REVIEW

Impact of COVID-19 vaccination on the risk of long COVID: An umbrella review of meta-analyses

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ABSTRACT

Background: Long COVID (post-acute COVID-19 syndrome) imposes a substantial burden on function, quality of life, and health services. Emerging evidence suggests COVID-19 vaccination may mitigate long-COVID risk, but estimates vary across syntheses and populations.

Objectives: To evaluate the impact of COVID-19 vaccination on the risk of long COVID by consolidating evidence from systematic reviews/meta-analyses, assessing methodological quality, and quantifying primary-study overlap.

Methods: We conducted an umbrella review of systematic reviews/meta-analyses indexed in PubMed, Scopus, and Web of Science (Dec 1, 2019–Sep 1, 2025; English). Eligibility followed PICOS; only SRs/MAs were included. Two reviewers screened, extracted data, and appraised quality with AMSTAR-2. Overlap of primary studies was quantified using the corrected covered area (CCA). Visual syntheses (AMSTAR-2 bubble plot; overlap matrix) were generated in RStudio (v4.3.1, ggplot2). Protocol registered on OSF.

Results: Five meta-analyses met inclusion criteria. Across adult populations, vaccination was consistently associated with reduced long-COVID risk, with pooled vaccine effectiveness (VE) commonly ~29–41% for primary series. Timing and dose mattered: protection was stronger when vaccinated before infection, and booster doses yielded the largest effects (VE ~70%). Pediatric evidence was inconclusive, with pooled estimates not reaching statistical significance. AMSTAR-2 ratings were High (2 reviews), Moderate (2), and Low (1, pediatric). CCA indicated moderate overlap across reviews, suggesting that portions of the apparent consistency derive from shared primary cohorts.

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Conclusions: COVID-19 vaccination reduces the incidence of long COVID in adults, particularly when a complete primary series and booster doses are received prior to infection. Evidence in children/adolescents remains limited and non-definitive. Policymakers should prioritize completion of primary series and boosters as part of long-COVID prevention, while future research should standardize outcomes, extend follow-up, compare platforms/boosting schedules, and strengthen pediatric data.

Key words: COVID-19 vaccines, post-acute COVID-19 syndrome, vaccination, meta-analysis as topic, systematic reviews as topic

Introduction

Long COVID—defined as a constellation of persistent and heterogeneous symptoms extending beyond the acute phase of SARS-CoV-2 infection—has emerged as a global public health concern due to its significant impact on functional status, quality of life, and healthcare utilization months after recovery (1). Symptoms can include fatigue, dyspnea, cognitive dysfunction, neuropsychiatric disorders, and multi-system involvement, with prevalence estimates ranging from 10% to 30% depending on the population studied and the definitions applied (2). The ongoing burden of long COVID underscores the need for effective preventive strategies (3). Increasing evidence indicates that vaccination can mitigate the risk and severity of these post-acute sequelae by reducing viral replication, limiting systemic inflammation, and promoting durable immune responses (4, 5). Observational data and meta-analyses suggest that vaccinated individuals not only experience lower incidence of long COVID but may also report reduced symptom severity and shorter symptom duration compared to unvaccinated counterparts (6). Recent clinical, immunologic, and bibliometric syntheses further support these associations across diverse study populations and vaccine platforms (7). Comparative analyses of vaccine-induced versus infection-acquired immunity highlight that vaccination generates more consistent and longer-lasting protection in the post-acute phase than natural infection alone (5, 8). At the immunological level, studies emphasize the role of memory T-cell–mediated responses, demonstrating that vaccination expands SARS-CoV-2–specific memory T-cell pools, thereby enhancing immune surveillance and potentially lowering the risk of chronic or relapsing symptomatology characteristic of long COVID (9, 10). This biological plausibility strengthens the case for vaccination as a preventive measure not only against acute disease but also against its long-term consequences (11). Despite this emerging evidence, uncertainties remain. The magnitude of vaccine protection against long COVID appears to vary across populations, vaccine types, timing of administration, and circulating viral variants (12). Booster doses show promise in amplifying protection, but data on durability and consistency are still evolving. Evidence in children and adolescents remains particularly limited, and definitions of long COVID differ across studies, complicating cross-study comparisons (13). Given the rapidly growing body of research, systematic reviews and meta-analyses have synthesized findings on vaccine effectiveness against long COVID (14). However, overlap between primary studies, methodological differences, and variation in outcome definitions pose challenges for drawing clear conclusions. An umbrella review—synthesizing evidence across multiple systematic reviews and meta-analyses—offers the highest level of evidence integration, allowing assessment of consistency, methodological quality, and redundancy in the available literature (15). The objective of this umbrella review is therefore to evaluate the impact of COVID-19 vaccination on the risk of long COVID by consolidating evidence from systematic reviews and meta-analyses, appraising their

methodological quality, quantifying overlap in primary studies, and identifying knowledge gaps to guide clinical practice and future research.

