Validation of acute myocardial infarction ICD-9 codes – Appendix

Full description of criteria for selection of potential post-IGIV acute myocardial infarction cases.

The study population consisted of new IGIV users who initiated treatment from January 1, 2006, through December 31, 2012. New IGIV users were defined as those with an IGIV treatment preceded by a period of 183 days of medical and pharmaceutical insurance coverage, during which no Ig treatments were observed. The first such IGIV treatment date was designated the patient's new use date. For the parent study on IGIV and thromboembolic event (TEE) risk, the arterial TEE endpoint included cases of acute myocardial infarction (AMI) and ischemic stroke.

Patients were followed from the IGIV new use date until the first occurrence of an inpatient arterial TEE diagnosis during a post-IGIV risk or control period, loss of health plan enrollment, or the end of the study period (December 31, 2012). For the arterial TEE endpoint, the risk period was defined as days 0-2 following an IGIV treatment, and the control period as days 14-27 following an IGIV treatment.

After identifying patients with a qualifying post-IGIV inpatient arterial TEE diagnosis, we applied the following exclusion criteria. A patient was excluded if (a) an inpatient encounter with an arterial TEE diagnosis was observed in the prior 30 days, (b) no medical procedure or diagnosis constituting a potential IGIV indication was observed in the prior 183 days, (c) the patient received IGIV within 20 days of a prior or subsequent IGIV treatment episode, or the end of the study period (to ensure that a control period was observable for the patient), or (d) the proximate IGIV treatment episode included an administration of a subcutaneous or intramuscular IG product or multiple branded IGIV products on or before the TEE admission date.

In this manuscript we report on the positive predictive value (PPV) associated with AMI diagnoses. PPVs for stroke diagnoses codes are reported separately.

For additional details, please see the protocol for the parent study, available online at

https://www.sentinelsystem.org/sites/default/files/Drugs/Assessments/Mini-Sentinel_Thromboembolic-Events-After-Immunoglobulin-Administration-Protocol_0.pdf .

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Appendix Table A1. Reasons charts could not be obtained for review.

Reason	Frequency
Chart not retrieved due to high cost	2
Unable to locate chart corresponding to requested encounter	9
Unable to map treatment record in SDD to provider name/identifiers needed for chart request	7
Insufficient information in chart	1
Provider did not reply	4
Provider refused to participate	5
Provider refused to participate due to legal/compliance/HIPAA concerns	5
Other or unspecified	4
Total	37

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AMI Adjudication Criteria

STEP 1. Criteria for Definite Acute Myocardial Infarction (AMI) or sudden cardiac death

Check if present:

Evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia (eg symptoms such chest pain, shortness of breath). Any one of the following, meets the definition for diagnosis of AMI:

- ☐ 1. Diagnostic cardiac biomarkers & EKG changes (**need BOTH A & B**)
  - ☐ A. Detection of rise and/or fall of cardiac biomarkers ([preferably cardiac troponin (cTn) but CK-MB or CK is acceptable if troponin is not available] with at least one value above the 99th percentile of the upper reference limit (URL)*
  - ☐ B. **AND** one or more of the following:
    - ☐ Ischemic symptoms
    - ☐ ECG changes indicative of new ischemia (new ST-T changes or new LBBB)
    - ☐ Development of pathological Q waves in ECG
    - ☐ Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality Identification of intracoronary thrombus by angiography or autopsy
- ☐ 2. Cardiac death with symptoms suggestive of myocardial ischemia and ischemic EKG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarkers would be increased.
- ☐ 3. Pathological findings postmortem of an acute AMI
- ☐ 4. PCI related AMI: elevations in cTn levels greater than 5x 99th percentile URL* in patients with normal baseline values (eg <99th percentile URL) or a rise in cTn values >20% if the baseline values were elevated or falling during the first 48 hours post-PCI. In addition, (i) symptoms suggestive of myocardial ischemia or (ii) new ischemic changes or (iii) angiographic findings consistent with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality.
- ☐ 5. Stent thrombosis AMI detected by coronary angiography or autopsy in the setting of myocardial ischemia with a rise/and or fall of cardiac biomarker values with at least one value above 99th percentile.
- ☐ 6. CABG related AMI: elevations in cardiac biomarkers greater than 10 x 99th percentile URL* in patients with normal baseline values (eg <99th percentile URL) during the first 72 hours post-CABG and one or more of the following:
  - ☐ New pathological Q waves
  - ☐ New LBBB
  - ☐ Angiographically documented new graft or native coronary artery occlusion

