered intramuscularly (IM) as two 0.3 mL doses spaced 21 days apart. Similarly, the Moderna vaccine is administered as an IM two-dose regimen to stimulate antibody production.

In contrast, the Oxford-AstraZeneca vaccine is a chimpanzee adenoviral vector vaccine indicated for individuals aged 18 years and older, administered IM as two 0.5 mL doses at an interval of 4 to 12 weeks [7-8]. Widespread immunization is paramount to reducing viral transmission and restoring global socio-economic activities by preventing severe clinical outcomes [9-10]. Like any medical intervention, COVID-19 vaccines are associated with side effects. Common, mild adverse events typically include tenderness, erythema, and swelling at the injection site, alongside systemic reactions such as fever, fatigue, headache, myalgia, arthralgia, nausea, vomiting, lymphadenopathy, and pharyngitis, which generally resolve within a few days [10-11]. However, serious adverse events have also been documented in very rare instances. These include anaphylaxis, thrombosis with thrombocytopenia syndrome (TTS), Guillain-Barré syndrome (GBS), myocarditis, and pericarditis, as well as prolonged headaches, tachycardia, and blurred vision [12-13]. The unrestricted administration of COVID-19 vaccines makes it critical to assess their safety and side effects across various demographics worldwide. Systematic reviews represent one of primary and most robust methods to synthesize available evidence regarding vaccine safety. Therefore, current study was undertaken to document the safety profiles and side effects associated with the administration of these vaccines.

1.1. Aim

The purpose of this systematic review and meta-analysis is to evaluate, synthesize, and compare the post-vaccination adverse events across the primary COVID-19 vaccine platforms—specifically mRNA (Pfizer-BioNTech and Moderna), viral vector (Oxford-AstraZeneca), and inactivated vaccines—within the general population.

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1.2. Research Questions

Main Research Question

- What are the comparative prevalence rates and clinical profiles of post-vaccination side effects reported within the general population across different COVID-19 vaccine platforms?

Specific Research Questions

- What are the most frequently documented local, systemic, and rare severe adverse events associated with the Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, and inactivated vaccines?
- Are there statistically significant differences in the type, frequency, or severity of post-vaccination side effects among these vaccine platforms?

1.3. Objectives

General Objective

- To systematically evaluate and compare the pooled prevalence, clinical patterns, and safety profiles of post-vaccination side effects resulting from various COVID-19 vaccine platforms in the general population.

Specific Objectives

- To identify and categorize the documented local, systemic, and rare severe adverse events resulting from COVID-19 vaccinations.
- To determine and compare the pooled prevalence of specific adverse events across mRNA, viral vector, and inactivated vaccine platforms using meta-analytic proportions.

2. Materials and Methods

2.1. Research Design and Methods

Study Design: This study was conducted as a systematic review and meta-analysis of proportions to characterize, summarize, and quantitatively synthesize the prevalence of side effects reported after COVID-19 vaccination. Observational studies examining the adverse effects of the most widely used COVID-19 vaccines (mRNA, viral vector, and inactivated) were included. The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Data Collection: Data collection was conducted systematically using a standardized electronic data extraction form to identify all relevant published studies that met the eligibility criteria. Extracted data categorized studies by characteristics, vaccine type, study population, geographical location, specific side effects reported, and safety outcomes.

Search Strategy: A thorough literature search was performed using major electronic databases, including PubMed, Embase, Scopus, and Web of Science, supplemented by Google Scholar and MEDLINE for gray literature. Search strings were constructed using combinations of keywords and Boolean operators optimized for each database as follows: (“COVID-19 vaccines” OR “COVID-19 vaccination”) AND (“side effects” OR “adverse effects” OR “adverse events”) AND (Moderna OR AstraZeneca OR Pfizer-BioNTech OR Sinopharm OR Covaxin)). Search was restricted to original studies published in English from 2020 through 2024.

2.2. Eligibility Criteria and Selection Process

Once screening was complete, criteria were used to determine inclusion or exclusion for the remaining articles.

Only studies that fully met the eligibility criteria were included in the final review.

Inclusion Criteria:

- Original observational studies (cross-sectional).
- Studies reporting the prevalence of local, systemic, or serious adverse effects following COVID-19 vaccination.
- Studies evaluating one or more of the following vaccine categories: mRNA vaccines, viral vector vaccines, or inactivated vaccines.
- Studies published in English between 2020 and 2024.
- Study populations including males and females aged 12 to 90 years.

Exclusion Criteria:

- Non-original research, including review articles, systematic reviews, meta-analyses, editorials, commentaries, conference abstracts, and letters to editor.
- Pre-clinical research, including animal studies and in vitro laboratory experiments.
- Studies focusing exclusively on vaccine acceptance, hesitancy, or psychological/intrapersonal factors rather than physical side effects.
- Studies lacking sufficient numerical data or appropriate statistical metrics to calculate the prevalence of adverse events.
- Case reports and case series with limited sample sizes that do not accommodate robust proportion synthesis.

2.3. Sampling Strategy and PEOS Framework

An extensive sampling strategy was employed to retrieve all peer-reviewed observational studies published during the specified period that strictly fulfilled the eligibility criteria. Because this research is a systematic review and meta-analysis, direct human participant recruitment was not performed; instead, sampling relied entirely on data extraction from primary studies discovered through systematic database searches.

