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RECORD Experience Event Ascertainment

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Overview

Key Messages

- Systematic strategies to identify events are critical
- Site Investigators typically under-report events
- Under-reporting of certain events may compromise detection of efficacy / safety signals

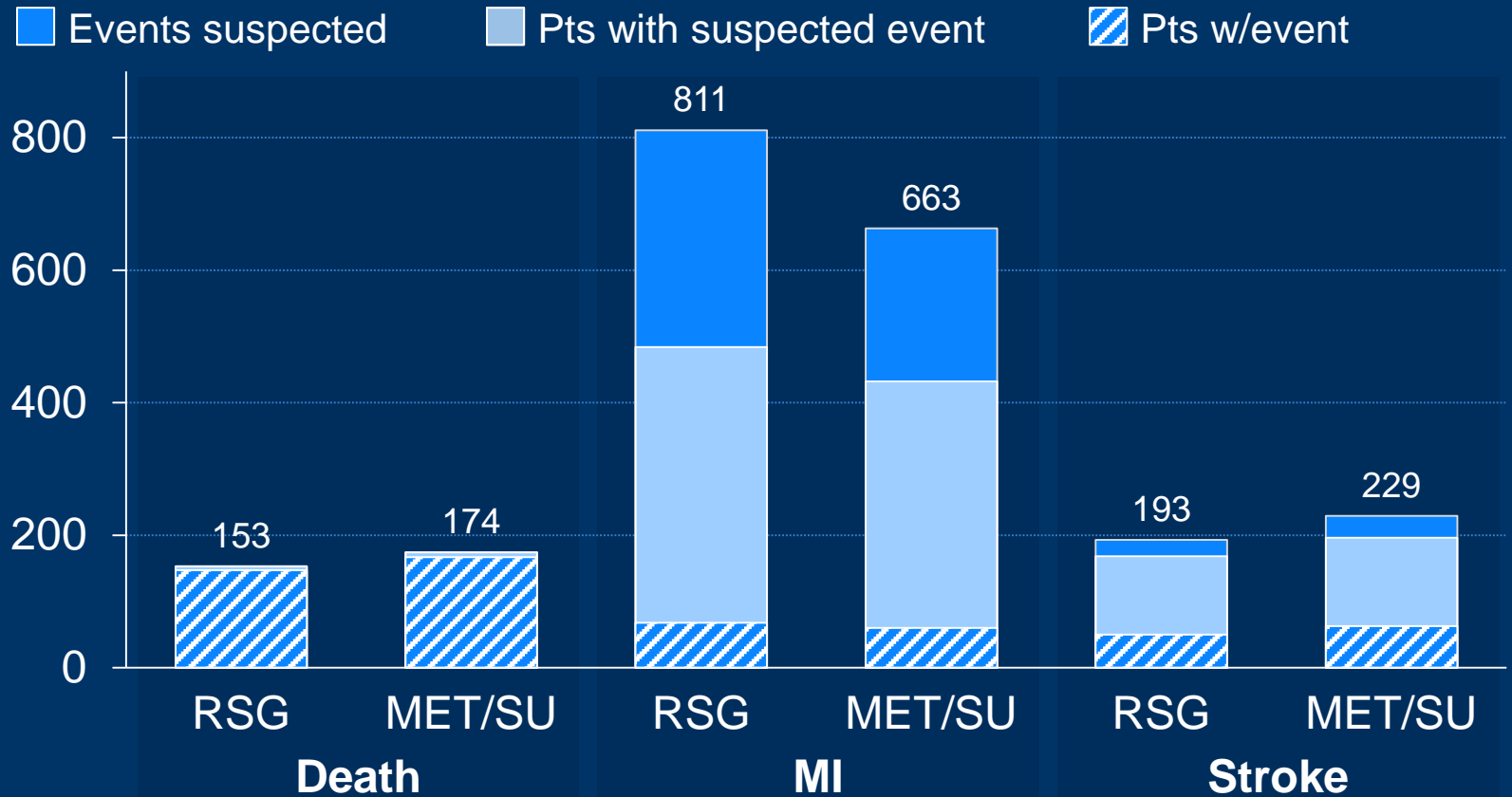


Identification of Suspected Events - RECORD

- Programmatic identification of suspected events included:
 - Screening of AE and SAE database
 - Pre-specified MedDRA coded terms
- Review of listings included:
 - Patients who withdrew
 - Patients who started new cardiac medications
 - Hospital admission with associated AEs
- Manual review of all source documents
- Manual review of all CRF pages including non-databased fields
- Review of deleted AEs and SAEs from original database audit trail

