# **ORIGINAL RESEARCH**

# Use of Cardiac Noninvasive Testing After Emergency Department Discharge: Association of Hospital Network Testing Intensity and Outcomes in Ontario, Canada

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**BACKGROUND:** The relationship between noninvasive cardiac diagnostic testing intensity and downstream clinical outcomes is unclear. Our objective was to examine the relationship between hospital network noninvasive cardiac diagnostic testing intensity and downstream clinical outcomes in patients who were discharged from the emergency department after assessment for chest pain.

**METHODS AND RESULTS**: We employed a retrospective cohort study design of 387 809 patients evaluated for chest pain in the emergency department between April 1, 2010 and March 31, 2016. Hospital networks were divided into tertiles based on usage of noninvasive cardiac diagnostic testing. The primary outcome was a composite of acute myocardial infarction or all-cause mortality. Adjusted Cox proportional hazards models were used to compare the hazard of the composite outcome of myocardical infarction and/or all-cause mortality between the tertiles. After adjustment for clinically relevant covariates, patients evaluated for chest pain in intermediate noninvasive cardiac diagnostic testing usage tertile hospital networks did not have significantly different hazards of the composite outcome when compared with those evaluated in low usage tertile hospital networks >90 days (hazard ratio [HR], 1.00; 95% CI, 0.83–1.21), 6 months (HR, 1.07; 95% CI, 0.92–1.24), and 1 year (HR, 1.03; 95% CI, 0.94–1.14). Patients evaluated in the high usage tertile also did not have significantly different hazards of the composite outcome usage tertile also did not have significantly different hazards of the composite outcome usage tertile also did not have significantly different hazards of the composite outcome usage tertile also did not have significantly different hazards of the composite outcome usage tertile also did not have significantly different hazards of the composite outcome compared with those evaluated in the low usage tertile at 90 days (HR, 0.98; 95% CI, 0.80–1.19), 6 months (HR, 1.01; 95% CI, 0.87–1.17); and 1 year (HR, 0.95; 95% CI, 0.86–1.05).

**CONCLUSIONS:** Our population-based study demonstrated that high noninvasive cardiac diagnostic testing use intensity was not associated with reductions in downstream myocardial infarction or all-cause mortality.

Key Words: cardiac noninvasive testing Coronary artery disease health services research

ore than 4 million cardiac noninvasive diagnostic tests (NITs) are performed annually in the United States for the evaluation of chest pain with increasing use despite stabilization in the incidence of coronary artery disease,<sup>1–6</sup> leading to concerns about possible overuse.<sup>7–11</sup> Variation in use of NIT among sites may be indicative of uncertainty regarding appropriate use. Indeed, a number of studies have reported significant regional variation in the use of cardiac testing for coronary artery disease.<sup>9,12–15</sup> However, the consequences of that variation are unclear. Specifically, it is unknown whether hospital networks with a physician strategy or culture of more NIT use are associated with improved downstream clinical outcomes when compared with hospital networks with a culture of less-intensive testing.<sup>3,5,16–19</sup> If associated with improved outcomes, a greater intensity of NIT may be justifiable. However, if not associated with improved

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# CLINICAL PERSPECTIVE

#### What Is New?

- Noninvasive diagnostic tests are often performed on patients undergoing chest pain evaluation in the emergency department; however, their association with downstream clinical outcomes is unclear.
- We employed a retrospective cohort study design of 387 809 patients evaluated for chest pain in the emergency department in Ontario, Canada.
- Hospital networks were divided into tertiles based on noninvasive diagnostic test usage, and patients evaluated for chest pain at high and intermediate usage tertile hospital networks did not have significantly different hazards of myocardial infarction or death compared with those evaluated in low usage hospital networks.

## What Are the Clinical Implications?

- Our results report that a strategy of more intense noninvasive diagnostic tests was not associated with improvements in important downstream clinical outcomes and suggest that significant opportunities exist to improve guidance regarding the appropriate indications for testing.
- Guidance regarding appropriate testing indications should be geared toward physicians practicing at high and intermediate noninvasive diagnostic test usage hospital networks.

# Nonstandard Abbreviation and Acronym

NIT noninvasive diagnostic test

outcomes, the strategy of increased NIT may be indicative of overuse.