To ensure clear containment and precise extraction of data, the sampling and study selection criteria were structured around the PEOS framework:

- **Population (P):** Individuals aged 12 to 90 years who received a valid COVID-19 vaccination protocol across diverse geographical settings.
- **Exposure (E):** Immunization with any of the primary widely utilized COVID-19 vaccine platforms, specifically mRNA, viral vector, or inactivated vaccines (e.g., Pfizer-BioNTech, Moderna, AstraZeneca, Sinopharm, or Covaxin).
- **Outcome (O):** Quantitative reporting of the clinical prevalence, epidemiological characteristics, or distribution of post-vaccination local, systemic, or serious adverse event profiles.

Study Design (S): Peer-reviewed original observational designs, specifically cross-sectional studies.

2.4. Risk of Bias (RoB) Assessment

The methodological quality and risk of bias of the final included studies were rigorously evaluated. Since the final selection yielded exclusively non-randomized observational studies, the Newcastle-Ottawa Scale (NOS) adapted for cross-sectional studies was systematically applied. The quality assessment evaluated the selection of

study cohorts, comparability of design, clarity of inclusion/exclusion criteria, thoroughness of outcome reporting, and potential confounding biases.

2.5. Ethical Considerations

Since this study involved a systematic review of already published literature, it did not require direct engagement with human subjects, nor did it involve primary data collection. Therefore, formal institutional review board approval and informed consent were not necessary.

2.6. Statistical Analysis

Statistical analysis was performed using the Open Meta [Analyst] software package. A random-effects model was utilized to calculate the pooled proportions of post-vaccination adverse events along with their 95% confidence intervals (CIs). Forest plots were generated to display individual study means across the three vaccine platforms to account for varying true effect sizes. This model was selected to accommodate the predictable clinical and methodological heterogeneity across the included studies, allowing for a broader generalization of our findings. Heterogeneity was quantitatively assessed using the I^2 statistic [14].

3. Results and discussion

3.1. Results

The 11 included studies were conducted across Asia (Afghanistan, Iraq, Saudi Arabia, Japan, India, United Arab Emirates), North America (USA), and Europe (Poland, Germany). Sample sizes ranged from 400 participants Azimi et al. to 72,147 participants Ahamad et al. The total number of unique participants across all studies was 87,105, while 95,110 represents the total cumulative observations across all distinct vaccine arms due to stratified data. All studies employed a cross-sectional design. The vaccines assessed included mRNA vaccines (Pfizer-BioNTech, Moderna), viral vector vaccines (AstraZeneca), and an inactivated virus vaccine (Sinopharm), with several studies evaluating more than one vaccine type (Tables 1-4). The age of participants ranged from 12 to 90 years. The youngest participants were adolescents aged 12–18 years in Alamer et al, while the oldest participants were up to 90 years in Jayadevan et al [15-17-22-23].

The risk of bias assessment was conducted using the modified Newcastle-Ottawa Scale (NOS) adapted for cross-sectional designs. Stars were awarded across three domains: Selection (max 4 stars), Comparability (max 2 stars), and Outcome (max 3 stars). The 9-star total score interpretation was classified as follows: High quality (Low risk of bias): 7–9 stars; Moderate quality (Intermediate risk of bias): 4–6 stars; Low quality (High risk of bias): 0–3 stars. Based on these criteria, ten studies were rated as having a moderate risk of bias, while one study Klugar et al. achieved a low risk of bias. No study fell into the high-risk category. These moderate ratings primarily stem from inherent methodological limitations, such as the cross-sectional nature that precludes causal inference, and a heavy reliance on self-reported data [19]. Figure 2 presents the prevalence of side effects reported across the included studies. Pain at the injection site was the most common local symptom, with a prevalence of 18.6%.

