# Development of a clinical prediction rule for 30-day cardiac events in emergency department patients with chest pain and possible acute coronary syndrome

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Speaker: R2 游姿寧

Supervisor: VS 吳柏衡

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# INTRODUCTION

- Chest pain:  > 6000000 visits in US yearly
- 2.1% of AMI was misdiagnosed, 30-day mortality: 9.1%
- However, some patients were low-risk but undergo prolonged evaluation
- Could low-risk patients be discharged earlier?

# GOAL OF THIS PAPER

- To derive a clinical prediction rule to identify adults with chest pain and at very low risk for cardiac event, for whom additional ED investigations might be unneccessary

# MATERIALS AND METHODS

- 3 academic EDs: 2 in Canada, 1 in US
- July 2007 to Feb 2010
- ≥ 24 y/o adults with typical anterior chest pain, initial normal ECG and Troponin level
- Excluding: acute ST-segment elevation, HR >100 or <50, SBP <90 mmHg, unreliable clinical history, a clear traumatic cause, cocaine usage, a terminal noncardiac illness, pregnancy, inability to follow-up…..

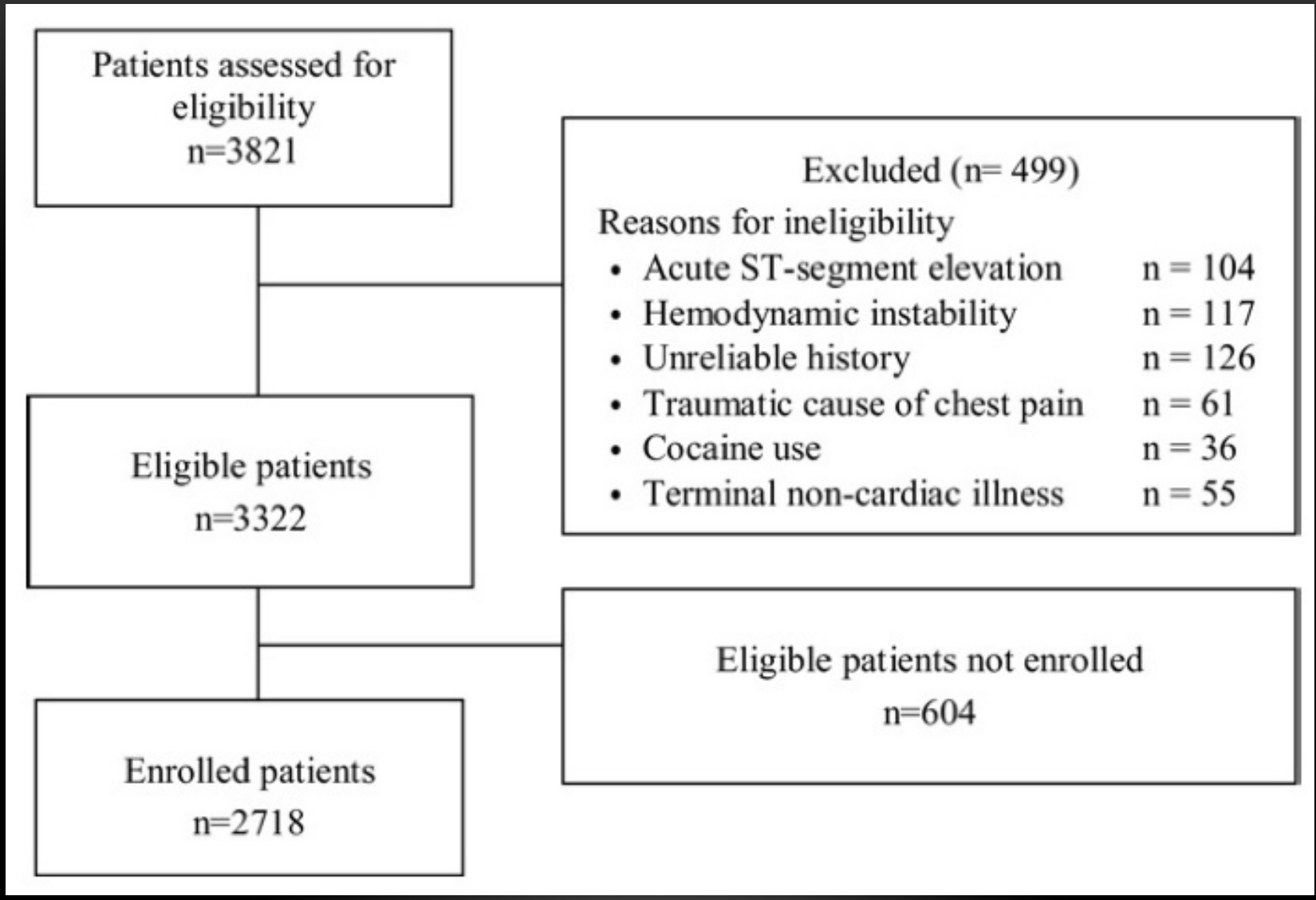
Patients assessed for eligibility n=3821
Excluded (n= 499)
Reasons for ineligibility
• Acute ST-segment elevation n = 104
• Hemodynamic instability n = 117
• Unreliable history n = 126
• Traumatic cause of chest pain n = 61
• Cocaine use n = 36
• Terminal non-cardiac illness n = 55
Eligible patients n=3322
Eligible patients not enrolled n=604
Enrolled patients n=2718

