Validation of ICD Code-Based Identification of Myocarditis Among mRNA COVID Vaccine Immunized Patients and COVID-Infected Patients

Chenan Zhang[1*], Claudia Ana Ianos[1], Stephen Edward Schachterle[1], Jill Dreyfus[1], Jonathan C. Johnson[2], Irene Margolin-Katz[2], Ankita Gupta[2], Cynthia Senerchia[2], Scott P. Kelly[1]

[1]Pfizer Inc, New York, New York, USA, [2]Optum, Eden Prairie, MN, USA

*Corresponding author email: chenan.zhang@pfizer.com

ISPOR 2025
Poster code: EPH125
Poster Session 4
Thursday, May 15, 2025
Discussion Period:
6:00 - 7:00 PM

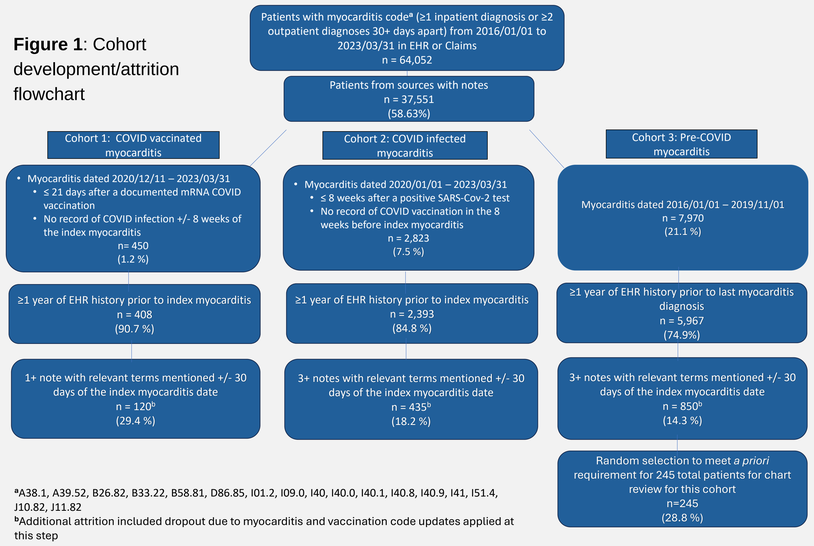
BACKGROUND:

- Myocarditis is an inflammatory disease of the myocardium (1). Diagnosis is challenging due to the heterogeneity of clinical presentations (2,3)
  - Endomyocardial biopsy (EMB) (the diagnostic gold standard) is infrequently used (2)
- International Classification of Diseases (ICD) codes are commonly used to identify myocarditis cases in real-world studies with recent efforts to validate such case-finding definitions (4)
  - Post-marketing safety surveillance for vaccines use case definition criteria for retrospective assessment of post-vaccination cases, such as CDC and the Brighton Collaboration (5,6)
- Study question: how do ICD-based myocarditis diagnoses perform when assessed with Brighton Collaboration criteria for myocarditis among:
  - Cohort 1: mRNA COVID-19 vaccine immunized patients
  - Cohort 2: SARS-CoV-2-infected patients
  - Cohort 3: myocarditis of any other cause prior to COVID era

METHODS:

- Data source: Optum's de-identified Market Clarity Data (Market Clarity) deterministically links medical and pharmacy claims with electronic health record data
- Study period: 01 Jan 2016 - 31 Mar 2023
- Study population:
  - Inclusion criteria:
    - Diagnosis of myocarditis identified using ICD-10 codes in EHR and/or claims
    - At least 1 myocarditis inpatient record or ≥2 myocarditis outpatient records dated ≥30 days apart
    - Myocarditis diagnosis:
      - Cohort 1: 11 Dec 2020 - 31 Mar 2023
      - Cohort 2: 01 Jan 2020 - 31 Mar 2023
      - Cohort 3: 01 Jan 2016 - 01 Nov 2019
    - ≥365 days of enrollment or activity in the EHR prior to the index myocarditis diagnosis
    - Availability of medical notes to use for confirmation of myocarditis 30 days -/+ the index event
  - Additional inclusion criteria by cohort:
    - Cohort 1: Record of mRNA vaccination within 21 days prior to the myocarditis diagnosis without a record of SARS-CoV-2 positive test within 8 weeks prior to myocarditis diagnosis
    - Cohort 2: Record of SARS-CoV-2 positive test within 8 weeks prior to myocarditis diagnosis, with no record of mRNA COVID-19 vaccination during that time
    - Cohort 3: No additional criteria
  - Exclusion criteria: <365 days between 1st recorded activity and index myocarditis