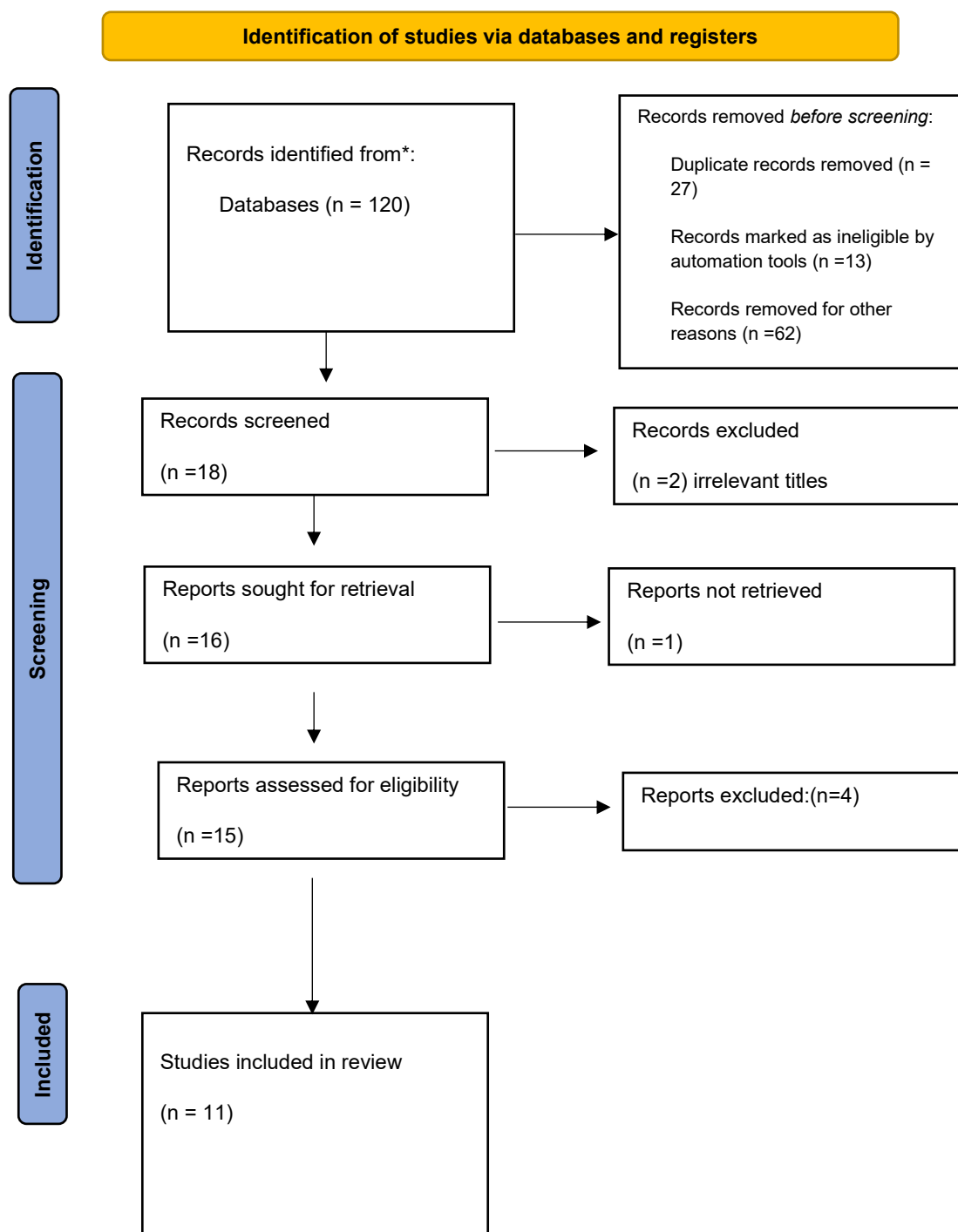


Figure 1: Prisma chart of the literature search and study selection processes.