**Table 1.** Baseline patient characteristics, ECG findings, and 30-day outcomes for 2,718 ED patients with chest pain.

| Characteristic | No. (%) of Patients (n=2,718)* |
|---|---|
| **Demographics** | |
| Mean age, y (SD) | 60.0 (14.9) |
| Age range, y | 25–99 |
| Male patient | 1,439 (52.9) |
| Arrival by ambulance | 661 (24.3) |
| Median length of stay in department, h (IQR) | 3.0 (3.1) |
| Range | 0.4–16.3 |
| **Cardiac risk factors** | |
| Hypertension | 1,592 (58.6) |
| Diabetes mellitus | 559 (20.6) |
| Hypercholesterolemia | 1,458 (53.6) |
| Family history of cardiac disease | 784 (28.8) |
| Smoking history | 1,393 (51.3) |
| Current | 483 (17.8) |
| Former (<1 y ago) | 155 (5.7) |
| Former (>1 y ago) | 755 (27.8) |
| No cardiac risk factors | 274 (10.1) |
| **Cardiovascular history** | |
| Previous myocardial infarction | 630 (23.2) |
| Angina (chest pain on exertion) | 626 (23.0) |
| Known coronary artery disease† | 892 (32.8) |
| Congestive heart failure | 185 (6.8) |
| Cardiac arrest | 41 (1.5) |
| Ventricular tachycardia | 31 (1.1) |
| Atrial fibrillation | 232 (8.5) |
| Stroke or transient ischemic attack | 190 (7.0) |
| Peripheral vascular disease | 133 (4.9) |
| No cardiovascular history | 1,395 (51.3) |
| **Initial ECG interpretation** | |
| Normal (%) | 1,169 (43.0) |
| Nonspecific ST-segment changes | 599 (22.0) |
| Abnormal, not diagnostic | 578 (21.3) |
| Ischemia known to be old | 241 (8.9) |
| Ischemia not known to be old | 131 (4.8) |
| **Other ECG findings** | |
| ST-segment depression >0.5 mm | 96 (3.5) |
| T-wave inversion | 195 (7.2) |
| Left bundle branch block | 91 (3.4) |
| Right bundle branch block | 118 (4.3) |
| Q waves | 247 (9.1) |
| **Management** | |
| Admitted to the hospital | 865 (31.8) |
| Admitted to the observation unit‡ (n=1,205) | 577 (47.9) |
| Cardiac stress testing performed | 896 (33.0) |
| Coronary angiography performed | 510 (18.8) |
| Coronary stenosis ≥70%§ | 329 (12.1) |
| **Outcomes** | |
| Cardiac event‖ | 336 (12.4) |
| Acute myocardial infarction | 167 (6.1) |
| Revascularization | 271 (10.0) |
| Death of cardiac/unknown cause | 6 (0.2) |
| Cardiac event occurring after ED disposition (inhospital or out-of-hospital) | 175 (6.4) |

**Table 1.** Continued.

| Characteristic | No. (%) of Patients (n=2,718)* |
|---|---|
| Acute myocardial infarction | 8 (0.3) |
| Revascularization | 171 (6.3) |
| Death of cardiac/unknown cause | 4 (0.2) |

IQR, Interquartile range.
*Unless otherwise indicated.
†Among the 892 patients with known coronary artery disease, 666 (74.7%) were confirmed with objective criteria in the medical record and 226 (25.3%) were ascertained by patient self-report.
‡Only 1 site (Rochester, MN) had an observation unit.
§In at least 1 major epicardial coronary artery.
‖Acute myocardial infarction, revascularization, or death of cardiac/unknown cause within 30 days of the ED visit. Some patients experienced more than one type of cardiac event.

