Supplementary Information 3: Derivation of Scores (D, Q, C, L, I, N)

We designed a novel quality assessment and data extraction tool, which included domains to capture information on study design (D) and quality of reporting (Q); confidence of comorbidity diagnosis (C); likelihood of a causal link between comorbidity and IMHA (L); confidence of IMHA diagnosis (I); and the number of patients with a given comorbidity (N).

Score D

Score D was assessed after positing the question: Does the study ask whether a comorbidity induces (or is associated with) IMHA as part of its hypothesis or specific aims, or is the question that a comorbidity induces (or is associated with) IMHA answered by study design? If the answer was yes, a D score was assigned; if the answer was no, the study was designated "Descriptive Association Only" for that comorbidity and assigned an arbitrary point of 1. A "'Retrospective case series or case report" was assigned 2 points; a "Cross-sectional study" was given 3 points; a "Retrospective cohort or case-control study" was assigned 4 points; both "Prospective case-control study" and "Prospective cohort study" were given 5 points; and an "'Unblinded randomized or non-randomized control trial or experiment" was assigned 7 points. Most of the comorbidities fell under "Descriptive Association Only"; there were 9 studies that were scored 7 points under "'Unblinded randomized or non-randomized control trial or experiment" design. Score D was derived by normalizing the assigned points (divided by 7, the maximum value).

Score Q

Score Q was assessed by evaluating 13 questions regarding the general quality of reporting of the study. Q1: Is (are) the study hypothesis (hypotheses) that a comorbidity or drug/vaccine

induces (or is associated with) IMHA clearly stated, OR is the question that a comorbidity or drug/vaccine induces (or is associated with) IMHA clearly answered by study design? Q2: Is (are) the specific aim(s)/objective(s) of the study clearly stated AND does at least one aim/objective include a means to identify whether a comorbidity or drug/vaccine induces (or is associated with) IMHA? Q3: Multi-center? Q4: Clear inclusion / exclusion criteria? Q5: Data on cases screened/excluded? Q6: Search terms described? Q7: Disease heterogeneity? Q8: Clear outcome measure definition? Q9: Clear presentation of results? Q10: Appropriate statistical testing? Q11: Variability measure reported (SD, range, interquartile range)? Q12: Conclusions supported by results? Q13: Clear conflict of interest statement? Answers to Q1-Q6 and Q8-Q13, were either "'No/absent/unclear/not applicable (NA)" (assigned 0 points), "Partially reported/suggested" (assigned 1 points) or "Yes" (assigned 2 points). For disease heterogeneity assessment in Q7, 2 points were given for "All cases are of one type or if diseases of disparate nature were analyzed in separate homogenous groups", 1 point was given for "Stratification is suggested but details are not explicitly stated" and 0 points were given for "All other references to disease heterogeneity". The general quality of reporting of the study was weighted according to our assessment of relative importance of these specific questions. A weighted sum of these 13 questions was then computed as:

2*Q1+2*Q2+Q3+Q4+Q5+Q6+2*Q7+2*Q8+3*Q9+3*Q10+2*Q11+3*Q12+Q13

General study quality for *Descriptive Association Only* was irrelevant to the question of the causal relationship between comorbidity and IMHA, and was therefore given 0 points. Score Q was then derived by normalizing the weighted sum (divided by 41, the maximum value in this dataset).

Score C

Score C assesses the confidence of comorbidity diagnosis. For infectious disease, “Direct organism detection (culture, cytology, PCR)” was given 3 points, “Serological detection of exposure” was given 2 points and “All other references to infection” was given 1 point; for cancer, “Consistent lesion with cytology or histopathology confirmation” was given 3 points, “Consistent lesion without cytology or histopathology confirmation” was given 2 points and “All other references to neoplasia” was given 1 point; for inflammatory disease, “Confident post mortem diagnosis” was given 3 points and “All other references to inflammatory disease” was given 1 point; for drugs and toxins, “Drug administered for ≥7d within 28d” was given 3 points, “Drug within 28d, no details” was given 2 points and “All other references to drugs” was given 1 point; for vaccines, both “Vaccinated within 14 days of diagnosis” and “Vaccinated within 30 days of diagnosis” were given 2 points and “All other references to vaccines” was given 1 point. Score C was then derived by normalizing the assigned points (divided by 3, the maximum value).

Score L

Score L assesses the likelihood of a causal link between comorbidity and IMHA, and each comorbidity was assigned either “'No/absent/unclear/NA” (1 point), “Partially reported/suggested” (2 points) or “Yes” (3 points). Score L was derived by normalizing the assigned points (divided by 3, the maximum value).

Score I

Score I assesses the confidence of IMHA diagnosis, and was assigned either “Suspicious” (1 point), “Supportive” (2 points), “Diagnostic” (3 points) or “Mechanistic study” (4 points). Score I was derived by normalizing the assigned points (divided by 4, the maximum value).

Score N

Score N accounts for the number of patients with a given comorbidity, and was given 1 point (1 patient), 2 points (2-5 patients), 3 points (6-10 patients), 4 points (11-20 patients), 5 points (21-50 patients) or 6 points (≥51 patients). Score N was derived by normalizing the assigned points (divided by 6, the maximum value).