NITs are often performed on patients undergoing evaluation for chest pain in the emergency department (ED) who were subsequently discharged home. According to recent guidelines, such patients should have NITs performed within 72 hours of discharge despite the lack of evidence of effectiveness in this clinical scenario.<sup>20</sup> Prior studies have not addressed institutional variations in NITs in patients evaluated in the ED for chest pain who were subsequently discharged and whether this variation is associated with changes in downstream clinical outcomes. Our objective was to evaluate the relationship between the use of noninvasive testing related to different hospital networks in Ontario, Canada, and downstream clinical outcomes of myocardial infarction (MI) and all-cause mortality in a cohort of patients who were recently discharged from the ED after assessment for chest pain.

## **METHODS**

The data set from this study is held securely in coded form at ICES. Although data-sharing agreements prohibit ICES from making the data set publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at http:// www.ices.on.ca/DAS. The full data set creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely on coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

# **Design and Derivation of the Cohort**

We employed a retrospective cohort study design. Patients entered the cohort if they were evaluated for chest pain in an ED in Ontario, Canada, between April 1, 2010 and March 31, 2016, and discharged home after evaluation. Date of the ED evaluation for chest pain served as the date of cohort entry or the index date. Moreover, to be included in the cohort, patients must have undergone an ECG test within 1 day of the ED visit or during the visit itself. Patients were followed for 30 days after the index chest pain visit to determine if they received 1 of 4 NITs currently available in Ontario: graded exercise stress test, stress echocardiography, MPI, or coronary computed tomography angiography. We excluded patients who underwent either an ED visit for chest pain or any NIT during the preceding 12 months.

#### **Hospital Networks**

Although the vast majority of NITs in Ontario are performed on an outpatient basis and not in the hospitals themselves, ~94% of all specialist physicians are affiliated with 1 hospital, with the hospital's ED at its hub.<sup>21</sup> Therefore, although NITs are not ordered by the hospital itself, they are very likely to be ordered by outpatient physicians affiliated with that hospital. Thus, hospital networks (which include emergency, inpatient, and outpatient physicians affiliated with the hospital network) can be considered single units of analysis. All 182 acute care hospital networks in Ontario that provide emergency care were included in this study. Hospital networks were categorized into 3 tertiles based on the rate of NIT use. Given the large number of hospital networks in our cohort, we believed that we would be able to draw more robust conclusions by grouping them into tertiles and comparing usage rates among them in a process similar to one used in the past to compare use of stress testing and angiography after stress testing.<sup>9</sup>

#### **Data Sources**

The National Ambulatory Care Reporting System (NACRS) was used to determine patient ED visits.

NACRS contains data for all hospital-based and community-based ambulatory care in Canada including information on ED discharge diagnosis.<sup>22,23</sup> Information to identify patient receipt of NIT and ECG was obtained from the Ontario Health Insurance Plan (OHIP) physician claims database using billing codes that were used in previous studies.<sup>6,15</sup> The Registered Person's Database (RPDB), a registry of Ontario residents who are registered for Ontario health insurance coverage, was used to obtain demographic information and to ascertain all-cause mortality. Median neighborhood income was obtained by linking the census area profile with patients' postal codes of residence from the RPDB using the postal code conversion file. Hospitalizations, including all-cause as well as hospitalization for acute MI and unstable angina, were determined using the Canadian Institutes for Health Information Discharge Abstract Database (CIHI-DAD). The CIHI-DAD is a database containing hospitalization information (including the reason for admission) for all hospitalizations in Ontario and has been validated and used extensively in prior research.<sup>12,24–29</sup> The Ontario Hypertension and Ontario Diabetes Databases were used to determine hypertension and diabetes mellitus status, respectively. Both databases have been validated with regard to their ability to accurately measure hypertension and diabetes mellitus status.30-32

The aforementioned databases were linked using unique encoded identifiers and analyzed at ICES. Data were linked with individual encrypted OHIP numbers used as the unique encoded identifiers to track health service use across the aforementioned databases. Thus, individual patients were followed longitudinally over time. After individual-level data were acquired, patients were categorized according to the hospital network in which they were evaluated. Given Canada's single-payer, -unded healthcare system, we were able to extract patient information with virtually 100% coverage of the population of Ontario. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a research ethics board or informed consent of study participants.