In 2718 patients:

- 336 had ≥ 1 cardiac event
- 167 had AMI
- 271 had revascularization
- 6 had death

**Table 2.** Univariate association between demographic, clinical, and ECG predictor variables and the primary outcome in 2,718 ED patients with chest pain.

| Variable | Group, No. (%) of Patients* | | | Interobserver Agreement, κ Value (n=250) |
|---|---|---|---|---|
| | Positive for Primary Outcome (n=336) | Negative for Primary Outcome (n=2,382) | Odds Ratio (95% CI) | |
| **Demographics** | | | | |
| Mean age, y (SD) | 66.4 (12.8) | 59.1 (15.0) | 1.03 (1.02–1.04) | NA |
| Male patient | 231 (68.8) | 1,208 (44.4) | 2.14 (1.68–2.73) | NA |
| Arrival by ambulance | 104 (31.0) | 557 (20.5) | 1.48 (1.15–1.89) | NA |
| **Cardiac risk factors** | | | | |
| Hypertension | 243 (72.3) | 1,349 (49.6) | 2.00 (1.56–2.58) | NA |
| Diabetes mellitus | 99 (29.5) | 460 (16.9) | 1.75 (1.35–2.25) | NA |
| Hypercholesterolemia | 239 (71.1) | 1,219 (44.8) | 2.35 (1.83–3.02) | NA |
| Family history of cardiac disease | 95 (28.3) | 689 (28.9) | 0.97 (0.75–1.25) | NA |
| Any history of smoking | 193 (57.4) | 1,200 (50.4) | 1.33 (1.06–1.67) | NA |
| **Cardiovascular history** | | | | |
| Acute myocardial infarction | 123 (36.6) | 507 (21.3) | 2.14 (1.68–2.72) | NA |
| Angina (chest pain on exertion) | 142 (42.3) | 484 (20.3) | 2.87 (2.26–3.64) | NA |
| Known coronary artery disease | 193 (57.4) | 699 (29.3) | 3.25 (2.57–4.11) | NA |
| Congestive heart failure | 33 (9.8) | 152 (6.4) | 1.60 (1.08–2.37) | NA |
| Cardiac arrest | 3 (0.9) | 38 (1.6) | 0.56 (0.17–1.81) | NA |
| Ventricular tachycardia | 5 (1.5) | 26 (1.1) | 1.37 (0.52–3.59) | NA |
| Atrial fibrillation | 34 (10.1) | 198 (8.3) | 1.24 (0.85–1.82) | NA |
| Stroke or transient ischemic attack | 35 (10.4) | 155 (6.5) | 1.67 (1.14–2.46) | NA |
| Peripheral vascular disease | 28 (8.3) | 105 (4.4) | 1.99 (1.14–3.49) | NA |
| **Chest pain history** | | | | |
| Present on ED arrival | 191 (56.8) | 1,583 (66.5) | 0.67 (0.53–0.84) | 0.63 |
| Present at rest | 275 (81.8) | 2,154 (90.4) | 0.48 (0.35–0.65) | 0.63 |
| Resolution of pain before evaluation | 176 (52.4) | 998 (41.9) | 1.53 (1.21–1.92) | 0.67 |
| Worse with exertion | 179 (53.3) | 688 (28.9) | 2.81 (2.23–3.54) | 0.53 |
| Pleuritic | 22 (6.5) | 441 (18.5) | 0.31 (0.20–0.48) | 0.74 |
| Similar to previous ischemia | 159 (47.3) | 504 (21.2) | 3.35 (2.65–4.24) | 0.74 |
| Change in usual pattern of angina in past 24 h | 92 (27.4) | 325 (13.6) | 2.39 (1.83–3.12) | 0.62 |
| ≥2 episodes of pain in past 24 h | 194 (57.7) | 987 (41.4) | 1.93 (1.53–2.43) | 0.61 |
| **Onset** | | | | |
| Abrupt (<1 h) | 255 (75.9) | 1,612 (67.7) | 1.50 (1.15–1.96) | 0.45 |
| Gradual (>1 h) | 71 (21.1) | 686 (28.8) | 0.66 (0.50–0.87) | 0.45 |
| **Location on chest** | | | | |
| Center | 236 (70.2) | 1,325 (55.6) | 1.88 (1.47–2.41) | 0.52 |
| Left anterior | 100 (29.8) | 847 (35.6) | 0.77 (0.60–0.99) | 0.51 |
| Left lateral | 19 (5.7) | 183 (7.7) | 0.72 (0.44–1.17) | 0.63 |
| Right anterior | 17 (5.1) | 154 (6.5) | 0.77 (0.46–1.29) | 0.48 |
| Right lateral | 4 (1.2) | 45 (1.9) | 0.63 (0.22–1.75) | 0.66 |
| **Pain description** | | | | |
| Pressure/squeezing | 188 (60.0) | 1,084 (45.5) | 1.52 (1.21–1.91) | 0.47 |
| Heavy | 60 (17.9) | 408 (17.1) | 1.05 (0.78–1.42) | 0.27 |
| Sharp | 40 (11.9) | 585 (24.6) | 0.42 (0.30–0.59) | 0.55 |
| Indigestion/burning quality | 39 (11.6) | 202 (8.5) | 1.42 (0.99–2.04) | 0.68 |