Methods

Protocol and registration

The methodology for this umbrella review was developed a priori and formally registered in the Open Science Framework (OSF) registry. The registration included the research objectives, eligibility criteria, search strategy, methods for study selection, data extraction procedures, risk of bias assessment, and the planned synthesis approach. The review was conducted in full compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, thereby ensuring transparency and reproducibility. The reporting structure, including the PRISMA flow diagram, followed the recommended standards for systematic evidence synthesis. The protocol is publicly accessible in OSF (https://doi.org/10.17605/OSF.IO/PU27Z).

Eligibility criteria

The inclusion criteria for this umbrella review were defined using the PICOS framework. We included studies that enrolled individuals with confirmed COVID-19 who were followed for the occurrence of long COVID outcomes. The intervention of interest was vaccination against COVID-19 with any vaccine platform, including mRNA, adenoviral vector, inactivated, or other types, as well as booster doses. Eligible comparators included unvaccinated individuals or different vaccine regimens, such as single versus double dose, or booster versus primary vaccination. The primary outcomes were the incidence and prevalence of long COVID, defined as symptoms persisting beyond the acute phase according to individual study definitions (≥4 weeks, ≥12 weeks, or ≥3 months). Secondary outcomes included the duration and severity of post-COVID symptoms. Only systematic reviews and meta-analyses were eligible for inclusion, while narrative reviews, preprints without peer review, clinical trials, case reports, case series, and primary observational studies were excluded.

Information sources and search strategy

A systematic literature search was conducted in PubMed, Scopus, and Web of Science. The searches covered the period from December 1, 2019, to September 1, 2025, corresponding to the timeline of COVID-19 vaccine deployment and subsequent research on long COVID. Only studies published in English were included.

The search strategy was developed using the PICOS framework and restricted to article titles to ensure specificity for systematic reviews and meta-analyses. The framework of concepts, codes, and Boolean logic used is presented in Table 1.

Study selection

The selection of studies was conducted in two stages. First, the titles and abstracts of all retrieved records were screened to exclude articles that were clearly irrelevant to the review question. In the second stage, the full texts of potentially eligible articles were

Table 1. Search strategy framework for identifying systematic reviews and meta-analyses on COVID-19 vaccination and long COVID

Concept	Code	Keywords	Search within
Population / Condition	#1	"long covid" OR "post covid" OR "post-covid" OR "post-acute covid" OR "post covid condition" OR "post covid-19 condition"	Article title
Intervention	#2	"vaccine" OR "vaccines"	Article title
Study type	#3	"systematic review" OR "meta-analysis"	Article title
Boolean logic	#4	#1 AND #2 AND #3	Article title

obtained and assessed in detail against the predefined inclusion and exclusion criteria.

Screening and eligibility assessment were performed independently by two reviewers. Any disagreements were resolved through discussion, and when consensus could not be reached, a third reviewer adjudicated. This process ensured consistency and minimized bias in study inclusion.

Data extraction

Data were extracted from each eligible study using a standardized, pre-tested extraction sheet to ensure consistency and accuracy. The following information was collected: author and year of publication, study population, vaccine type and dose, comparator group, number of studies included in each review, effect size estimates with corresponding confidence intervals (CIs), and reported outcomes. The extraction sheet was piloted on a sample of studies prior to full data collection to refine the process and minimize errors.

Quality assessment

The methodological quality of the included systematic reviews and meta-analyses was assessed using the AMSTAR-2 (A Measurement Tool to Assess Systematic Reviews, version 2) instrument. This tool evaluates 16 domains of methodological rigor, including protocol registration, adequacy of the literature search, study selection and data extraction procedures, assessment and interpretation of risk of bias, appropriateness of meta-analytical methods, and consideration of heterogeneity and publication bias. Based on the AMSTAR-2 criteria, each review was assigned an overall confidence rating. Reviews with no or only one non-critical weakness were classified as High, indicating high confidence in their results. Reviews with more than one non-critical weakness but no critical flaws were rated as Moderate, reflecting moderate confidence. Reviews with a single critical flaw, with or without additional non-critical weaknesses, were rated as Low, indicating low confidence in their findings. Finally, reviews with more than one critical flaw were rated as Critically Low, meaning their results should not be relied upon. This appraisal provided a transparent evaluation of the reliability of the included reviews and guided the interpretation of evidence in this umbrella review.