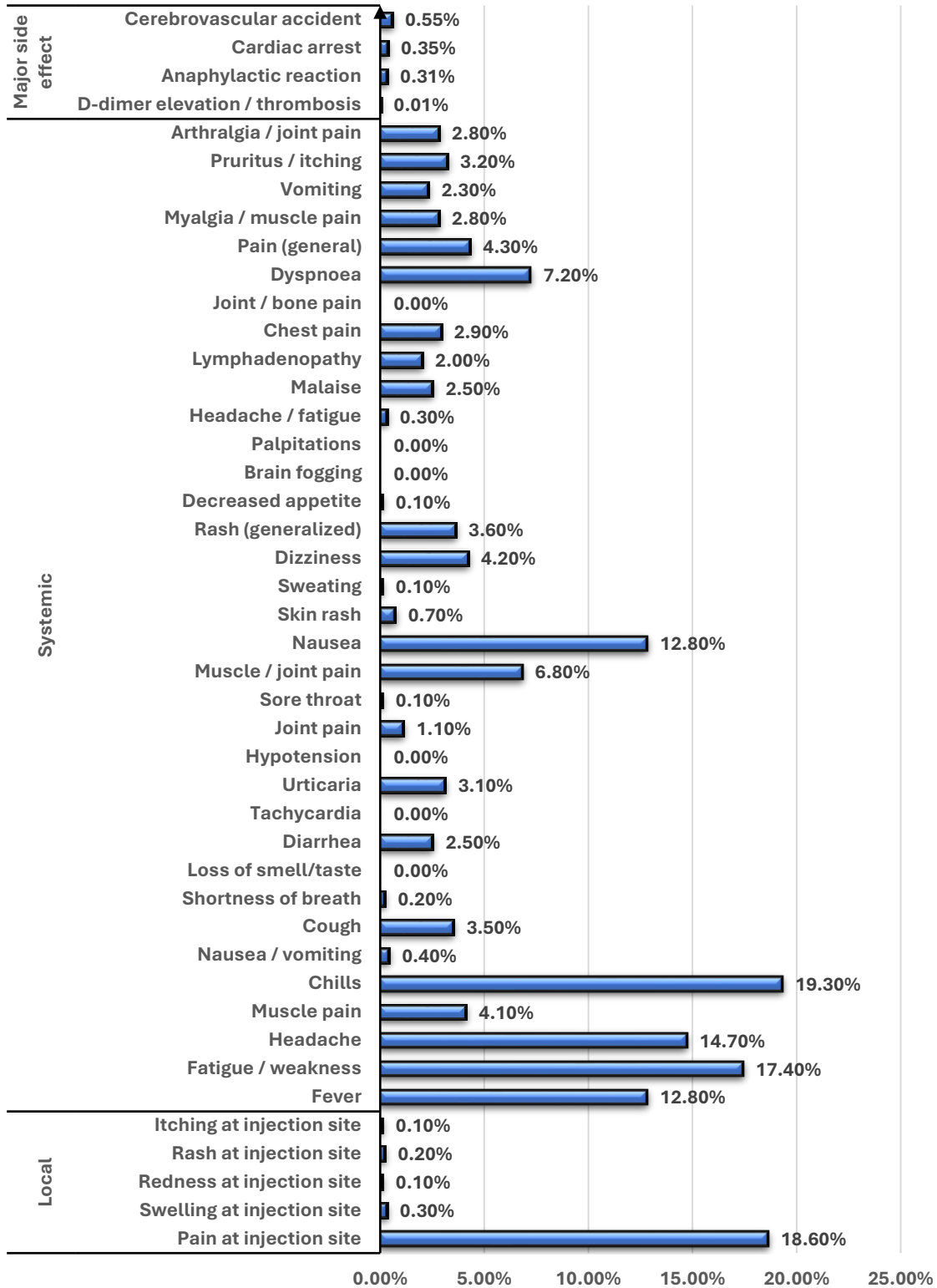


Figure 2: Prevalence of local side effects prevalence in included studies