Figure 1: Cohort development/attrition flowchart



[a]A38.1, A39.52, B26.82, B33.22, B58.81, D86.85, I01.2, I09.0, I40, I40.0, I40.1, I40.8, I40.9, I41, I51.4, J10.82, J11.82
[b]Additional attrition included dropout due to myocarditis and vaccination code updates applied at this step

- Analysis:
  - Two clinicians reviewed medical records for myocarditis using the Brighton Collaboration criteria and diagnostic certainty levels:
    - Validated: Levels 1 (Confirmed), 2 (Probably) and 3 (Possible)
    - Not validated: Levels 4 (Insufficient Evidence), 5 (Not a case)
  - Concordance of ICD based myocarditis diagnoses with Brighton Collaboration case definitions and level of certainty (% validated among all ICD-code based diagnoses) calculated for each cohort overall and by strata: diagnosis setting, age, and comorbidity status

RESULTS

- Lowest concordance (myocarditis ICD codes validated by clinician review) observed in Cohort 1 (49%) compared to Cohort 2 (77%) and Cohort 3 (65%)
- In Cohort 1, concordance was higher in patients <25 vs 25+ years old (90% vs 41%), in Hispanic vs non-Hispanic patients (89% vs 46%), in patients with 0 vs 1+ Charlson Comorbidity Index (CCI) (63% vs 39%); and in inpatient/emergency department (IP/ED) vs outpatient settings (70% vs 30%)
- In Cohorts 2 and 3, concordance was also higher in IP/ED vs outpatient settings (80% vs 62% and 76% vs 51%, respectively), but similar by age, ethnicity, and CCI
- No concordance differences were noted by sex, race, geographical region, insurance type, or prior healthcare utilization for any cohort
- Notably, among the 65 unvalidated myocarditis codes (Brighton levels 4 and 5) from patients in Cohort 1, 37 (57%) were D86.85, sarcoid myocarditis
  - 17/24 (71%) were D86.85 for sarcoid myocarditis among Brighton level 5 cases

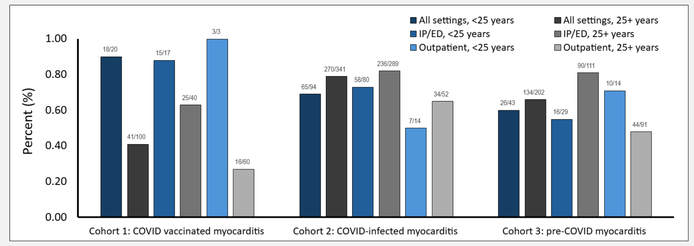
Table 1 Myocarditis patient characteristics stratified by case definition and cohort