Data synthesis

A narrative synthesis was undertaken to summarize the findings of the included systematic reviews and meta-analyses. Key characteristics and results were extracted to allow comparison across reviews in terms of populations, vaccine types, comparators, outcomes, and main effect estimates. Where possible, a quantitative synthesis was also performed. The degree of overlap in primary studies across the included reviews was assessed using the Corrected Covered Area (CCA) method to evaluate redundancy and ensure that pooling of results did not disproportionately weight repeated evidence. In addition, visualizations of quality assessments (AMSTAR-2 ratings) and overlap patterns were generated using RStudio (version 4.3.1). Specifically, custom R code with the ggplot2 package was applied to produce bubble plots summarizing AMSTAR-2 ratings and to generate an overlap matrix for the CCA analysis. These graphical outputs complemented the narrative and tabular summaries, improving the transparency of evidence presentation and facilitating interpretation of methodological quality and redundancy across reviews.

Results

Search results

A total of 29 records were identified through database searching (Web of Science, n=10; Scopus, n=9; PubMed, n=10). After removal of 17 duplicates, 12 records remained for screening. Following title and abstract review, 6 records were excluded because they were not systematic reviews or meta-analyses. Subsequently, six full-text articles were assessed for eligibility. Of these, one article was excluded due to absence of required data, insufficient information, or poor quality. No records were excluded for indirect relationship to the research question. Ultimately, five systematic reviews and meta-analyses were included in both the

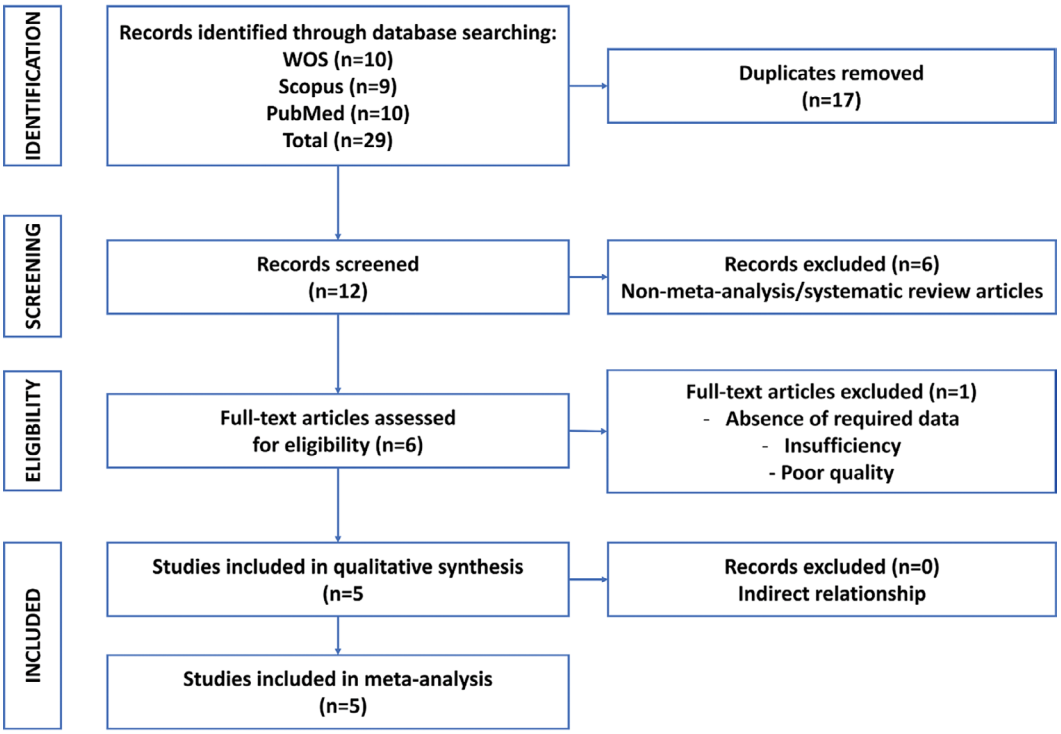

Figure 1. PRISMA flow diagram of study selection for the umbrella review on COVID-19 vaccination and risk of long COVID.

qualitative synthesis and quantitative meta-analysis. The study selection process is illustrated in Figure 1, which presents the PRISMA flow diagram of records retrieved, screened, excluded, and included.