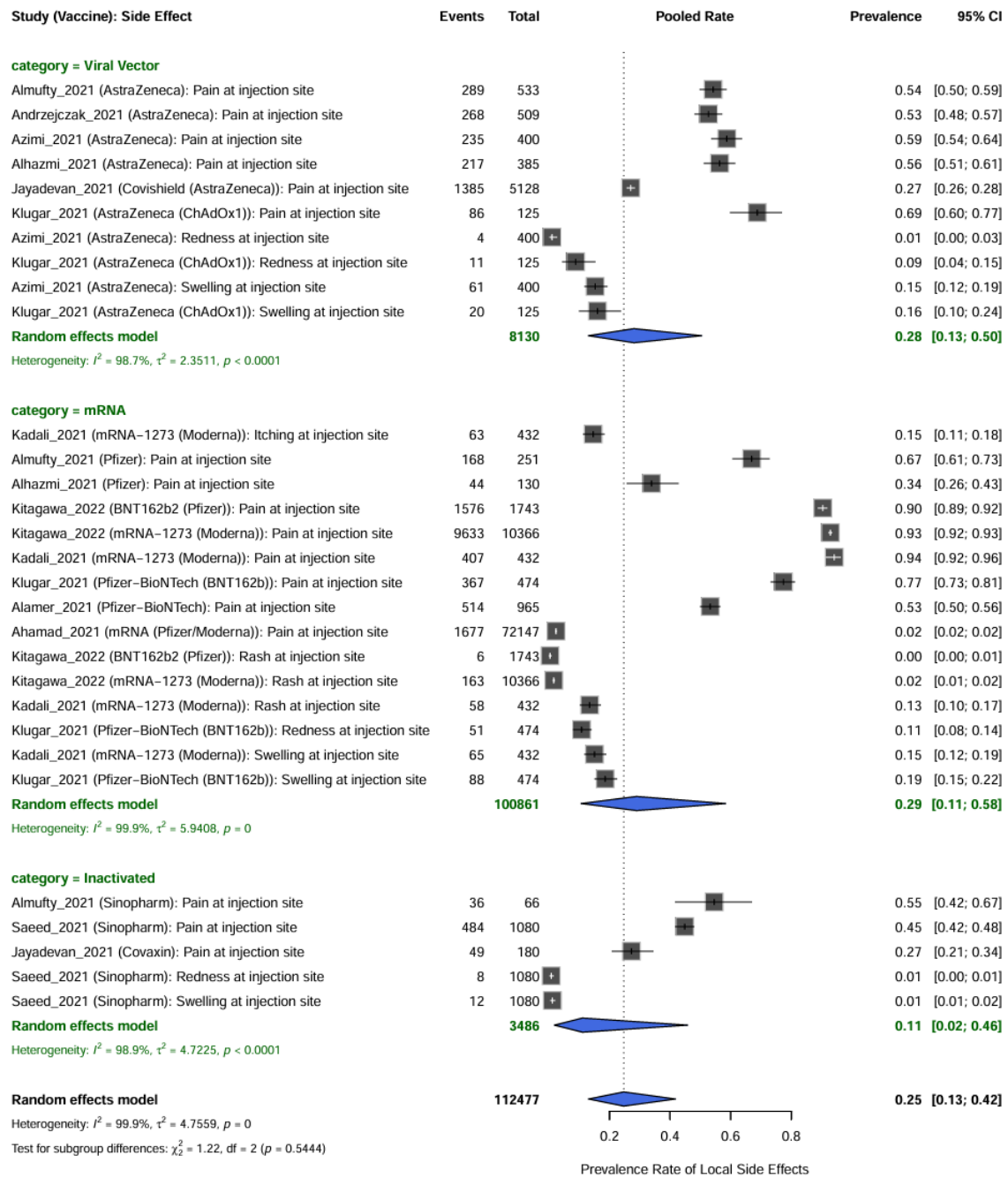
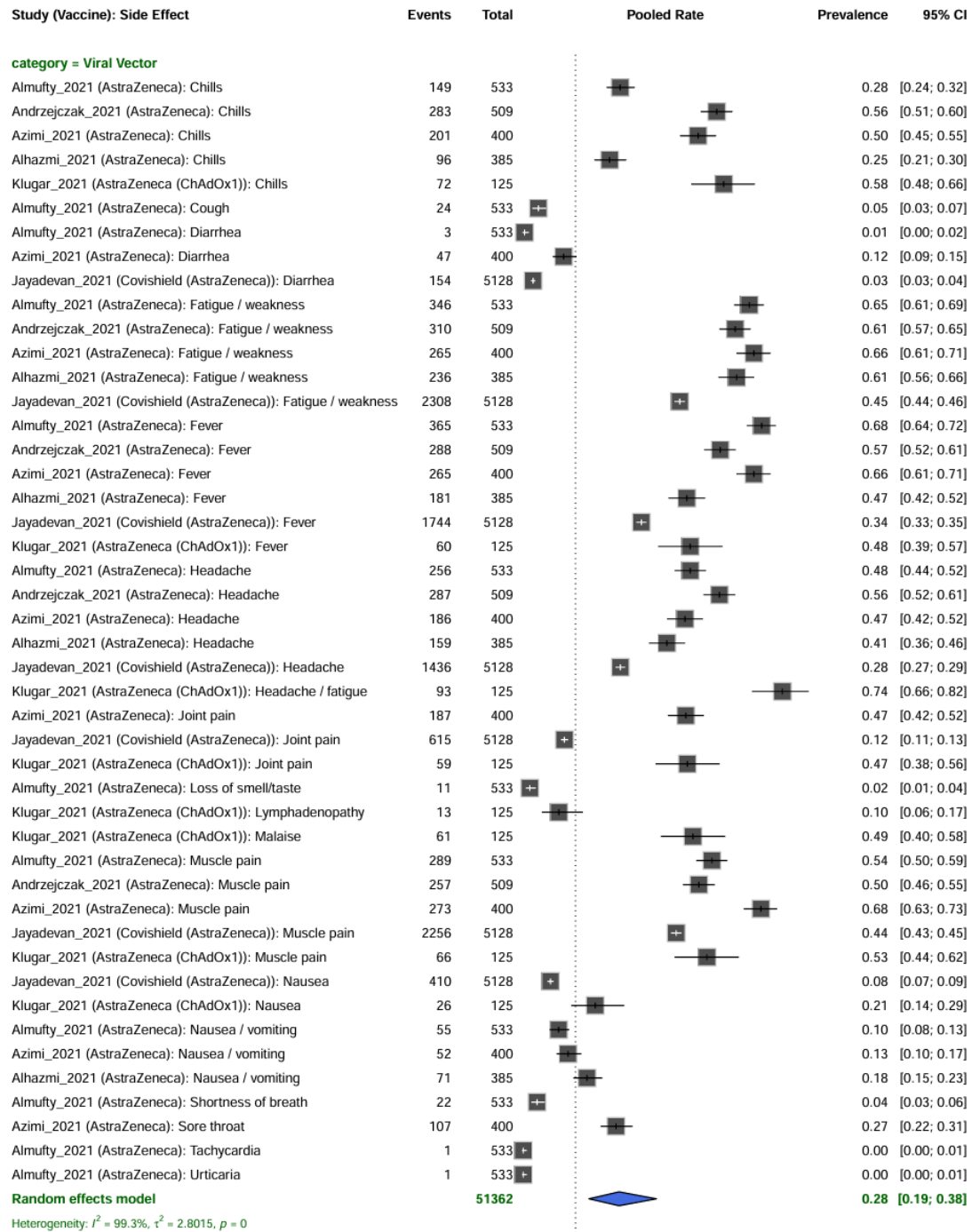
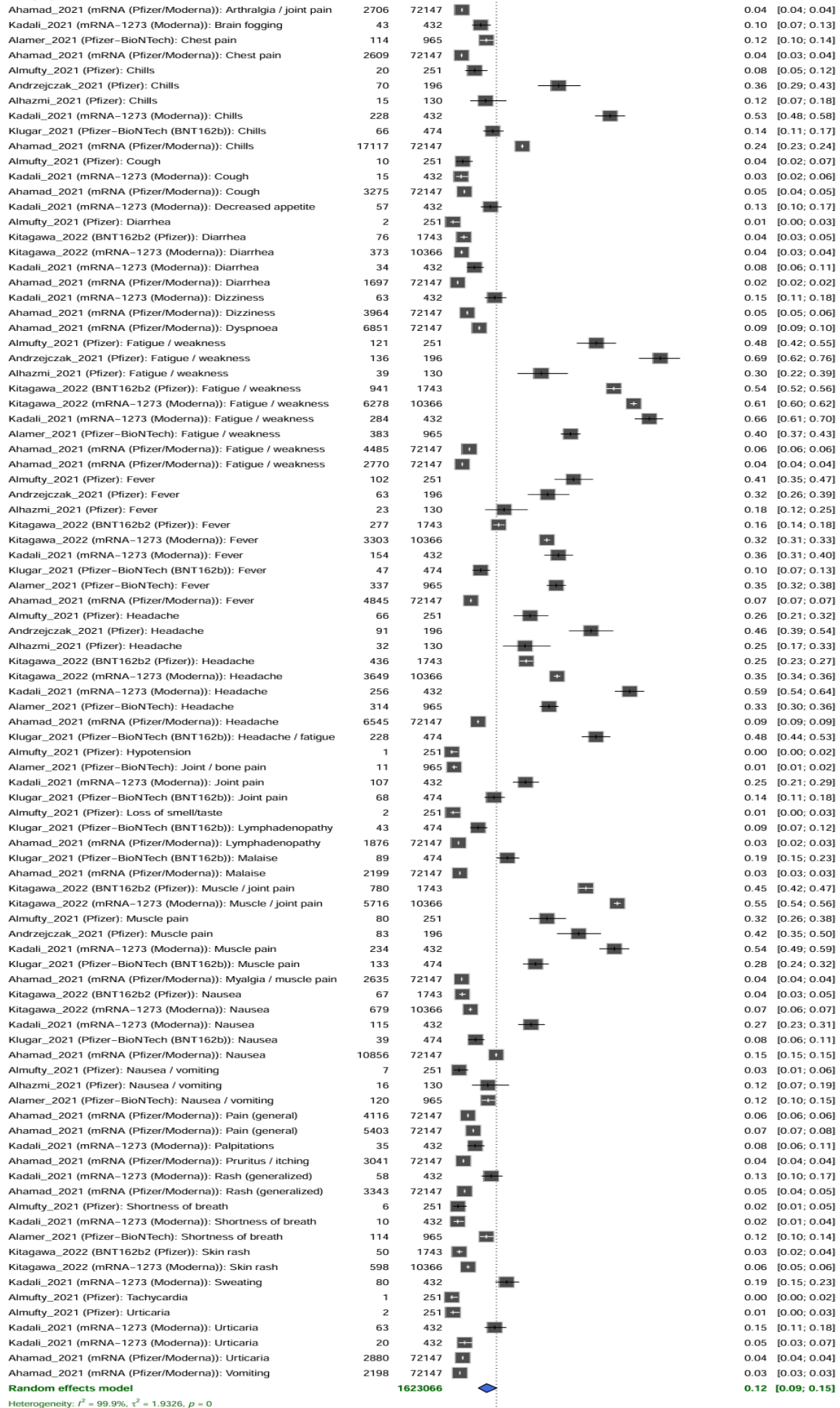