| | | | | |
|---|---|---|---|---|
| **Radiation** | | | | |
| Left arm/shoulder | 95 (28.3) | 582 (24.4) | 1.22 (0.95–1.57) | 0.55 |
| Right arm/shoulder | 18 (5.4) | 101 (4.2) | 1.28 (0.76–2.14) | 0.33 |
| Both arms/shoulders | 38 (11.3) | 103 (4.3) | 2.82 (1.91–4.17) | 0.34 |
| Neck/jaw | 79 (23.5) | 361 (15.2) | 1.72 (1.31–2.27) | 0.45 |
| Back | 39 (11.6) | 316 (13.3) | 0.86 (0.60–1.22) | 0.63 |
| Abdomen | 2 (0.6) | 41 (1.7) | 0.34 (0.08–1.42) | 0.66 |
| **Associated symptoms** | | | | |
| Nausea or vomiting | 71 (21.1) | 550 (23.0) | 0.89 (0.68–1.18) | 0.54 |
| Shortness of breath | 158 (47.0) | 923 (38.8) | 1.40 (1.12–1.77 | 0.42 |
| Diaphoresis | 95 (28.3) | 496 (20.8) | 1.50 (1.16–1.94) | 0.61 |
| Worse with movement | 50 (14.9) | 481 (20.2) | 0.69 (0.50–0.95) | 0.43 |
| Typical for acute coronary syndrome[†] | 250 (74.4) | 778 (32.6) | 5.99 (4.62–7.77) | 0.75 |
| Atypical for acute coronary syndrome[†] | 79 (23.5) | 1,527 (64.1) | 0.17 (0.13–0.22) | 0.75 |
| **Initial interpretation of the ECG[§] (n for κ=80)** | | | | 0.85 |
| Normal (%) | 84 (25.0) | 1,076 (45.2) | 0.40 (0.31–0.51) | NA |

**Table 2.** Continued.

| Variable | Group, No. (%) of Patients* | | | Interobserver Agreement, κ Value (n=250) |
|---|---|---|---|---|
| | Positive for Primary Outcome (n=336)* | Negative for Primary Outcome (n=2,382) | Odds Ratio (95% CI) | |
| Nonspecific ST-segment changes (%) | 67 (19.9) | 532 (22.3) | 0.86 (0.65–1.15) | NA |
| Abnormal but not diagnostic of ischemia (%) | 82 (24.4) | 496 (20.8) | 1.22 (0.94–1.60) | NA |
| Infarction or ischemia known to be old (%)[‖] | 36 (10.7) | 205 (8.6) | 1.24 (0.85–1.82) | NA |
| Infarction or ischemia not known to be old (%) | 67 (19.9) | 64 (2.7) | 9.03 (6.30–12.95) | NA |
| **Other ECG findings** | | | | |
| ST-segment depression >0.5 mm | 58 (17.3) | 67 (2.8) | 7.21 (4.97–10.47) | NA |
| T-wave inversion | 50 (14.9) | 145 (6.1) | 2.70 (1.91–3.81) | NA |
| Left bundle-branch block | 24 (7.1) | 67 (2.8) | 2.66 (1.64–4.30) | NA |
| Right bundle-branch block | 18 (5.4) | 100 (4.2) | 1.29 (0.77–2.16) | NA |
| Q waves | 39 (11.6) | 208 (8.7) | 1.37 (0.96–1.97) | NA |

*Unless otherwise indicated.