	All Cohort 1: COVID vaccinated myocarditis (N=120)	Validated Cohort 1: COVID vaccinated myocarditis (N=59)	All Cohort 2: COVID infected myocarditis (N=435)	Validated Cohort 2: COVID infected myocarditis (N=335)	All Cohort 3: Pre COVID myocarditis (N=245)	Validated Cohort 3: Pre COVID myocarditis (N=160)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Index age, Median (Q1 - Q3)	54.5 (34 - 63.5)	40 (21 - 61)	51 (28 - 64)	52 (29 - 64)	48 (32 - 61)	46. 5 (31.5 , 59)
Gender						
Female	44 (36.7%)	22 (37.3%)	188 (43.2%)	153 (45.7%)	101 (41.2%)	68 (42.5%)
Male	76 (63.3%)	37 (62.7%)	247 (56.8%)	182 (54.3%)	144 (58.8%)	92 (57.5%)
Race						
African American	31 (25.8%)	15 (25.4%)	100 (23.0%)	85 (25.4%)	50 (20.4%)	33 (20.6%)
White	78 (65.0%)	40 (67.8%)	266 (61.1%)	197 (58.8%)	168 (68.6%)	109 (68.1%)
Other/Unknown	11 (9.1%)	<5	69 (15.9%)	53 (15.8%)	27 (11.0%)	18 (11.2%)
Ethnicity						
Hispanic	9 (7.5%)	8 (13.6%)	50 (11.5%)	36 (10.7%)	24 (9.8%)	16 (10.0%)
Not Hispanic	84 (70.0%)	36 (61.0%)	285 (65.5%)	225 (67.2%)	200 (81.6%)	133 (83.1%)
Unknown	27 (22.5%)	15 (25.4%)	100 (23.0%)	74 (22.1%)	21 (8.6%)	11 (6.9%)
Region						
Midwest	35 (29.2%)	17 (28.8%)	127 (29.2%)	94 (28.1%)	87 (35.5%)	60 (37.5%)
Northeast	57 (47.5%)	28 (47.5%)	164 (37.7%)	126 (37.6%)	100 (40.8%)	63 (39.4%)
Other/Unknown	5 (4.2%)	<5	18 (4.1%)	12 (3.6%)	16 (6.5%)	9 (5.6%)
South	15 (12.5%)	8 (13.6%)	113 (26.0%)	92 (27.5%)	34 (13.9%)	23 (14.4%)
West	8 (6.7%)	<5	13 (3.0%)	11 (3.3%)	8 (3.3%)	5 (3.1%)
Insurance type (At Index)						
Commercial	66 (55.0%)	34 (57.6%)	214 (49.2%)	169 (50.4%)	123 (50.2%)	79 (49.4%)
Medicaid	17 (14.2%)	9 (15.3%)	93 (21.4%)	73 (21.8%)	48 (19.6%)	35 (21.9%)
Medicare	18 (15.0%)	7 (11.9%)	83 (19.1%)	66 (19.7%)	56 (22.9%)	34 (21.3%)
Other/Unknown	19 (15.8%)	9 (15.3%)	45 (10.3%)	27 (8.1%)	18 (7.3%)	12 (7.5%)
Healthcare Utilization in previous 182 days						
Inpatient Hospitalization	32 (26.7%)	15 (25.4%)	168 (38.6%)	131 (39.1%)	124 (50.6%)	90 (56.3%)
Emergency Department	29 (24.2%)	11 (18.6%)	108 (24.8%)	84 (25.1%)	76 (31.0%)	53 (33.1%)
Outpatient Visit	105 (87.5%)	48 (81.4%)	326 (74.9%)	249 (74.3%)	200 (81.6%)	120 (75.0%)
Charlson Comorbidity Index in previous 365 days						
0	49 (40.8%)	31 (52.5%)	210 (48.3%)	159 (47.5%)	91 (37.1%)	62 (38.8%)
1+	71 (59.2%)	28 (47.5%)	225 (51.7%)	176 (52.5%)	154 (62.9%)	98 (61.3%)

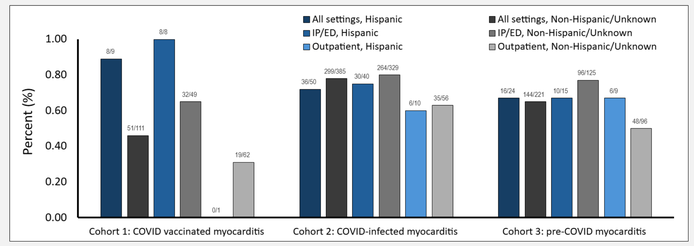
Note: To reduce risk of re-identification, cells with fewer than n=5 were masked as "<5"