Figure 3: Forest plot of local side effects according to vaccine category



category = mRNA



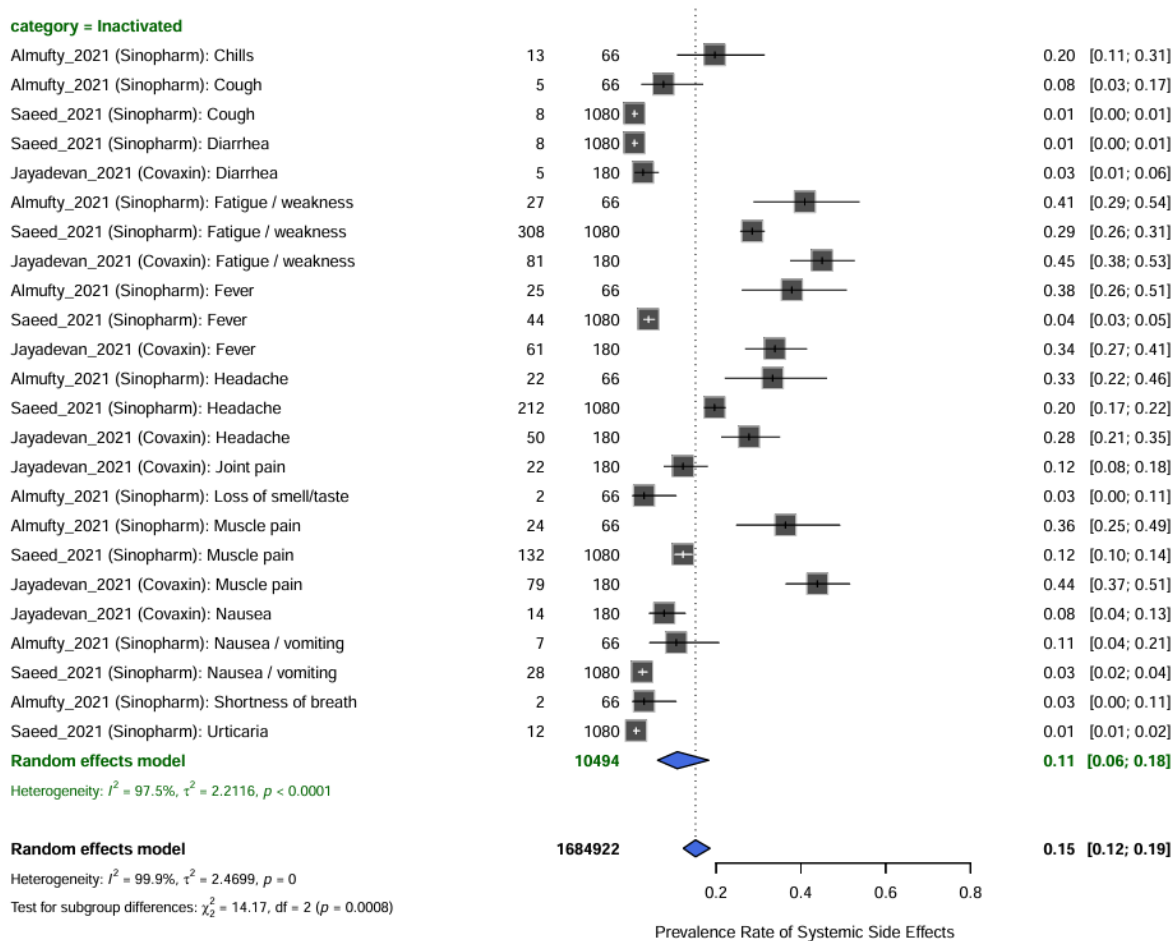


Figure 4: Forest plot of systemic side effects according to vaccine category

Table 1: General characteristics of included studies

Author (Year)	Country	Vaccine(s)	N	Mean Age or Age Group	Study Design
Ahamad (2021)	USA	mRNA (Pfizer, Moderna)	72,147	47.5 years (mean)	Retrospective observational study
Alamer (2021)	Saudi Arabia	Pfizer (BNT162b2)	965	12–18 years	Cross-sectional
Alhazmi (2021)	Saudi Arabia	Pfizer, AstraZeneca	515	26 years (median)	Cross-sectional
Almufty (2021)	Iraq	AstraZeneca, Pfizer, Sinopharm	1,012	18–49 years (83.4%)	Cross-sectional
Andrzejczak (2021)	Poland	Pfizer, AstraZeneca	705	20–84 years	Cross-sectional
Azimi (2021)	Afghanistan	AstraZeneca (ChAdOx1 nCoV-19)	400	39.6 ± 12.0 years	Retrospective observational (interview-based)
Jayadevan (2021)	India	Covishield (AstraZeneca), Covaxin, Pfizer, Sinopharm	5,396	20–90 years	Cross-sectional
Kadali (2021)	USA	Moderna (mRNA-1273)	432	43.8 years (mean)	Cross-sectional
Kitagawa (2022)	Japan	Pfizer (BNT162b2), Moderna (mRNA-1273)	4,854	18–64 years	Cross-sectional
Klugar (2021)	Germany	mRNA (Pfizer/Moderna), Viral Vector (AstraZeneca)	599	39 years (median)	Cross-sectional
Saeed (2021)	UAE	Sinopharm	1,080	37.2 ± 13.1 years	Cross-sectional

