

Examples describing the different types of decisions that were made in the process of matching SAE types to AESI terms

Example 1, SAE types that matched an AESI term verbatim. The SAE term “hyperglycemia” was matched to the AESI list term “hyperglycemia” whereas we excluded the SAE “hypoglycemia” as the term was not on the AESI list. Similarly, “diarrhea” was on the AESI list, whereas “vomiting” was not.

Example 2, SAEs with alternative diagnostic names. The SAE term “facial paralysis” was included as this is an alternative diagnostic name for the AESI term “Idiopathic Peripheral Facial Nerve Palsy.” In contrast, the SAE term “facial swelling” was excluded as the term was not on the AESI list, and no other AESI types were likely to cause facial swelling.

Example 3, Applying the plausibility of disease time course to potential vaccine induced AESIs. The SAE term “osteoarthritis” was excluded although “arthritis” was on AESI list, as it was judged that osteoarthritis is a pathology that develops over many years and is unlikely to be caused by a vaccine within a period of months. In contrast, the SAE term “rheumatoid arthritis” was matched to the AESI “arthritis” as an exacerbation of an autoimmune arthritis, and is plausibly induced in a short time frame by a vaccine.

We included the SAE arthritis given it matched the term arthritis on the AESI list, which did not offer further specification of type of arthritis. In this situation SAEs would be included rather than excluded as sensitivity was desired over specificity. Again, including an SAE not associated with vaccine would only produce further noise and thus be expected to push associations toward the null.

Example 4, Applying the plausibility of causative mechanism to potential vaccine induced AESIs. The SAE term “gastrointestinal hemorrhage” was matched to the AESI term “bleeding disorder,” as gastrointestinal hemorrhage is a likely presentation for those with bleeding disorders. The SAE term “duodenal ulcer hemorrhage” was excluded because, while it is a subcategory of gastrointestinal hemorrhage, the causative mechanism for duodenal ulcer hemorrhage is duodenal ulcer. The latter is not an AESI term, and bleeding disorders do not typically present with duodenal ulcers as they do with the more general category of gastrointestinal hemorrhage.

Example 5, Judgment on likelihood of AESI term resulting in the SAE. The SAE term “abdominal pain” was matched to the AESI of “colitis/enteritis” as abdominal pain is the most likely presenting symptoms of colitis/enteritis. The SAE term “volvulus” was not matched; this is a relatively rare cause of abdominal pain, and there was no AESI term that would cause volvulus. The SAE “psychotic disorder” was matched to the AESI “psychosis,” whereas the SAE “suicidal ideation” was not matched, as psychosis does not typically present as suicidal ideation.

Example 6, Determining single AESI term to categorize SAE when multiple AESI terms can be applied. The SAE “chest pain” was matched with multiple AESIs including pulmonary embolism, and pericarditis, and multiple others. When this occurred the AESI judged to be the most likely was chosen by the clinician reviewers. This was done to ensure all included SAEs were given a single AESI category, to allow for any trends in AESI body systems to be noted, but none were identified clearly. This could limit the interpretation of which body systems of AESI are increased, but would not influence the total count of AESIs in each group. However, criticisms have helped identify a legitimate limitation of this method choice. A better way to handle cases like this would be to note that the SAE fits multiple AESI categories rather than a single AESI category.

Example 6 also applies to the SAE “non-cardiac chest pain” that was matched to the AESI of pericarditis. Non-cardiac chest pain was judged to be an SAE in which a cardiac nature had likely been ruled out after finding normal troponin levels and thus most likely explained by one of two serious causes: pulmonary embolism or pericarditis. Both of these diagnoses are frequently missed causes of chest pain that would be categorized as serious, and both would likely have normal troponin levels allowing a “non-cardiac chest pain” SAE categorization, in particular if these diagnoses had been missed. Undiagnosed pericarditis was therefore judged as the most likely cause of this SAE. There has been some questioning of how non-cardiac chest pain could be judged as pericarditis considering the relationship between pericarditis and the heart. The rationale for matching non-cardiac chest pain to the AESI of pericarditis was not related to whether pericarditis would be considered cardiac or non-cardiac, but instead based on the concern that pericarditis is frequently a cause of serious chest pain which is never diagnosed that could result in a SAE labeled as non-cardiac chest pain.