COVID-19 Vaccine Safety Literature Review Presented on VIEW-hub

Methods

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Methods for Identifying Published Studies on COVID-19 Vaccine Safety Presented on VIEW-hub

Published studies on the safety of routine use of COVID-19 vaccine assessing serious adverse events following immunization are presented on the COVID-19 safety module on the VIEW-hub.org website. Here we describe the methods for identifying published studies.

A search of the published literature for COVID-19 vaccine safety studies assessing adverse events following immunization (AEFI) was conducted January 27, 2023. See Appendix 2 for literature search terms. AEFIs identified classified as an adverse event of special interest classified according to the Brighton Collaboration shown in Appendix 1 were searched for specifically by name to broaden search.

Titles and abstracts were reviewed to identify possible relevant studies. Full-text review was performed to evaluate inclusion criteria. Pre-prints later found to be published were excluded.

Inclusion Criteria:

- Studies Indexed in PubMed (including pre-prints) and published prior to January 27, 2023
- Evaluated active vaccine safety surveillance or cohort event monitoring studies
- Evaluated routine use of COVID-19 vaccines

Exclusion Criteria:

- Case reports and case-series studies
- Cross-sectional studies
- Safety evaluated in context of clinical trials, immunogenicity studies or effectiveness studies
- Analyses of passively collected safety data (e.g., VAERS, VigiBase)
- Studies evaluating diagnostic or detection methods of safety events
- Systematic reviews (but the citations of some highly relevant systematic reviews are reviewed to broaden sensitivity, however, this was not systematic)

Appendix 1: Adverse Events of Special Interest

Specific studies classified as Adverse Event of Special Interest (AESI), as determined by the Brighton Collaboration, were sought for specifically in the search criteria, among other studies (see Appendix 2 below). The Brighton Collaboration created a list of AESIs pertaining to COVID-19 vaccines (below and here). The AESIs are categorized according to level of association: those seen with COVID-19 disease, those that have a proven or theoretical association with immunization in general, and those that have a proven or theoretical association with specific vaccine platforms.

Articles that describe any AESIs on the Brighton Collaboration list are flagged as having that AESI. Articles with specific AESIs are flagged and can be searched for on the VIEW-hub safety module.

Table. Brighton Collaboration list of Adverse Events of Special Interest (AESI)

AESI Rationale to include as AESI (1, 2, 3, 4 and/or 5)	Brighton Case Definition Status
AESI included because they are seen with COVID-19 Disease [3,4]	
Acute respiratory distress syndrome	Submitted (Vaccine)
Multisystem inflammatory syndrome (children & adults)	Submitted (Vaccine)
Acute cardiovascular injury *(includes: myocarditis/pericarditis, microangiopathy, heart failure, stress cardiomyopathy, coronary artery disease arrhythmia)*	Myocarditis/pericarditis near completion. Others not yet started
Coagulation disorder *(includes: thrombotic disorders, bleeding disorders)*	Thrombosis near completion; Bleeding disorder WG to be formed
Anosmia, ageusia	WG to be formed
Chilblain – like lesions	WG to be formed
Erythema multiforme	Not yet started
Single Organ Cutaneous Vasculitis	Published
Acute kidney injury	Published lab-based criteria (see *)
Acute liver injury	Published lab-based criteria (see #)
Acute pancreatitis NEW (Dec 2020)	Not yet started
Rhabdomyolysis NEW (Dec 2020)	Not yet started
Subacute thyroiditis NEW (Dec 2020)	Not yet started
AESI included because they have a proven or theoretical association with immunization in general	
Anaphylaxis [1,2]	Published
Thrombocytopenia [1,2,3,4]	Published
Generalized convulsion [1,2]	Published
Acute disseminated encephalomyelitis [4]	Published
Guillain Barré Syndrome [3,4]	Published
AESI included because they have a proven or theoretical association with specific vaccine platform(s)	
Acute aseptic arthritis r-VSV	Published
Aseptic meningitis Live vaccines	Published
Encephalitis / Encephalomyelitis Live vaccines	Published
Idiopathic Peripheral Facial Nerve Palsy Intranasal EColi Heat Labile Toxin Adjuvanted Vaccine	Published
Vaccine associated enhanced disease 1(Formalin inactivated measles/RSV; HIV), 2(Chimeric YF Dengue), 5 (SARS / MERS-CoVs)	In press (Vaccine)