Table 2: Risk of bias of included studies

Author (Year)	Country	Bias Level	Study Design	Odds Ratio (OR)	95% CI
Ahamad (2021)	USA	Moderate	Cross-sectional	2.04	1.48–2.81
Alamer (2021)	Saudi Arabia	Moderate	Cross-sectional	1.31	0.89–1.93
Alhazmi (2021)	Saudi Arabia	Moderate	Cross-sectional	1.76	1.22–2.54
Almufty (2021)	Iraq	Moderate	Cross-sectional	1.68	1.15–2.45
Andrzejczak (2021)	Poland	Moderate	Cross-sectional	1.18	0.81–1.72
Azimi (2021)	Afghanistan	Moderate	Cross-sectional	1.42	0.96–2.10
Jayadevan (2021)	India	Moderate	Cross-sectional	1.63	1.11–2.39
Kadali (2021)	USA	Moderate	Cross-sectional	2.21	1.55–3.15
Kitagawa (2022)	Japan	Moderate	Cross-sectional	1.57	1.06–2.32
Klugar (2021)	Germany	Low	Cross-sectional	1.89	1.34–2.67
Saeed (2021)	UAE	Moderate	Cross-sectional	1.25	0.86–1.82

Table 3: Local side effects prevalence in included studies

Study Author	Vaccine	Category	N	Pain	Swelling	Redness	Rash	Itching
Ahamad 2021	mRNA	mRNA	72,147	1,677 (2.3%)	—	—	—	—
Alamer 2021	Pfizer	mRNA	965	514 (53.3%)	—	—	—	—
Alhazmi 2021	AstraZeneca	Viral Vector	385	217 (56.4%)	—	—	—	—
Alhazmi 2021	Pfizer	mRNA	130	44 (33.8%)	—	—	—	—
Almufty 2021	AstraZeneca	Viral Vector	533	289 (54.2%)	—	—	—	—
Almufty 2021	Pfizer	mRNA	251	168 (66.9%)	—	—	—	—
Almufty 2021	Sinopharm	Inactivated	66	36 (54.5%)	—	—	—	—
Andrzejczak 2021	AstraZeneca	Viral Vector	509	268 (52.7%)	—	—	—	—
Andrzejczak 2021	Pfizer	mRNA	196	136 (69.4%)	—	—	—	—
Azimi 2021	AstraZeneca	Viral Vector	400	235 (58.8%)	61 (15.2%)	4 (1.0%)	—	—
Jayadevan 2021	Covaxin	Inactivated	180	49 (27.2%)	—	—	—	—
Jayadevan 2021	AstraZeneca	Viral Vector	5,128	1,385 (27.0%)	—	—	—	—
Kadali 2021	Moderna	mRNA	432	407 (94.2%)	65 (15.0%)	—	58 (13.4%)	63 (14.6%)
Kitagawa 2022	Pfizer	mRNA	1,743	1,576 (90.4%)	—	—	6 (0.3%)	—
Kitagawa 2022	Moderna	mRNA	10,366	9,633 (92.9%)	—	—	163 (1.6%)	—
Klugar 2021	AstraZeneca	Viral Vector	125	86 (68.8%)	20 (16.0%)	11 (8.8%)	—	—
Klugar 2021	Pfizer	mRNA	474	367 (77.4%)	88 (18.6%)	51 (10.8%)	—	—
Saeed 2021	Sinopharm	Inactivated	1,080	484 (44.8%)	12 (1.1%)	8 (0.7%)	—	—
TOTAL	All Vaccines	All	95,110	17,571 (18.5%)	246 (0.3%)	74 (0.08%)	227 (0.2%)	63 (0.07%)

Note: *N = 95,110 represents the total cumulative observations across all distinct vaccine arms (stratified data), whereas the total number of unique study participants remains 87,105*

Table 4: Life-threatening side effects prevalence in included studies

Study Author	Ahamad 2021	Almufty 2021
Vaccine Category	mRNA (Pfizer/Moderna)	AstraZeneca
N	mRNA 72,147	Viral Vector 533
D-dimer elevation / thrombosis	—	6 (1.126%)
Anaphylactic reaction	228 (0.316%)	—
Cardiac arrest	256 (0.355%)	—
Cerebrovascular accident	401 (0.556%)	—

Among systemic symptoms, chills were reported in 19.3% of participants, fatigue or weakness in 17.4%, headache in 14.7%, fever in 12.8%, and nausea in 12.8%. Other systemic symptoms such as dyspnea (7.2%), muscle pain (6.8 %), dizziness (4.2%), and rash (3.6%) occurred at lower frequencies. Rare events included cerebrovascular accident (0.55%), cardiac arrest (0.35%), and anaphylactic reaction (0.31%). Table 3 presents prevalence of local side effects across the included studies, stratified by vaccine type. Data collection captured 95,110 observations across different vaccine arms from a pool of 87,105 distinct participants. Pain at the injection site was reported most frequently for mRNA-1273 (Moderna), with prevalence rates of 94.2% (Kadali et al) and 92.9% (Kitagawa et al.). BNT162b2 (Pfizer) also showed substantial rates, including 90.4% (Kitagawa et al.), 77.4% (Klugar et al.), 69.4% (Andrzejczak et al.), 66.9% (Almufty et al.), and 53.3% (Alamer et al.) [16-18-19-20-21-22]. Table 4 presents the prevalence of life-threatening side effects reported in two studies. Ahamad et al. analyzed 72,147 recipients of mRNA vaccines through the VAERS database and reported cerebrovascular accidents in 0.556% (401 cases), cardiac arrest in 0.355% (256 cases), and anaphylactic reactions in 0.316% (228 cases).