CEC Adjudicated Events

Total: 2223
Death: 327
MI: 1474
Stroke: 422

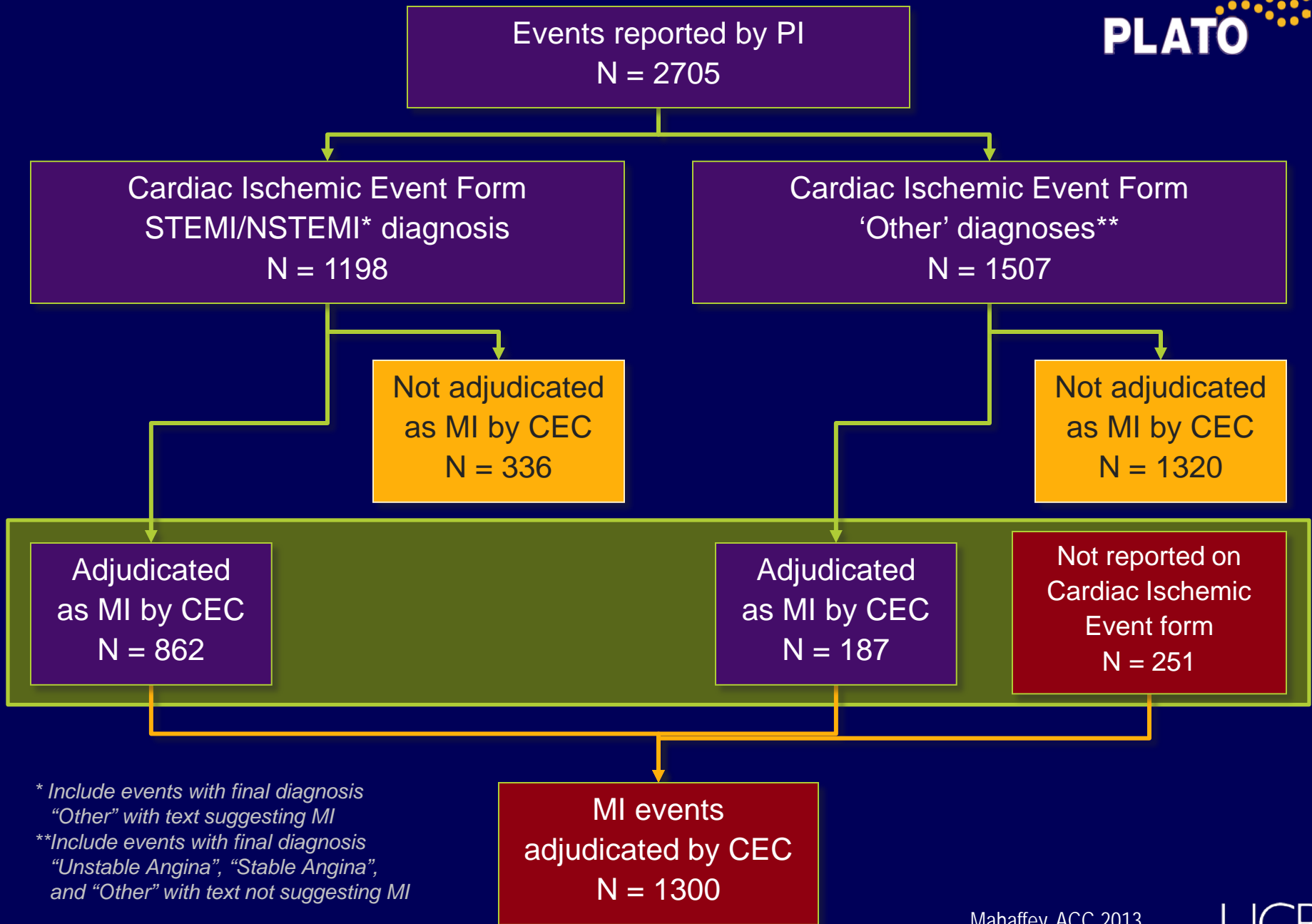


| | | | | | | |
|--------------------------|-----|-----|-----|-----|-----|-----|
| Pts with suspected event | 153 | 174 | 482 | 431 | 168 | 195 |
| Pts w/event | 147 | 167 | 68 | 60 | 50 | 63 |

RECORD Readjudication Disagreements

- **MI Disagreement**
 - 14 not reported by both
 - 11 reported by DCRI CEC
 - 3 reported by Original CEC
- **Stroke Disagreements**
 - 18 not reported by both
 - 11 reported by DCRI CEC
 - 7 reported by Original CEC