†The primary outcome was acute myocardial infarction, coronary revascularization, or death within 30 days of the ED visit.

‡Attending physicians were instructed to record whether the chest pain syndrome was cardiac (typical for acute coronary syndrome) or noncardiac (atypical for acute coronary syndrome) in cause.

§κ Was dichotomously assessed according to whether ECGs were classified as infarction or ischemia not known to be old (acute ischemia) or "other."

‖Infarction or ischemia on ECG was defined as T-wave inversion greater than or equal to 0.2 mm or ST-segment depression greater than or equal to 1 mm in at least 2 contiguous leads.

Patients who had primary outcome:

- Demographics: older, more male, more arrival by ambulance
- Cardiac risk factors: HTN, DM, lipid, smoking
- CV Hx: AMI, Angina, CAD, CHF, CVA, PVD
- Chest pain Hx: resolution of pain before evaluation, worse with exertion, similar episode, change in usual pattern, ≥ 2 pain episodes
- Onset: abrupt
- Location: center
- Pain: pressure/squeezing
- Radiation: both arms/shoulders, neck/jaw
- Associated symptoms: SOB, diaphoresis, worse with movement, typical for ACS
- ECG: ST depression, TWI, LBBB

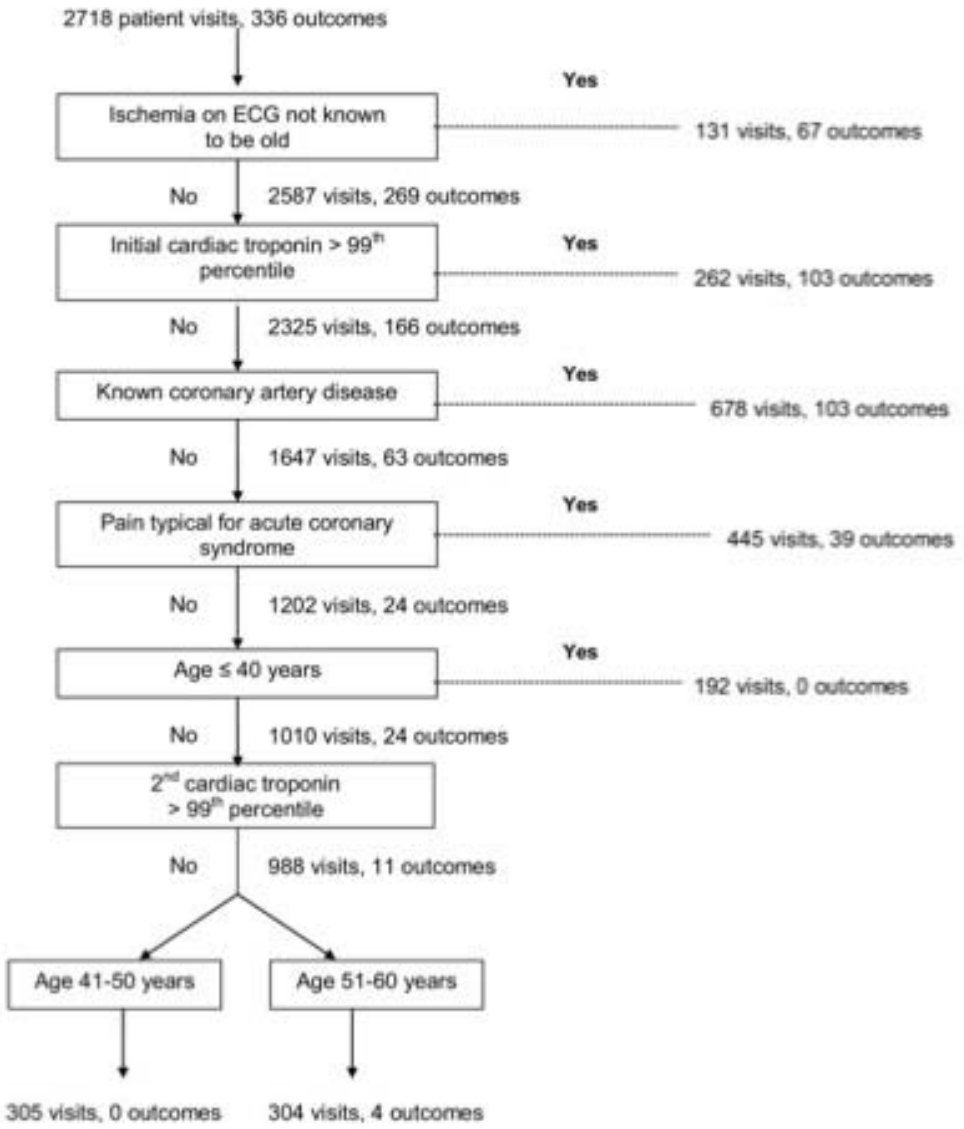


**Figure 2.** Derivation of clinical decision rule by recursive partitioning.

**Table 3.** Prognostic accuracy of clinical decision rule for 30-day cardiac events in 2,718 patients with chest pain and possible acute coronary syndrome.

***A*, Age cutoff 50 years or younger**

| Decision Rule | Cardiac Event Within 30 Days | No Cardiac Event Within 30 Days |
|---|---|---|
| Yes | 336 | 1,885 |
| No | 0 | 497 |

Sensitivity 100.0% (95% CI 97.2% to 100.0%); specificity 20.9% (95% CI 16.9% to 24.5%); positive predictive value 15.1% (95% CI 13.7% to 16.7%); negative predictive value 100.0% (95% CI 99.0% to 100.0%); stress testing proportion 81.7% (95% CI 80.2% to 83.1%).

***B*, Age cutoff 60 years or younger**

| Decision Rule | Cardiac Event Within 30 Days | No Cardiac Event Within 30 Days |
|---|---|---|
| Yes | 332 | 1,581 |