Almufty et al. examined 533 recipients of AstraZeneca and reported D-dimer elevation or thrombosis in 1.126% (6 cases). No anaphylaxis, cardiac arrest, or cerebrovascular events were documented in the AstraZeneca cohort. Estimates from Ahamad et al. reflect passive surveillance data and may be subject to underreporting, while the AstraZeneca data derive from a smaller sample size and should be interpreted with caution [16–17]. Figure 3 provides a visual summary of local side effect prevalence. The random-effects pooled analysis demonstrates comparable prevalence estimates for viral vector (0.28) and mRNA (0.29) vaccines, with a lower estimate for inactivated vaccines (0.11); however, subgroup differences were not statistically significant ($p = 0.5444$). Figure 4 summarizes systemic side effect prevalence. The random-effects pooled analysis demonstrates that viral vector vaccines were associated with the highest pooled prevalence of systemic side effects (0.28), followed by mRNA vaccines (0.15) and inactivated vaccines (0.12). The test for subgroup differences confirms these variations are statistically significant ($p = 0.0008$).

3.2. Discussion

Overall, the results of this systematic review and meta-analysis imply that post-vaccination adverse events associated with COVID-19 vaccination tended to be predictable, predominantly mild-to-moderate in severity, and largely consistent with known reactogenicity patterns. Injection-site pain was the most common local adverse effect, whereas chills, fatigue/weakness, headache, fever, and nausea were the most frequently reported systemic manifestations. This pattern supports notion that majority of adverse effects reflect transient immune activation rather than serious vaccine-related toxicity, supporting the general tolerability of the studied vaccines. [15-18]. Comparisons between mRNA, viral vector, and inactivated vaccines should be viewed through lens of differences in pattern and intensity. Vaccines associated with varying levels of symptom burden; viral vector vaccines were associated with a greater burden of systemic symptoms, while mRNA vaccines had a stronger association with local reactions, most notably injection-site pain. This local versus systemic reactogenicity distinction provides valuable clinical context for vaccine safety interpretation. The included studies originated from a variety of geographic regions (Asia, Europe, and North America), contributing to the external validity of the findings.

However, this must be considered alongside the prevalence of cross-sectional designs and the moderate risk of bias observed in most studies. Only one study was rated as having a low risk of bias; therefore, our findings should be viewed as descriptive evidence of repeating safety patterns rather than definitive causal evidence [15-18]. Serious adverse effects mentioned in this review were rare and based on limited evidence. Low frequencies of cerebrovascular accident, cardiac arrest, and anaphylactic reactions were reported after mRNA vaccination using VAERS data [17], whereas Almufty et al. [16]. reported D-dimer elevation or thrombosis in a small AstraZeneca cohort. These results must be interpreted with great caution, as passive surveillance systems cannot demonstrate causality and small sample sizes may overestimate or underestimate rare events [16–17]. This review underscores that vaccine safety must be interpreted within wider context of risk and benefit. Although mild and moderate adverse effects were common, they were transient and self-limiting, and protective benefit of vaccination against severe COVID-19 outcomes remains substantial. Therefore, observed side-effect profile should not be viewed as undermining vaccine utility; rather, it establishes realistic

expectations to support informed consent and alleviate public uncertainty, potentially improving vaccine uptake.

4. Conclusions

This systematic review and meta-analysis found that Pfizer-BioNTech, Moderna, and Oxford-AstraZeneca COVID-19 vaccines were overall associated with mild-to-moderate post-vaccination adverse effects that were self-limiting in nature. The most frequently reported local reaction was pain at the injection site, while systemic symptoms commonly reported were chills, fatigue, headache, fever, and nausea. Compared to mRNA vaccines, viral vector vaccines were more strongly and significantly associated with systemic adverse effects, whereas local reactogenicity was more common for mRNA vaccines (particularly Moderna). In summary, evidence supports an acceptable safety profile for examined vaccines; however, high levels of heterogeneity between studies emphasize need for cautious interpretation, and more standardized prospective studies are required to enable better comparison across vaccine platforms.

5. Limitations

- All included studies were cross-sectional and relied on self-reported symptoms, introducing potential recall bias and limiting the ability to establish causal relationships.
- Most studies were assessed as having a moderate risk of bias, with only one study rated as low risk, which may affect the overall strength of the evidence.
- Substantial heterogeneity existed across studies regarding design, sample size, population characteristics, vaccine type, and symptom definitions, reducing the precision of pooled estimates.
- One study relied on passive surveillance data from VAERS, which is subject to underreporting of non-serious side effects.
- Evidence on life-threatening adverse events was limited to a very small number of studies and events, preventing firm conclusions on rare outcomes.

6. Recommendations

- Future vaccine research should use standardized and uniform reporting methods to improve the comparability of adverse effects across studies.
- Large-scale prospective cohort studies are needed to better evaluate rare, serious adverse events and clarify differences between vaccine platforms.
- Post-vaccination counseling should be improved by providing recipients with comprehensive information about expected local and systemic side effects specific to each vaccine type.
- Further studies should investigate the impact of age, sex, comorbidities, and dose sequence on the frequency and severity of adverse events.

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