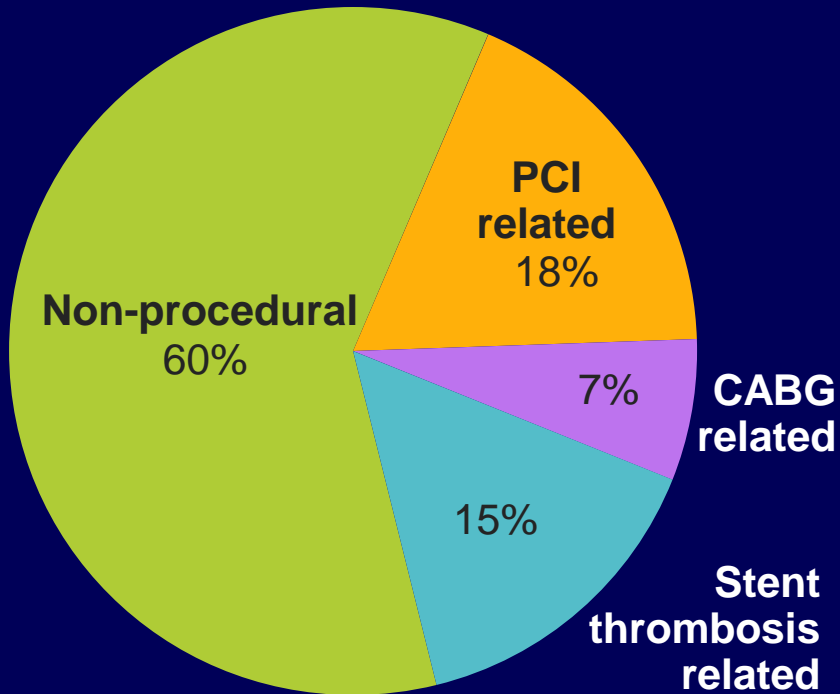




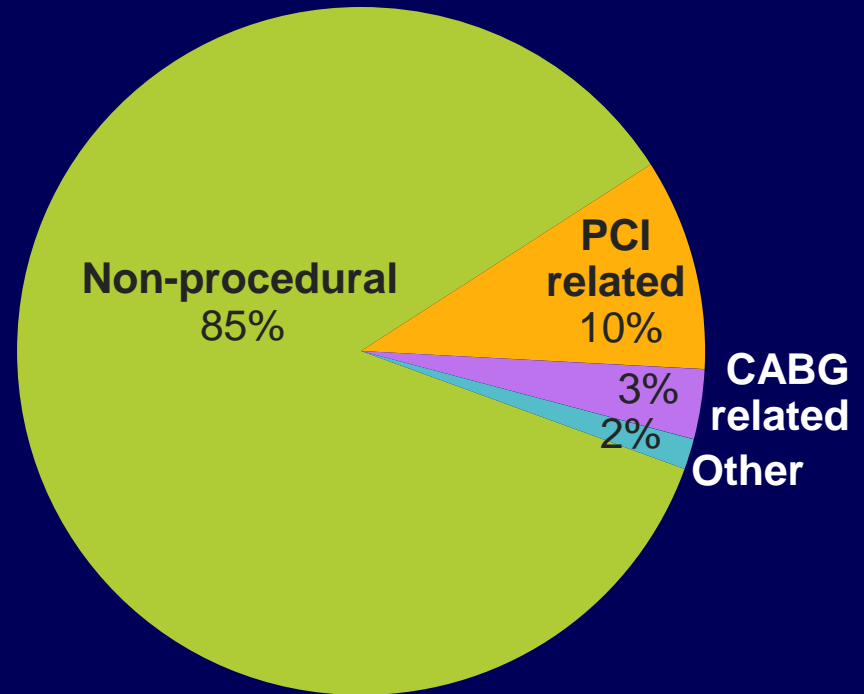
* Include events with final diagnosis "Other" with text suggesting MI