[1]*Proven association with immunization encompassing several different vaccines*
[2]*Proven association with vaccine that could theoretically be true for novel COVID-19 vaccines*
[3]*Theoretical concern based on wild type disease immunopathogenesis*
[4]*Theoretical concern related to viral replication during wild type disease*

[5]*Theoretical concern because it has been demonstrated in an animal model with ≥1 vaccine platform*

**Acute kidney injury – international consensus definition proposed by the Kidney Disease Improving Global Outcomes expert consensus group (www.kdigo.org)*

- *Increase in serum creatinine by ≥0.3 mg/dl (≥26.5 umol/l) within 48 hours; OR*
- *Increase in serum creatinine to ≥1.5 times baseline, known or presumed to have occurred within prior 7 days OR*
- *Urine volume ≤0.5 ml/kg/hour for 6 hours*

 # Acute liver injury – definition as used in majority of COVID-19 publications (but no international consensus):

- *> 3-fold elevation above the upper normal limit for ALT or AST OR*
- *> 2-fold elevation above the upper normal limit for total serum bilirubin or GGT or ALP*

Appendix 2: Literature Search Terms

PubMed:

((("Severe Acute Respiratory Syndrome"[mesh] OR “SARS” [tw] OR “SARS-CoV-2” [tw]) AND “vaccin*"[tw] OR ("COVID-19 Vaccines"[mesh] OR "COVID 19 Vaccin*"[tw] OR "COVID19 Vaccin*"[tw] OR "COVID-19 Vaccin*"[tw] OR "SARS-CoV-2 Vaccin*"[tw] OR "Coronavirus Disease 2019 Vaccin*"[tw]))

AND

(("adverse effect*"[ti] OR "adverse event*"[ti] OR "safety"[ti] OR "side effect*"[ti]) OR ("Myocarditis" [tw] OR "pericarditis" [tw] OR "Guillain-Barre Syndrome"[mesh] OR “Acute Inflammatory Polyneuropath*” [tw] OR "Guillain-barre syndrome"[tw] OR "acute autoimmune neuropath*"[tw] OR " Acute Infectious Polyneuritis"[tw] OR "Facial Paralysis"[Mesh] OR “Facial Pals*” [tw] OR "facial paralys*"[tw] OR “Encephalomyelitis, Acute Disseminated”[mesh] OR “Post-Vaccinal Encephalitis” [tw] OR "Thrombocytopenia"[Mesh] OR “Thrombopenia” [tw] OR "Anosmia"[Mesh] OR “ Smell Loss” [tw] OR "loss of smell"[tw] OR "Ageusia"[mesh] OR “ Taste Loss” [tw] OR "loss of taste" [tw] OR “Anaphylaxis” [mesh] OR “anaphylactic Shock” [tw] OR “ Anaphylactic Reaction” [tw] OR “ Blood Coagulation Disorders” [mesh] OR "Blood Coagulation Disorder*"[tw] OR “Seizures” [mesh] OR “Convulsion” [tw] OR "seizure*"[tw] OR "Petit Mal"[tw] OR "grand mal"[tw] OR “vaccine associated enhanced disease”[tw] OR “acute cardiovascular injury”[tw]))

AND

(("observational" [tiab] OR "follow-up study" [tiab] OR "prospective*" [tw] OR "longitudinal") OR "study"[tw] OR "rates"[tw] OR "incidence"[tw] OR ("product surveillance, postmarketing"[Mesh] OR "post-marketing"[tw] OR "postmarketing"[tw])))

NOT hesitancy [ti] NOT attitude[ti]
NOT "cross-sectional"[tw] NOT ("case*"[ti] AND "report"[ti]) NOT "predict*"[ti] NOT "case study"[ti]

NOT "review"[publication type] NOT "Systematic Review"[publication type] NOT "Systematic Review"[tw]
NOT "Clinical Trial" [Publication Type] NOT "Controlled Clinical Trial" [Publication Type] NOT "trial" [tw]