#### Outcomes

To mitigate issues related to immortal time bias/survivorship bias, we performed landmark analyses in which time zero for follow-up was at 30 days post-initial chest pain evaluation. Patients were then followed up to March 31, 2017, for outcomes. The primary outcome was a composite of time to hospitalization for acute MI or all-cause mortality. We also evaluated each component of the primary outcome separately. Definitions that we used to determine these outcomes have been previously validated using administrative data from CIHI-DAD and have been extensively used in the literature.<sup>12,25,29,33,34</sup>

### **Covariates**

Covariates were selected a priori based on clinical importance.<sup>26,35–41</sup> The following covariates were used in our statistical models: average ED volume; evaluation in hospitals with cardiac catherization capabilities; rural location of the hospital where the patient was evaluated; cardiovascular risk factors such as age, sex, hypertension, dyslipidemia, diabetes mellitus, and income strata; prior cardiovascular history; and measures of comorbidity, such as chronic obstructive pulmonary disease and active cancer.

## **Statistical Analysis**

Characteristics of patients undergoing testing were compared between the 3 usage groups using  $\chi^2$  for categorical variables and analysis of variance for continuous variables.

#### **Unadjusted Analyses**

The  $\chi^2$  test was used to compare the occurrence of the outcomes within 90 days, 6 months, and 1 year between the 3 groups.

#### **Adjusted Analyses**

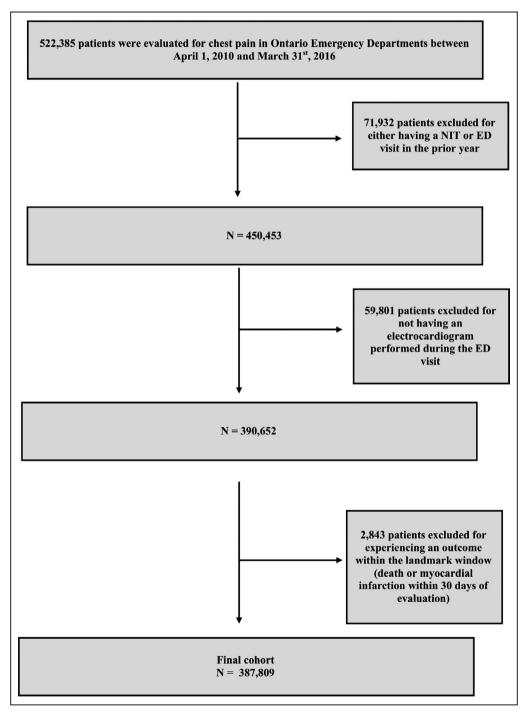
Adjusted Cox proportional hazards models were used to compare the hazard of the composite outcome of MI and/or all-cause death between the groups. A robust sandwich variance estimator was used to account for clustering of patients within hospital networks and because the primary exposure variable was measured at the hospital network level. We adjusted for the covariates listed previously. All statistical analyses were conducted using SAS version 9.3 (SAS Institute Inc., Cary, NC). All statistical tests were 2-sided, with a significance level of 0.05.

#### **Sensitivity Analyses**

We performed 2 sensitivity analyses to evaluate the robustness of our results. First, to mitigate the risk that our results were impacted by very low volume networks, we excluded networks who evaluated less than 1 chest pain patient per month during our study period and subsequently repeated our statistical analyses. Second, to account for patients who possibly had their NIT late, we performed a sensitivity analysis using a 60-day inclusion period for receipt of NIT coupled with a 60-day landmark period.

# RESULTS

There were 522 385 adult patients who were discharged after evaluation for chest pain in the ED in Ontario hospitals between April 1, 2010, and March 31, 2016. Of these, 71 932 were excluded for either having a NIT or ED visit in the prior year. Of these patients, 390 652 had an ECG performed at the time of ED visit. Of these patients, 2843 were excluded as part of the landmark analysis because they died or had a MI within 30 days of the index event. The final cohort of patients was 387 809 (see Figure 1). NITs were predominantly performed after discharge from the ED in an outpatient setting. In fact, only 3144 patients (0.81%) had NIT performed on the same day as their presentation for chest pain in the ED setting.



**Figure 1. Derivation of the study population.** ED indicates emergency department; and NIT, noninvasive diagnostic test.

#### Hospital Network Tertiles for NIT Use

Of 182 hospital networks in Ontario, 60 were categorized in the low testing use group, and 61 hospital networks were categorized into both the intermediate and high testing use groups. The low testing use group used NITs at a mean rate of 12% (range, 0%–16%) versus mean testing rates of 20% (range, 16%-25%) and 35% (range, 25%-60%) for the intermediate and high testing intensity groups, respectively. Figure S1 displays the site-specific variation for our study. Of the patients, 215 725 (55.6% of the cohort) were tested after discharge from high use hospital networks, 123 163 patients (31.8% of the cohort) were tested after discharge from intermediate use hospital networks, and 48 921 patients (12.6% of the cohort) were tested after discharge from low use hospital networks.