Characteristics of included studies

A total of five meta-analyses were included in this umbrella review, each examining the impact of COVID-19 vaccination on the risk of long COVID or post-COVID conditions. Table 2 provides a structured summary of the key characteristics and findings from these reviews. The included studies consistently assessed vaccination status in relation to the occurrence of long COVID, though definitions of outcomes (≥4 weeks, ≥12 weeks, or ≥3 months after infection) varied across reviews. Despite heterogeneity in design and populations, most analyses indicated a protective effect of vaccination, particularly when a complete primary series or booster doses were administered prior to SARS-CoV-2 infection. The included reviews encompassed evidence from multiple geographic regions, including the United States, United Kingdom, Spain, Switzerland, Italy, France, Israel, India, Brazil, Saudi Arabia, Morocco, South Africa, Turkey, and Norway. Populations studied ranged from adults in the general population to healthcare workers, veterans, children, and adolescents. The majority of primary studies involved non-randomized observational designs, most commonly cohort studies, with sample sizes ranging from a few hundred to several million participants. A broad spectrum of vaccine types was represented. The most frequently studied were mRNA vaccines (Pfizer-BioNTech [BNT162b2] and Moderna [mRNA-1273]), followed by adenoviral vector vaccines (Oxford–AstraZeneca [ChAdOx1 nCoV-19] and Janssen/Johnson & Johnson [Ad26.COV2.S]). Several reviews also included data on inactivated vaccines (CoronaVac, Covaxin, Sinopharm) and other platforms (e.g., Gamaleya). The analyses stratified by number of doses indicated that vaccine effectiveness against long COVID was strongest after a complete

Table 2. Summary of included meta-analyses on the impact of COVID-19 vaccination on long COVID

Authors, Year (Reference)	Population	Vaccine Type / Dose	Comparator	No. of Studies	Outcomes	Main Findings	Quality (AMSTAR-2)
Gao et al., 2022 (16)	Patients with confirmed COVID-19 (adults and children); mainly from USA, UK, Spain, also India, Switzerland, Saudi Arabia, Italy, France	Primarily mRNA vaccines (BNT162b2, mRNA-1273); also ChAdOx1 nCoV-19, Ad26.COV2.S, inactivated vaccines; 1 or 2 doses; given before or after infection	Unvaccinated individuals	18 observational studies (12 cohort, 1 case-control, 5 cross-sectional); 185,689 vaccinated vs. 759,987 unvaccinated	Long COVID incidence; specific symptoms (cognitive dysfunction, kidney disease, myalgia, sleep disorder, etc.)	Vaccinated group had 29% lower risk of long COVID (RR=0.71, 95% CI 0.58–0.87, p<0.01). Effect protective for two doses (RR=0.83), but not one dose. Protective both if vaccinated before infection (RR=0.82) and after infection (RR=0.83). Reduced risk of cognitive dysfunction, kidney problems, myalgia, and sleep disorders.	High (AMSTAR-2, as it is a registered PROSPERO review, followed PRISMA, included risk of bias assessment, sensitivity analyses)
Gutfreund et al., 2024 (17)	Children & adolescents (<21 years); 23,995 participants across 8 studies (Israel, UK, Norway, Thailand, USA, Italy)	Pfizer-BioNTech, Moderna, AstraZeneca, Sinopharm; at least 1 dose; some studies with 2 doses	Unvaccinated pediatric individuals	8 studies (5 in meta-analysis: 20,325 participants)	Post-COVID condition (symptoms ≥4 weeks, ≥12 weeks, or ≥6 months)	Pooled prevalence: 21.3% unvaccinated vs. 20.3% vaccinated. Pooled DOR = 1.07 (95% CI, 0.77–1.49). For 2 doses before infection, DOR = 0.82 (95% CI, 0.63–1.08). Overall: no statistically significant protection of vaccination against pediatric long COVID.	Low–Moderate (most studies good quality by Downs & Black tool, but overall certainty low due to observational designs; AMSTAR-2 rating = Low)
Marra et al., 2023 (18)	Adults with confirmed COVID-19; 1,600,830 individuals across 10 studies (UK, USA, France, Israel, Italy)	Pfizer-BioNTech, Moderna, AstraZeneca, Janssen; ≥1 dose; some studies with 2 doses; before or after infection	Unvaccinated	10 observational studies (6 included in quantitative synthesis; 251,123 individuals)	Post–COVID-19 condition (symptoms persisting ≥3–12 weeks depending on study definition)	Pooled DOR = 0.708 (95% CI 0.692–0.725) → Vaccine effectiveness ≈ 29.2%. VE higher when given before infection (35.3%) than after (27.4%). Overall, vaccination reduced risk of long COVID, though protection was modest.	Moderate–High (8 studies "good quality," 1 fair, 1 poor by Downs & Black; overall AMSTAR-2 = Moderate)