| No | 4 | 801 |

Sensitivity 98.8% (95% CI 95.4% to 100.0%); specificity 33.6% (95% CI 28.9% to 38.1%); positive predictive value 17.4% (95% CI 15.7% to 19.1%); negative predictive value 99.5% (95% CI 98.6% to 99.8%); stress testing proportion 70.4% (95% CI 68.6% to 72.1%).

- If the age cufoff: 50 y/o
  - Sensitivity: 100%, specificity 20.9%
- If the age cufoff: 60 y/o
  - Sensitivity: 98.8%, specificity 33.6%

## North American Chest Pain Rule*

**A patient with chest pain and possible acute coronary syndrome can be safely discharged from the ED without additional diagnostic testing if NONE of the following four criteria are met:**

(1) New ischemia on initial ECG†

(2) History of coronary artery disease

(3) Pain is typical for acute coronary syndrome‡

(4) Initial cardiac troponin is positive

AND

(5) Age ≤ 40 years

OR

Age 41-50 years and repeat troponin at least 6 hours from symptom onset is negative.§

# LIMITATION

- Only enrolled the patients with a chest pain syndrome
- The primary outcome did not include ACS with medical management
- The initial ECG and Trop level were not sufficient to indicate ischemic heart disease

# DISCUSSION

- The new clinical decision rule: patients without risk factors with normal initial Trop level
  - ≤ 40 y/o: discharge
  - 41-50 y/o: F/U Trop after ≥ 6 hr, if normal → discharge
- TIMI score, HEART score, Vancouver Chest Pain Rule…. were not good enough!
  - TIMI score: sensitivity 97%, specificity 25%, miss rate (score: 0) 2%
  - HEART (History, ECG, Age, Risk factors, Troponin) score: sensitivity 98.1%, specificity 15.5%, miss rate 2.5%
  - Vancouver Chest Pain rule: no typical chest pain → discharge (ever > 40 y/o)

# DISCUSSION

- Marsan (2005): < 40 y/o, normal ECG and enzymes, no risk factor, no abnormal cardiac Hx → no cardiac events at 30 days
- Collin (2011): with similar characteristics, no cardiac events at 1 year
- This clinical prediction rule:
  - Increase the efficiency of diagnostic investigation
  - Patients without any of the high-risk criteria could be safely discharged

# THANKS