Duke Clinical Research Institute

Cardiovascular Event Identification in EHR & Claims Data

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Disclosures for

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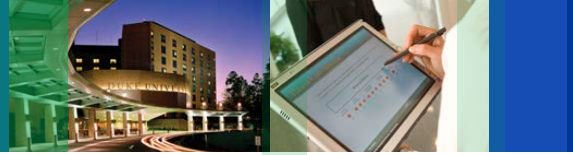
Amgen, Novartis, GlaxoSmithKline (pending), Boston Scientific (pending), St Jude Medical (pending)

Endpoint Selection in Electronic Healthcare Data

Most reliable if *serious* and *results in immediate healthcare episode*

Typical MACE components

- Myocardial infarction
- Stroke
- Congestive heart failure
- Coronary revascularization
- Major bleeding
- Cardiovascular death



Reliability of Endpoint Ascertainment is Variable

Mortality

Occurrence (but not cause) s/b highly reliable in claims

Procedure-based endpoints

Highly reliable due to need for reimbursement

Hospitalization-based endpoints

Dependent on coding of condition

Less Questionable → ***More Questionable***

MI	***Stroke***	***Bleeding***
~10 ICD-9-CM Dx codes w/in 1 3-digit code series	*~15 ICD-9-CM Dx codes w/in 5 3-digit code series*	*~80 ICD-9-CM Dx codes w/in ~20 3-digit code series*

Comparing to Adjudicated Trial Rates

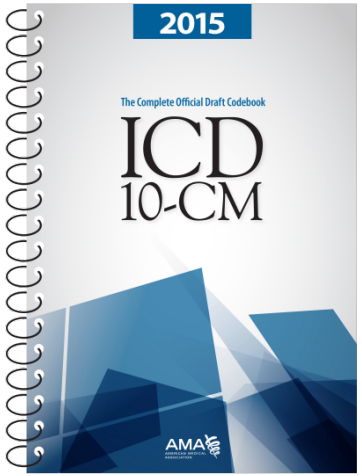
Myocardial Infarction	
Claims criteria	Adjudication criteria
Inpatient encounter w/ ICD-9-CM diagnosis code 410.x0, 410.x1 in primary position	ECG or changes consistent with acute infarction or ischemia MI: • New diagnostic Q waves (Q wave in leads V2 and V3 ≥ 0.02 sec or QS complex in leads V2 and V3; Q wave ≥ 0.03 sec and ≥ 0.1 mV deep or QS complex in leads I, II, aVL, aVF or V4-V6 in any two leads of a contiguous lead grouping (I and aVL; V1-V6; II, III, aVF, R wave ≥ 0.04 sec in V1 and V2 and R/S ≥ 1 with a concordant positive T wave)) in the absence of conduction abnormalities • New significant ST-segment- T-wave changes in two or more contiguous leads: ST elevation at the J point ≥ 0.1 mV in all leads other than leads V2 and V3 where the following cut points apply: ≥ 0.2 mV in men ≥ 40 years; 0.25 mV in men < 40 years, or ≥ 0.15 mV in women. ST depression horizontal or downsloping ≥ 0.05 mV; or T wave inversion ≥ 0,1mV with prominent R wave or R/S ratio ≥ 1. • Development of new left bundle branch block (LBBB) • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality • Intracoronary thrombus by angiography *AND* Elevated cardiac biomarkers (values according to each hospital's laboratory): A rise and/or fall in cardiac biomarker values (preferably troponin, CKMB, AST, LDH or myoglobin) with at least one value above the 99th percentile of the upper reference limit.

Case-Identification Algorithms

Sources include…

- Validation studies
- Other published studies
- Quality measure definitions
- Reimbursement guidance (esp. procedures)
- .
- .
- .

Direct code searches



Using Existing Algorithms

Validation study caveats

- Based on small sample?
- Based on single site data?
- Do not report sensitivity or specificity?
- Based on claims data, not EHR data?
- Discordant results from another study?

General considerations

- Algorithm for incident events or prevalent disease?
- Based on code sets you need?

New Algorithm: ADAPTABLE Major Bleeding

Hospitalization for Bleeding
(Based on primary Dx)

+

Blood Product Transfusion
(Based on many things)

Need to understand…

- All possible coding for transfusions
- Insurance coverage allowances
- Reimbursement documentation requirements

Good practice: Validate a sample of your endpoints

EHR Data and Endpoint Ascertainment

Issues to consider

- Less structured and less consistent than claims
  e.g. primary diagnosis not necessarily an EHR concept
- Different coding systems
  e.g., SNOMED-CT, site-specific
- Mortality outside of the system is not well captured
- Potential for site-specific differences in…
  …completeness of patient healthcare received
  …coding practices
  …data availability

Other safety endpoints using EHR data?

"Additional parameters such as increase in body weight, oedema/fluid retention, occurrence of hypertension, significant changes in heart rate/arrhythmias, or increases in LDL-cholesterol could also be systematically collected whenever this is considered relevant (e.g. based on mechanism of action or pre-clinical findings). Clinically relevant changes in cardiac function should be evaluated by cardiac imaging, if there is an indication of a detrimental effect on cardiac function."

Source: EMA, Reflection Paper on Assessment of Cardiovascular Safety Profile of Medicinal Products