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Marra et al., 2022(19)	Adults with confirmed COVID-19; 775,931 individuals across 32 studies (USA, UK, Switzerland, India, Brazil, France, Israel, Italy, Morocco, Netherlands, Norway, Saudi Arabia, Scotland, South Africa, Spain, Turkey)	Pfizer-BioNTech, Moderna, AstraZeneca, Janssen; also CoronaVac, Covaxin, Sinopharm, Gamaleya; ≥2 doses (fully vaccinated); some with boosters	Unvaccinated individuals	32 studies (24 meta-analyzed; 620,221 participants)	Post-COVID condition (long COVID; ≥4–12 weeks, ≥6 months depending on study)	Pooled DOR = 0.680 (95% CI: 0.523–0.885) → VE ≈ 32%. VE higher before infection (36.9%) than after (no protection, DOR=1.303). Booster doses (3rd dose) showed strongest effect (VE ≈ 68.7%). Protection confirmed even in Omicron era (VE ≈ 31.6%).	High (28/32 studies rated "good" quality on Downs & Black; overall AMSTAR-2 = High)
Peine et al., 2025 (14)	>5.7 million participants across 89 non-randomized studies (global; adults, children, elderly, healthcare workers, veterans, special subgroups)	Any COVID-19 vaccine (mRNA, vector, inactivated); ≥1 dose before SARS-CoV-2 infection; some 2–3 doses; booster analyses	Unvaccinated or placebo groups	65 studies with adjusted estimates (22 included in PCC meta-analysis; 42 in LC meta-analysis)	Post-COVID condition (PCC, ≥3 months), Long COVID (LC, ≥1 month), secondary outcomes (QoL, daily function, return to work)	VE against PCC: 41.0% (95% CI 27.8–51.7). By dose: 1 dose: 19.1% (NS), 2 doses: 43.2%, 3 doses: 70%. VE against LC: 34.1% (95% CI 25.0–42.2). VE lower after Omicron (20.9%) vs pre-Omicron (32.1%). In elderly >75 yrs: VE 41%; in children <18: VE 26% (NS). Booster doses and immunocompromised groups showed strongest protection (~70%).	Moderate (AMSTAR-2) – downgraded to Low certainty due to non-randomized designs and residual confounding, but broad dataset and robust sensitivity analyses.

Abbreviations: Ad26.COV2.S, Janssen/Johnson & Johnson COVID-19 vaccine (adenoviral vector-based); AMSTAR-2, A Measurement Tool to Assess Systematic Reviews, version 2; critical appraisal tool for systematic reviews of healthcare interventions; BNT162b2, Pfizer-BioNTech mRNA COVID-19 vaccine; ChAdOx1 nCoV-19, Oxford-AstraZeneca adenovirus vector COVID-19 vaccine; CI, Confidence Interval; statistical range within which the true effect size is expected to lie with a given probability (commonly 95%); CoronaVac, Inactivated COVID-19 vaccine developed by Sinovac Biotech; Covaxin, Inactivated COVID-19 vaccine developed by Bharat Biotech; DOR, Diagnostic Odds Ratio; in this context, used to estimate vaccine effectiveness against long COVID outcomes; LC, Long COVID; persistence or occurrence of symptoms at least 1 month after acute SARS-CoV-2 infection; mRNA-1273, Moderna mRNA COVID-19 vaccine; NS, Not Significant; statistical result that did not reach conventional thresholds for significance; PCC, Post-COVID-19 Condition; WHO definition: symptoms continuing ≥3 months after infection, lasting ≥2 months, not explained by another diagnosis; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; evidence-based guidelines for reporting systematic reviews; PROSPERO, International Prospective Register of Systematic Reviews; QoL, Quality of Life; patient-reported assessment of well-being and daily functioning; RR, Risk Ratio; measure of relative risk comparing event probability in vaccinated vs. unvaccinated groups; VE, Vaccine Effectiveness; reduction in disease or condition incidence among vaccinated vs. unvaccinated groups, expressed as a percentage; WHO, World Health Organization.

primary course or booster dose, while protection was less consistent after a single dose or when vaccination occurred post-infection.