**Include events with final diagnosis "Unstable Angina", "Stable Angina", and "Other" with text not suggesting MI

CEC MIs



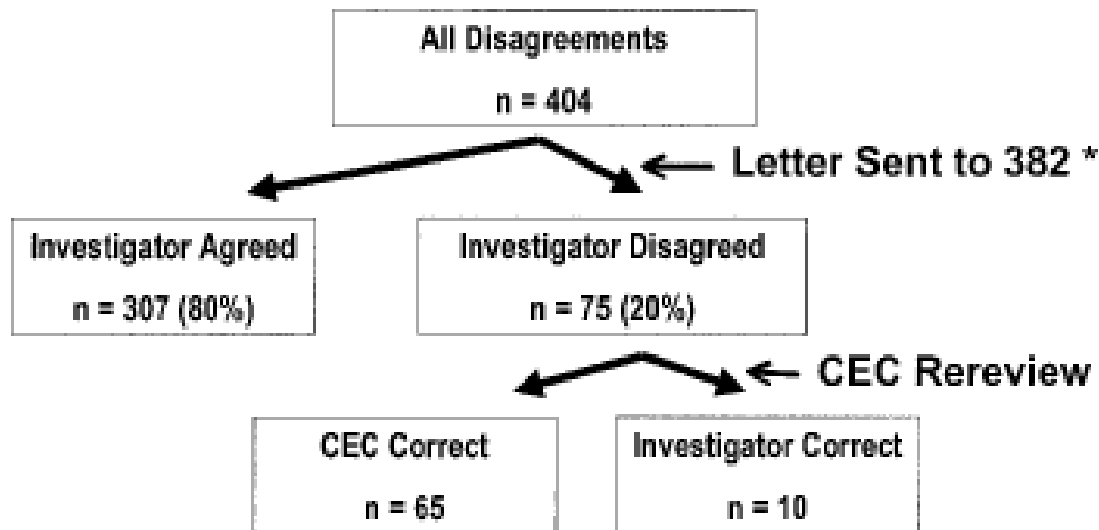
Investigator Reported MIs



Reconciliation of Disagreements

PARAGON B

Figure 2

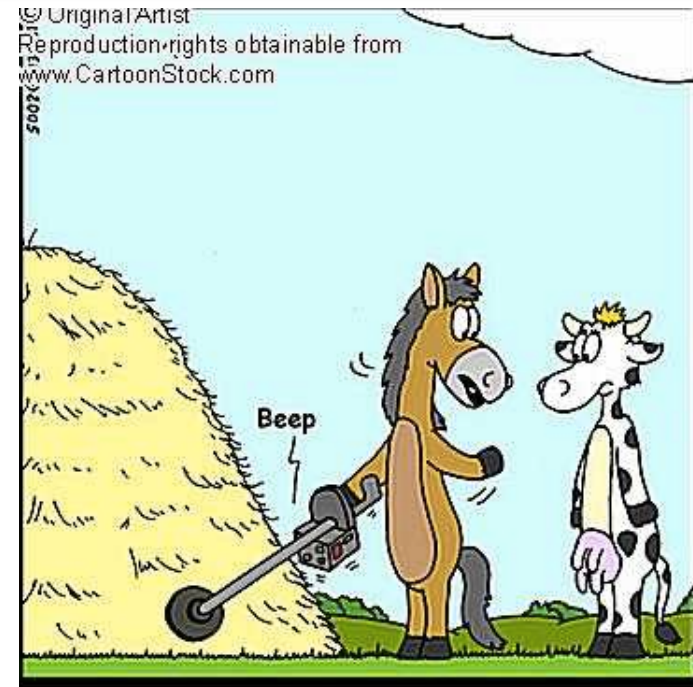


Reconciliation of disagreements between site-investigator and CEC assessments of MI.

*Twenty patients had core laboratory data identifying MI, and 2 patients had MI >24 hours before enrollment.

Summary

- Systematic screening is important to ascertain events.
- Need data collection that supports event identification
- Site Investigators under-report endpoint events
- Lack of reporting may impact drug evaluation



You were right: There's a needle in this haystack...



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Treatment Effect: CEC and Site Investigator

| | Ticagrelor | Clopidogrel | HR (95% CI) (Tic vs. Clo) |
|--------------------------|------------|-------------|------------------------------|
| CEC | | | |
| All MI | 508 | 599 | 0.840 (0.746–0.945) |
| STEMI | 117 | 159 | 0.731 (0.576–0.928) |
| NSTEMI | 356 | 404 | 0.875 (0.758–1.008) |
| Not evaluable | 45 | 57 | 0.785 (0.531–1.160) |
| Q-wave | | | |
| Q-wave | 42 | 46 | 0.909 (0.598–1.381) |
| Non Q-wave | | | |
| Non Q-wave | 333 | 375 | 0.881 (0.761–1.022) |
| Not evaluable | 160 | 208 | 0.763 (0.621–0.938) |
| Site Investigator | | | |
| All MI | 459 | 516 | 0.883 (0.779–1.001) |
| STEMI | 156 | 196 | 0.791 (0.641–0.976) |
| NSTEMI | 287 | 307 | 0.929 (0.791–1.091) |
| Other | 29 | 31 | 0.931 (0.561–1.545) |