#### **Patient Characteristics**

Patients evaluated for chest pain at hospital networks in the highest NIT use tertile were more likely to be female and have dyslipidemia, diabetes mellitus, and hypertension, but less likely to have a prior MI or angina, peripheral vascular disease, and chronic renal disease when compared with those patients treated in the lowest NIT use tertile (see Table 1). In terms of noncardiac comorbidities, patients in the highest use tertile were less likely to have chronic obstructive pulonary disease or prior malignancy and had a lower mean Charlson comorbidity risk score. They were also ≈4-fold less likely to reside in rural areas (8.0% versus 33.4%; P<0.01) and almost 3-fold more likely to be evaluated in an ED of a hospital network with cardiac catheterization capabilities (36.4% versus 11.7%; P<0.01). We have summarized the baseline characteristics of those patients undergoing NIT in Table S1. Baseline characteristics

#### Table 1. Baseline Characteristics of the Patient Population

|  | Low NIT Use<br>(First Tertile) | Intermediate NIT<br>Use (Second Tertile) | High NIT Use<br>(Third Tertile) | Total Cohort    | P Value |
|--|--------------------------------|--|---------------------------------|-----------------|---------|
| No. of hospital networks   | 60                             | 61                                       | 61                              | 182             |         |
| No. of patients evaluated for chest pain                                 | 48 921                         | 123 163                                  | 215 725                         | 387 809         |         |
| Age, y, mean±SD  | 57.06±10.85                    | 56.93±10.86                              | 56.15±10.74                     | 56.51±10.80     | <0.001  |
| Female sex, n (%)  | 26 146 (53.45)                 | 66 322 (53.85)                           | 116 830 (54.16)                 | 209 298 (53.97) | 0.01    |
| Average ED volume, mean±SD   | 985.33±821.85                  | 1482.16±729.46                           | 2304.12±1096.95                 | 1876.71±1083.90 | <0.001  |
| Rural (%)  | 16 327 (33.37)                 | 19 424 (15.77)                           | 17 219 (7.98)                   | 52 970 (13.66)  | <0.01   |
| Neighborhood income, n (%)   | 1                              |  | 1                               |                 |         |
| 1  | 9237 (18.88)                   | 27 867 (22.63)                           | 39 609 (18.36)                  | 76 713 (19.78)  | <0.001  |
| 2  | 9756 (19.94)                   | 24 767 (20.11)                           | 42 353 (19.63)                  | 76 876 (19.82)  |         |
| 3  | 9849 (20.13)                   | 22 917 (18.61)                           | 45 288 (20.99)                  | 78 054 (20.13)  |         |
| 4  | 9712 (19.85)                   | 23 385 (18.99)                           | 47 972 (22.24)                  | 81 069 (20.90)  |         |
| 5  | 9997 (20.43)                   | 23 495 (19.08)                           | 39 993 (18.54)                  | 73 485 (18.95)  |         |
| Evaluation in hospitals with cardiac catheterization capabilities, n (%) | 5712 (11.68)                   | 37 005 (30.05)                           | 78 617 (36.44)                  | 121 334 (31.29) | <0.001  |
| Cardiovascular history and risk factors, n (%)                           |                                |  |                                 |                 |         |
| Congestive heart failure   | 792 (1.62)                     | 1916 (1.56)                              | 2889 (1.34)                     | 5597 (1.44)     | <0.001  |
| Previous MI  | 2395 (4.90)                    | 5854 (4.75)                              | 8624 (4.00)                     | 16 873 (4.35)   | <0.001  |
| Peripheral vascular disease  | 1590 (3.25)                    | 4089 (3.32)                              | 6270 (2.91)                     | 11 949 (3.08)   | <0.001  |
| Chronic renal disease  | 394 (0.81)                     | 1086 (0.88)                              | 1607 (0.74)                     | 3087 (0.80)     | <0.001  |
| Diabetes mellitus  | 9115 (18.63)                   | 24 089 (19.56)                           | 44 939 (20.83)                  | 78 143 (20.15)  | <0.001  |
| Dyslipidemia   | 20 838 (42.60)                 | 55 789 (45.30)                           | 107 199 (49.69)                 | 183 826 (47.40) | <0.001  |
| Hypertension   | 20 822 (42.56)                 | 53 762 (43.65)                           | 96 063 (44.53)                  | 170 647 (44.00) | <0.001  |
| Previous cerebrovascular disease   | 480 (0.98)                     | 1165 (0.95)                              | 1815 (0.84)                     | 3460 (0.89)     | <0.001  |
| Previous revascularization, PCI, or CABG                                 | 1779 (3.64)                    | 4845 (3.93)                              | 7230 (3.35)                     | 13 854 (3.57)   | <0.001  |
| Comorbidities  |                                |  |                                 |                 |         |
| COPD, n (%)  | 941 (1.92)                     | 2382 (1.93)                              | 3467 (1.61)                     | 6790 (1.75)     | <0.001  |
| Cancer, n (%)  | 1617 (3.31)                    | 4334 (3.52)                              | 6595 (3.06)                     | 12 546 (3.24)   | <0.001  |
| Charlson score, mean±SD  | 0.37±1.04                      | 0.38±1.07                                | 0.33±0.98                       | 0.35±1.02       | <0.001  |