Findings of meta-analyses

Across the five eligible meta-analyses, vaccination was consistently associated with a lower risk of long COVID in the general (mostly adult) population. Gao et al. pooled 15 observational studies (≈945k participants) and found a 29% relative risk reduction (RR = 0.71, 95% CI 0.58–0.87) for any vaccination versus none (16). Marra et al. (6 studies in the meta-analysis; 251,123 participants) reported a pooled DOR = 0.708 (95% CI 0.692–0.725), corresponding to VE ≈ 29.2% (19). Updating and restricting to fully vaccinated cohorts (≥2 doses), Marra et al. (24 studies; 620,221 participants) estimated DOR = 0.680 (95% CI 0.523–0.885; VE ≈ 32.0%) (18). The most comprehensive review to date (44 adjusted studies in main PCC analysis, >2 million participants) estimated VE = 41.0% (95% CI 27.8–51.7) against post-COVID-19 condition (PCC; ≥3 months) and VE = 34.1% (95% CI 25.0–42.2) against long COVID (LC; ≥4 weeks) (14). Dose number and timing were consistent determinants of protection. In Gao et al., two doses were protective (RR = 0.83, 95% CI 0.74–0.94) whereas one dose was not (RR = 0.83, 95% CI 0.65–1.07). Vaccination was beneficial whether given before infection (RR = 0.82, 95% CI 0.74–0.91) or after infection (RR = 0.83, 95% CI 0.74–0.92) (16). Marra et al. similarly observed higher VE when vaccination occurred before infection (DOR = 0.647; VE ≈ 35.3%) than after infection (DOR = 0.726; VE ≈ 27.4%) (19). In the fully vaccinated update, Marra et al. found protection before infection (DOR = 0.631; VE ≈ 36.9%), no protection when vaccination was given after infection (DOR = 1.303; 95% CI 0.890–1.907), and sustained benefit during the Omicron era among those vaccinated before infection (DOR = 0.684; VE ≈ 31.6%) (18). Peine et al. corroborated a dose-response and a variant effect: VE for 1 dose was 19.1% (not statistically significant), 2 doses 43.2%, and 3 doses 70.0%; VE after pre-Omicron infections was 32.1% versus 20.9% after Omicron (wide CIs), and among those >75 years VE was 41% (one NRSI) (14). Evidence consistently indicates additional protection from booster dosing. Marra et al. reported first-booster VE ≈ 68.7% (DOR = 0.313, 95% CI 0.278–0.353) for reviews where vaccination occurred before infection (18). Peine et al. likewise showed the highest VE (~70%) after three doses compared with unvaccinated, including in immunocompromised individuals in one included study (14). The pediatric-focused meta-analysis (5 studies in the meta-analysis, 20,325 children/adolescents) did not detect a significant protective effect of vaccination on post-COVID conditions overall (pooled DOR = 1.07, 95% CI 0.77–1.49) (17). A two-dose analysis before infection (DOR = 0.82, 95% CI 0.63–1.08) also did not reach significance, reflecting limited and heterogeneous pediatric evidence (17). In Peine et al., a single pediatric NRSI suggested VE = 26% (–4% to 48%) for ≥1 dose against PCC, again not statistically significant, underscoring the lower certainty in youth compared with adults (14). Taken together, the meta-analytic evidence indicates that COVID-19 vaccination reduces the incidence of long COVID in adults, with the greatest protection when a complete primary series and booster doses are received before infection; protection appears smaller or absent when vaccination occurs after infection, and pediatric evidence remains inconclusive.

Quality of evidence

The methodological quality of the included systematic reviews and meta-analyses was assessed using the AMSTAR-2 tool. As summarized in Figure 2, one review (16) was rated as High confidence, while another (18) also achieved a High rating. Two reviews (14, 19) were judged to be of Moderate confidence, reflecting minor methodological limitations but overall reliable results. In contrast, the pediatric-focused review (17) was rated as Low, primarily due to the limited number of included studies and concerns regarding observational design bias. Overall, the quality assessment indicates that the evidence base is dominated by moderate-to-high quality reviews, supporting the robustness of findings that COVID-19 vaccination provides protection against long COVID. However, the confidence in pediatric evidence remains low, underscoring the need for more high-quality studies in younger populations.

Figure 2. AMSTAR-2 ratings of included systematic reviews and meta-analyses on COVID-19 vaccination and long COVID.