- ☐ Imaging evidence of new loss of viable myocardium or a regional wall motion abnormality

* Note: if the 99th percentile of the upper reference limit (URL) from the respective laboratory performing the assay is not available then the URL for the myocardial necrosis from the laboratory should be used. If the 99th percentile of the URL or the URL for myocardial necrosis is not available, the AMI decision limit for the particular laboratory should be used as the URL.

If the above criteria are met then check box below and form is finished, if not proceed to step 2.

☐ Definite AMI

Step 2. If criteria above for definite AMI are not met, use the table below to determine probability of AMI based on symptoms, cardiac biomarkers, and ECG

Cardiac Enzymes				
	Abnormal	**Equivocal**	**Incomplete**	**Normal**
ECG Pattern/Symptoms				
Cardiac pain present:				
Evolving, diagnostic ECG: Evolving Q wave and evolving ST-T abnormalities	Definite MI	Definite MI	Definite MI	Definite MI
Positive ECG: Equivocal Q wave evolution with ST-T depression/inversion; or evolving ST-T elevation alone; or new left bundle branch block	Definite MI	Definite MI	Probable MI	No MI
Nonspecific ECG: evolution of minor ST-T depression/inversion or minor Q-wave evolution alone and not classified above	Definite MI	Probable MI	No MI	No MI
ECG negative for ischemia: Normal ECG, other ECG, or ECG absent	Definite MI	No MI	No MI	No MI
Cardiac pain absent:				
Evolving, diagnostic ECG: Evolving Q wave and evolving ST-T abnormalities	Definite MI	Definite MI	Definite MI	Probable MI
Positive ECG: Equivocal Q wave evolution with ST-T depression/inversion; or evolving ST-T elevation alone; or new left bundle branch block	Definite MI	Probable MI	No MI	No MI
Nonspecific ECG: evolution of minor ST-T depression/inversion or minor Q-wave evolution alone and not classified above	Probable MI	No MI	No MI	No MI
ECG negative for ischemia: Normal ECG, ECG absent or unreadable	No MI	No MI	No MI	No MI

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	Interpretation of cardiac enzymes		
Cardiac Enzyme	**Abnormal**	**Equivocal**	**Normal**
CK-MB (highest value)	$\geq 99^{th}$ percentile URL	>ULN and $<99^{th}$ percentile URL	WNL
Troponin (highest value)	$\geq 99^{th}$ percentile URL	>ULN and $<99^{th}$ percentile URL	WNL
CK (no MB available- consider highest value)	N/A	$\geq 99^{th}$ percentile URL	WNL

Abbreviations: electrocardiogram (ECG), within normal limits (WNL), upper reference limit (URL), upper limit of normal (ULN), creatine kinase (CK).

Step 2 Adjudication decision

- ☐ Definite AMI
- ☐ Probable AMI
- ☐ Possible AMI (criteria for definite or probable AMI not met, but physician diagnosis of AAMI documented in chart)
- ☐ No AMI (ruled out)
- ☐ Insufficient information / unknown

If 'Probable', 'possible' or 'insufficient information / unknown', what data were needed but not available:

- ☐ Cardiac biomarkers
- ☐ ECGs
- ☐ Information on ischemic symptoms
- ☐ Other _____
- ☐ None
- ☐ If this information is obtained return for adjudication