ED indicates emergency department; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NIT, noninvasive diagnostic test; and PCI, percutaneous coronary intervention.

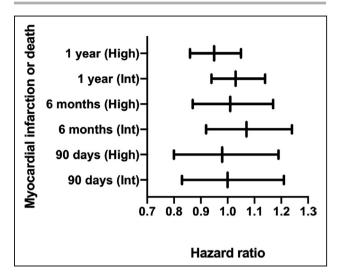
for this subgroup were qualitatively similar to those of the overall cohort.

#### **Unadjusted Outcomes**

Overall, event rates for our outcomes were low. Only 6295 patients (1.62% of our cohort) had either a MI or died within 1 year post–chest pain evaluation in the ED. Patients who presented to hospital networks in the highest NIT use group were significantly less likely to experience the outcome of all-cause mortality or MI compared with patients presenting to hospital networks in the lowest usage group (0.37% versus 0.43% at 90 days, 0.80% versus 0.94% at 6 months, and 1.46% versus 1.83% at 1 year; P<0.05 for all; see Table 2).

#### **Adjusted Outcomes**

After adjustment for clinically relevant covariates, those patients evaluated for chest pain at hospital networks in the high or intermediate use groups did not have significantly different rates of the composite outcome of MI or death compared with those evaluated at hospital networks in the lowest use group. The intermediate use group did not have a significantly different hazard of MI or death when compared with the low use group over 90 days (hazard ratio [HR], 1.00; 95% CI, 0.83-1.21), 6 months (HR, 1.07; 95% Cl, 0.92-1.24), and 1 year (HR, 1.03; 95% Cl, 0.94-1.14) post ED evaluation. The high use group also did not have significantly different hazards of MI or death compared with the low use group over 90 days (HR, 0.98; 95% CI, 0.80-1.19), 6 months (HR, 1.01; 95% Cl, 0.87-1.17), and 1 year (HR, 0.95; 95% CI, 0.86–1.05) (see Figure 2). The same relationships were observed for each constituent component of the composite outcome; MI and all-cause



**Figure 2.** Myocardial infarction (MI) or all-cause mortality for the high and intermediate (Int) use tertiles vs the low use tertile (reference).

mortality with all the CIs of the respective HRs crossing 1 (see Figures 3 [MI] and 4 [all-cause mortality]).

#### **Sensitivity Analyses**

Our results were similar after exclusion of low volume hospital networks. The intermediate use group did not have significantly different hazards of MI or death when compared with the low use group over 90 days (HR, 1.01; 95% CI, 0.81–1.26), 6 months (HR, 1.06; 95% CI, 0.89–1.26), and 1 year (HR, 1.00; 95% CI, 0.89–1.12) post ED evaluation. The high use group also did not have significantly different hazards of MI or death compared with the low use group over 90 days (HR, 0.99; 95% CI, 0.79–1.23), 6 months (HR, 1.00; 95% CI, 0.82–1.03). Furthermore, our results were not impacted by a

| Table 2. | Unadjusted Outcomes Compared Among the NIT Use Tertiles |  |
|----------|---|--|
|----------|---|--|