Corrected covered area

The extent of overlap among the included systematic reviews and meta-analyses was evaluated using the Corrected Covered Area (CCA) method. Across the five reviews (14, 16-19), several primary studies were included in more than one review. For example, large-scale cohort studies appeared repeatedly across different analyses. This overlap resulted in a moderate CCA value, indicating that while redundancy exists, it is not excessive (Figure 3). The presence of overlap has important implications for interpreting umbrella review findings. Repeated inclusion of the same primary studies across different reviews can inflate the weight of evidence and give the impression of a larger body of independent data than actually exists. In this case, the moderate overlap highlights the need for careful interpretation: although findings across reviews are consistent in showing a protective effect of vaccination against long COVID, much of this consistency stems from reliance on a shared set of key observational studies. Thus, while the umbrella review demonstrates that vaccination is associated with a reduced risk of long COVID, the true breadth of evidence is narrower than the number of systematic reviews might suggest. This underscores the importance of transparent overlap assessment in evidence synthesis and suggests that future reviews should explicitly account for study duplication to avoid redundancy-driven bias.

Discussion

This umbrella review synthesizing five systematic reviews and meta-analyses demonstrates that COVID-19 vaccination is consistently associated with a reduced risk of long COVID in adults. Across reviews, pooled estimates indicate a modest but statistically significant protective effect, with vaccine effectiveness ranging from approximately 29% to 41% depending on study populations, timing of vaccination, and number of doses received (20). The evidence was strongest for individuals who completed a full primary series prior to SARS-CoV-2 infection and particularly when booster doses were administered, with protection approaching 70% in some analyses (21). Pediatric evidence, however, remains inconclusive, as meta-analyses of children and adolescents did not show significant protective effects (17). These findings are broadly consistent with large observational studies