Figure 2. Concordance between ICD code and Brighton Collaboration-defined myocarditis by diagnosis setting and (A) age, race/ethnicity (B), and CCI (C)

A



B



C

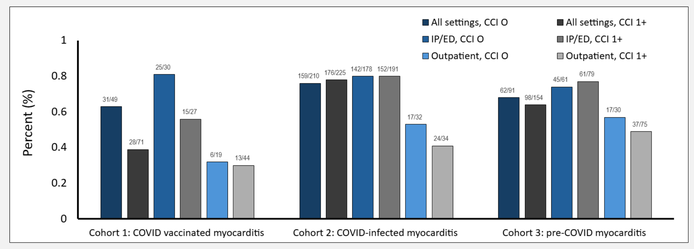


Table 2 Most common myocarditis ICD codes by cohort and Brighton Collaboration category

Code	Description	Cohort 1 Brighton Category 1, 2, 3	Cohort 1 Brighton Category 4, 5	Cohort 2 Brighton Category 1, 2, 3	Cohort 2 Brighton Category 4, 5	Cohort 3 Brighton Category 1, 2, 3	Cohort 3 Brighton Category 4, 5
	Total	66	65	378	109	186	88
B33.22	Viral myocarditis	<5	<5	12 (3.2%)	8 (7.3%)	11 (5.9%)	<5
D86.8	Sarcoid myocarditis	12 (18.2%)	37 (56.9%)	<5	<5	<5	<5
I40.0	Infective myocarditis	<5	<5	47 (12.4%)	10 (9.2%)	7 (3.8%)	<5
I40.1	Isolated myocarditis	<5	<5	<5	5 (4.6%)	12 (6.5%)	8 (9.1%)
I40.8	Other acute myocarditis	5 (7.6%)	<5	13 (3.4%)	<5	6 (3.2%)	<5
I40.9	Acute myocarditis, unspecified	8 (12.1%)	<5	44 (11.6%)	10 (9.2%)	30 (16.1%)	12 (13.6%)
I51.4	Myocarditis, unspecified	29 (43.9%)	17 (26.2%)	254 (67.2%)	70 (64.2%)	114 (61.3%)	56 (63.6%)

Note: To reduce risk of re-identification, cells with fewer than n=5 were masked as "<5"

CONCLUSIONS

The concordance of myocarditis ICD-code with Brighton Collaboration criteria varies by age, ethnicity, comorbidities, care setting, and cohort. Future directions include the development of ICD-code based algorithms using correlates of concordance for improved myocarditis case identification in both COVID and non-COVID contexts in the real-world setting.

ACKNOWLEDGEMENTS: Thanks to Jake Thistle for supporting poster development
DISCLOSURES: This study was sponsored by Pfizer Inc

REFERENCES:

1. Al-Akchar M, Shams P, Kiel J. Acute Myocarditis. [Updated 2023 Feb 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441847/
2. Heymans S, Dawson D, Fuster V, et al. Myocarditis following SARS-CoV2 mRNA vaccination against COVID-19: facts and open questions. J Am Coll Cardiol. 2022;80(14):1363-65.
3. Caforio AL, Pankuweit S, Arbustini E, et al; European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2013 Sep;34(33):2636-48, 2648a-2648d. doi: 10.1093/eurheartj/eht210. Epub 2013 Jul 3. PMID: 23824828.
4. Lufkin BC, Wong HL, Amend KL, et al. Validation of a claims-based algorithm for myocarditis/pericarditis using medical chart review. Pharmacoepidemiology and Drug Safety (Vol. 32, pp. 183-184).
5. Gargano JW, Wallace M, Hadler SC, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: update from the advisory committee on immunization practices — United States, June 2021. MMWR Morb Mortal Wkly Rep 2021;70:977-82.
6. Sexson Tejtel SK, Munoz FM, Al-Ammouri I, et al. Myocarditis and pericarditis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine 2022;40:1499-511