|                 | Low NIT Use (First<br>Tertile) | Intermediate NIT Use<br>(Second Tertile) | High NIT Use (Third<br>Tertile) | Overall Cohort | <i>P</i> Value |
|-----------------|--------------------------------|--|---------------------------------|----------------|----------------|
| MI, n (%)       |                                |  |                                 |                |                |
| 90 d            | 74 (0.15)                      | 146 (0.12)                               | 267 (0.12)                      | 487 (0.13)     | 0.211          |
| 6 mo            | 155 (0.32)                     | 336 (0.27)                               | 520 (0.24)                      | 1011 (0.26)    | 0.007          |
| 1 y             | 285 (0.58)                     | 613 (0.50)                               | 955 (0.44)                      | 1853 (0.48)    | <0.001         |
| All-cause morta | ality, n (%)                   |  |                                 |                |                |
| 90 d            | 142 (0.29)                     | 390 (0.32)                               | 557 (0.26)                      | 1089 (0.28)    | 0.008          |
| 6 mo            | 318 (0.65)                     | 894 (0.73)                               | 1242 (0.58)                     | 2454 (0.63)    | < 0.001        |
| 1 y             | 633 (1.29)                     | 1697 (1.38)                              | 2278 (1.06%)                    | 4608 (1.19)    | < 0.001        |
| MI or all-cause | mortality, n (%)               |  |                                 |                |                |
| 90 d            | 212 (0.43)                     | 527 (0.43)                               | 806 (0.37)                      | 1545 (0.40)    | 0.02           |
| 6 mo            | 462 (0.94)                     | 1204 (0.98)                              | 1718 (0.80)                     | 3384 (0.87)    | < 0.001        |
| 1 y             | 896 (1.83)                     | 2256 (1.83)                              | 3143 (1.46)                     | 6295 (1.62)    | <0.001         |

MI indicates myocardial infarction; and NIT, noninvasive diagnostic test.

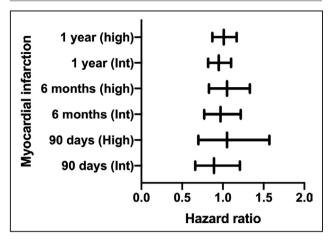
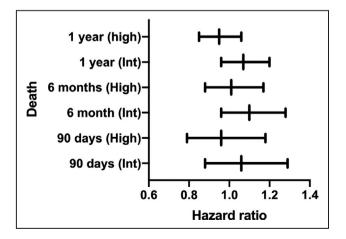


Figure 3. Myocardial infarction (MI) for the high and intermediate (Int) use tertiles vs the low use tertile (reference).

60-day inclusion period for receipt of NIT. The intermediate use group did not have significantly different hazards of MI or death when compared with the low use group over 90 days (HR, 1.04; 95% CI, 0.82–1.32), 6 months (HR, 1.09; 95% CI, 0.94–1.26), and 1 year (HR, 1.04; 95% CI, 0.95–1.14) post ED evaluation. The high use group also did not have significantly different hazards of MI or death compared with the low use group over 90 days (HR, 1.02; 95% CI, 0.81–1.29), 6 months (HR, 1.04; 95% CI, 0.90–1.19), and 1 year (HR, 0.98; 95% CI, 0.90–1.07).

#### **Downstream Resource Use**

Downstream all-cause ED visits, hospitalizations, and cardiovascular interventional/revascularization procedures (invasive angiography, percutaneous coronary intervention, coronary artery bypass grafting) are reported in Table 3. At 1 year, those in the highest NIT use tertile were significantly less likely to visit the ED or be hospitalized for any cause. However, they were



**Figure 4.** All-cause mortality for the high and intermediate (Int) use tertiles vs the low use tertile (reference).

significantly more likely to undergo cardiovascular invasive/revascularization procedures.

#### DISCUSSION

In our large, population-based, real-world study, we demonstrated significant between-hospital network variation in subsequent NIT in Ontario, Canada, among patients evaluated in the ED for chest pain and discharged home. MI and all-cause mortality were not significantly different among patients being evaluated in high or intermediate use hospital networks when compared with those evaluated at low use hospital networks. Thus, we could not demonstrate that higher NIT intensity was related to improved downstream major adverse cardiovascular events. These findings were consistent among 3 different outcome assessment time frames and for each of the constituent outcomes of MI and all-cause mortality. Furthermore, our results were robust to the exclusion of low volume hospital networks and to the extension of the inclusion period for receipt of NIT to 60 days.