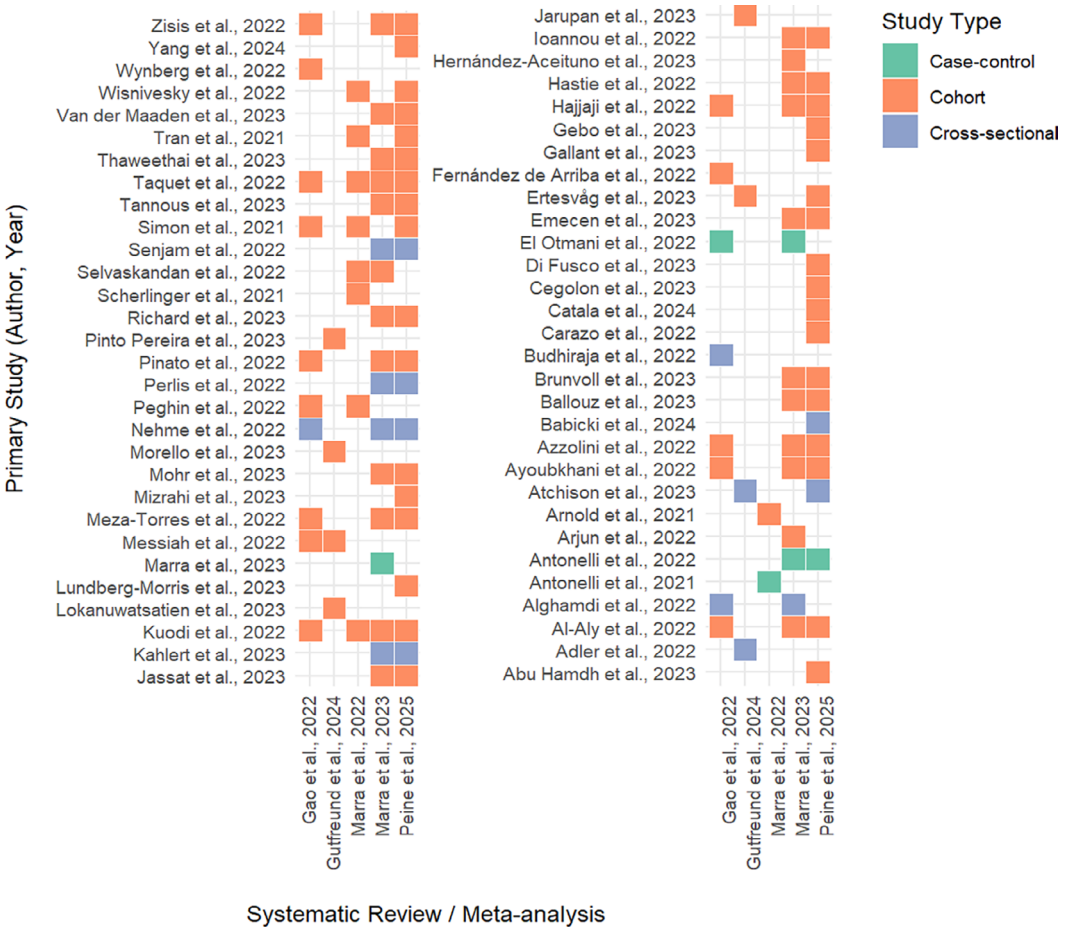

Figure 3. Corrected Covered Area (CCA) analysis showing the extent of overlap in primary studies across included systematic reviews and meta-analyses.

that reported lower risks of persistent post-COVID symptoms among vaccinated individuals (22). The protective effect aligns with real-world vaccine effectiveness data against severe COVID-19 outcomes, although the magnitude of benefit against long COVID appears smaller (23). Importantly, while randomized controlled trials (RCTs) evaluating vaccination and long COVID are lacking, the consistency across large-scale observational data and multiple systematic reviews supports the robustness of the observed association (24). The protective effect of vaccination against long COVID is biologically plausible (25). Vaccines may reduce the risk of viral persistence, lower systemic inflammation, and prevent severe acute disease—factors that have been implicated in the pathogenesis of long COVID (26). Enhanced immune responses following booster doses may explain the stronger protection observed in individuals receiving three vaccine doses compared with those with incomplete schedules (27). The findings of this umbrella review support the integration of vaccination strategies into long COVID prevention efforts. Ensuring completion of the primary vaccine series and expanding booster campaigns could substantially reduce the long-term burden of COVID-19 (28). Policymakers should also recognize the importance of boosters, which demonstrated the strongest protective effect against post-COVID conditions (29). While the adult evidence is convincing, further research is required to clarify the role of vaccination in children and adolescents before targeted recommendations can be confidently made for younger populations (30).

Strengths and limitations

A key strength of this umbrella review is the synthesis of the highest level of evidence, focusing exclusively on systematic reviews and meta-analyses. The use of AMSTAR-2 ensured rigorous evaluation of methodological quality and overlap analysis using the Corrected Covered Area (CCA) helped account for redundancy in primary studies. However, several limitations must be acknowledged. First, all included reviews relied on observational data, introducing risks of confounding and bias. Second, definitions of long COVID varied considerably across primary studies (≥4 weeks, ≥12 weeks, or ≥3 months), limiting comparability. Third, overlap in primary studies was moderate, indicating that much of the evidence base draws upon a relatively narrow set of large cohorts, which may exaggerate consistency across reviews. Finally, pediatric evidence remains sparse and inconclusive, underscoring an important evidence gap.

Future research directions

Future studies should adopt standardized definitions of long COVID, in line with WHO and NICE guidance, to enhance comparability. Long-term prospective follow-up studies are needed to assess the durability of vaccine-induced protection against long COVID. Comparative analyses of different vaccine platforms, mixed regimens, and booster intervals are also warranted. Importantly, pediatric-specific studies should be prioritized to address the current evidence gap. Finally, high-quality systematic reviews must continue to evaluate emerging data while minimizing redundancy and clearly reporting study overlap.

Conclusion

This umbrella review demonstrates that COVID-19 vaccination consistently reduces the risk of long COVID in adults, with effectiveness estimates ranging from 29% to 41% for primary series and up to 70% following booster doses. Protection is strongest when vaccination occurs before SARS-CoV-2 infection, whereas post-infection vaccination shows limited or no benefit. Pediatric evidence remains inconclusive, highlighting the need for further studies in younger populations. Overall, the findings reinforce the role of vaccination not only in preventing acute COVID-19 outcomes but also in mitigating long-term sequelae. These results underscore the public health importance of complete vaccination and booster campaigns as a strategy to reduce the global burden of long COVID. Continued research is essential to refine dose strategies, evaluate vaccine platforms, and establish standardized outcome measures that will inform future vaccination policies and long COVID prevention programs.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Declaration on the Use of AI: Artificial intelligence–assisted tools (ChatGPT, OpenAI, San Francisco, CA, USA) were used exclusively to improve the clarity, grammar, and style of the manuscript text. The authors confirm that AI was not used for data collection, data analysis, interpretation of results, or drawing scientific conclusions. All content, findings, and interpretations presented in this article are the sole responsibility of the authors.

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