It is currently unclear if more NIT leads to improved outcomes in patients undergoing evaluation for coronary artery disease.<sup>2,42</sup> Currently, the American Heart Association advocates for performing NIT for patients presenting for chest pain to the ED in whom an acute coronary syndrome has been excluded.<sup>43</sup> However, this recommendation is largely based on older data reporting relatively high rates of MI and death in those discharged from the ED after presentation with chest pain.<sup>44</sup> In the present study, we found significant practice variation in the percentage of patients undergoing NIT after discharge, ranging from 0% to 60% across all hospital networks providing emergency care in Ontario. Patients evaluated in the highest NIT intensity hospital networks were tested at a mean rate ≈3.5-fold greater when compared with those evaluated in the lowest NIT intensity hospital network group.

Our findings are consistent with and expound on other studies reported in the medical literature. For example, a recent study demonstrated that NIT after PCI ranged significantly between 17% and 73% in a large, population-based study using Medicare data in the United States.<sup>9</sup> This study categorized NIT use after PCI into quartiles and concluded that increased test use was not associated with improved downstream clinical outcomes such as MI and mortality. Building on that work, we report in this article that intensity of NIT, as defined by institutional practice, was similarly not associated with significantly different rates of MI and/or all-cause mortality in those patients evaluated for chest pain in the ED who were discharged home. Our results also build on recent

|                  | Low NIT Use (First<br>Tertile)  | Intermediate NIT Use<br>(Second Tertile) | High NIT Use (Third<br>Tertile) | Overall Cohort  | <i>P</i> Value |
|------------------|---------------------------------|--|---------------------------------|-----------------|----------------|
| ED visits, n (%) | )                               |  |                                 |                 |                |
| 90 d             | 10 556 (21.58)                  | 23 336 (18.95)                           | 37 566 (17.41)                  | 71 458 (18.43)  | <0.001         |
| 6 mo             | 16 066 (32.84)                  | 35 314 (28.67)                           | 56 682 (26.28)                  | 108 062 (27.86) | <0.001         |
| 1 y              | 23 155 (47.33)                  | 52 251 (42.42)                           | 84 866 (39.34)                  | 160 272 (41.33) | <0.001         |
| Hospitalization  | ıs, n (%)                       |  |                                 |                 |                |
| 90 d             | 2410 (4.93)                     | 6165 (5.01)                              | 10 250 (4.75)                   | 18 825 (4.85)   | <0.001         |
| 6 mo             | 3909 (7.99)                     | 9634 (7.82)                              | 15 641 (7.25)                   | 29 184 (7.53)   | <0.001         |
| 1 y              | 6056 (12.38)                    | 14 836 (12.05)                           | 24 109 (11.18)                  | 45 001 (11.60)  | <0.001         |
| Invasive angio   | graphy or revascularization, PC | Cl, or CABG, n (%)                       |                                 |                 |                |
| 90 d             | 1018 (2.08)                     | 2695 (2.19)                              | 6731 (3.12)                     | 10 444 (2.69)   | <0.001         |
| 6 mo             | 1528 (3.12)                     | 3850 (3.13)                              | 8559 (3.97)                     | 13 937 (3.59)   | <0.001         |
| 1 y              | 2013 (4.11)                     | 4899 (3.98)                              | 10 532 (4.88)                   | 17 444 (4.50)   | < 0.001        |

Table 3. Downstream Resource Use Compared Among the NIT Use Tertiles

CABG indicates coronary artery bypass grafting; ED, emergency department; NIT, noninvasive diagnostic test; and PCI, percutaneous coronary intervention.

work from our group that reported that NIT was not associated with reductions in MI or mortality in the majority of patients discharged home from the ED after evaluation for chest pain when compared with patients who were not tested.<sup>10</sup>

A possible explanation for the observed lack of impact of NIT on outcomes may be related to the low event rates that occurred in our cohort. Of the patients in our cohort, ~1.8% experienced a MI or died after 1 year of follow-up. The low event rates reflect an overall low-risk population who were evaluated for chest pain in an ED and in whom the ECG and other cardiac testing did not reveal high-risk features allowing them to be discharged home safely. Our low event rates parallel those of other similar studies evaluating the clinical effectiveness of NIT.<sup>42</sup>

#### **Clinical Importance**

Our results suggest that a strategy of more intense NIT was not associated with improvements in important downstream clinical outcomes and suggest that significant opportunities exist to improve guidance regarding appropriate indications for testing. Guidance regarding appropriate testing indications should be geared to physicians practicing at high and intermediate use hospital networks. Furthermore, more intense NIT was not consistently associated with reductions in downstream resource use. Although we observed lower ED visits and hospitalizations in high NIT hospital networks, we also observed higher rates of cardiac invasive and revascularization procedures. Overall, the absolute differences in resource use metrics between the NIT use tertiles were small.

# Limitations

A main strength of this article lies in its large sample size and the fact that we have virtually 100% coverage of the population of Ontario. Every resident of Ontario is entitled to receive health insurance through the OHIP. Because of the universality of this single-payer healthcare system, we are able to capture accurate and complete information on the entire population. This study must also be interpreted in the context of its potential limitations. First, our databases lacked granularity in a number of domains. For example, we lacked data on chest pain characteristics. We could therefore not account for the traditional pretest likelihood of obstructive coronary artery disease based on chest pain characteristics in our cohort. We also lacked data on patient smoking status and thus were unable to calculate 10-year aggregate cardiovascular risk scores for our patients. Second, as this is an observational study, there is the potential that patient characteristics differ across the tertiles of NIT. To address this limitation, we used Cox regression analyses to account for observed differences between the groups, allowing for adjustment for many clinically important covariates. However, there is the possibility that patients differed in unmeasured ways across tertiles. Third, these results reflect patterns of care and outcomes in Ontario and may not necessarily be generalizable to other jurisdictions. However, Ontario is a diverse province with a population of  $\approx$ 15 million people and is similar to many diverse jurisdictions around the world. Fourth, our study was not designed as an equivalence clinical trial and as such the absence of evidence for the efficacy of more intense NIT may not necessarily translate to evidence of an absence of such an impact. However, we believe that our results are clinically meaningful given the large sample size studied in addition to the consistency of our results across all constituents of the composite outcome and the robustness of the results to both the exclusion of low-volume hospital networks and to a 60-day inclusion window for receipt of NIT.

#### CONCLUSIONS

Our large, population-based, real-world study demonstrated significant variation in hospital network NIT intensity in Ontario, Canada. High NIT use was not associated with reductions in downstream MI or all-cause mortality.

#### **ARTICLE INFORMATION**

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**Disclosures** 

None.

Supplementary Material Table S1 Figure S1

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# SUPPLEMENTAL MATERIAL

|                     | Low NIT<br>utilization<br>(first<br>tertile) | Intermediate<br>NIT<br>utilization<br>(second<br>tertile) | High NIT<br>utilization<br>(third<br>tertile) | Total<br>cohort | p-value |
|---------------------|--|---|---|-----------------|---------|
| Number of patients  |  |   |   |                 |         |
| evaluated for chest |  |   |   |                 |         |
| pain                | N=5,947                                      | N=24,159  | N=75,402                                      | N=105,508       |         |
| Age in years (mean, | 57.73  |   | 56.55   | 56.86           |         |
| standard deviation) | (10.26)                                      | 57.59 (10.34)   | (10.27)                                       | (10.30)         | <.001   |
| Female Sex (%)      | 2,775  | 11,663  | 37,905  | 52,343          |         |
|                     | (46.66%)                                     | (48.28%)  | (50.27%)                                      | (49.61%)        | <.001   |
| Average emergency   |  |   |   |                 |         |
| department volume   |  |   |   |                 |         |
| (mean, standard     | 1107.10                                      | 1471.82   | 2317.97                                       | 2055.97         |         |
| deviation)          | (846.39)                                     | (727.46)  | (1069.25)                                     | (1075.43)       | <.001   |
| Rural (%)           | 1,806  | 3,925   | 5,726   | 11,457          |         |
|                     | (30.37%)                                     | (16.25%)  | (7.59%)                                       | (10.86%)        | < 0.001 |
| Neighbourhood       |  |   |   |                 |         |
| income              |  |   |   |                 |         |
|                     | 1,015  | 4,893   | 13,017  | 18,925          |         |
| 1                   | (17.07%)                                     | (20.25%)  | (17.26%)                                      | (17.94%)        | < 0.001 |
|                     | 1,146  | 4,650   | 14,609  | 20,405          |         |
| 2                   | (19.27%)                                     | (19.25%)  | (19.37%)                                      | (19.34%)        |         |
|                     | 1,176  | 4,492   | 15,791  | 21,459          |         |
| 3                   | (19.77%)                                     | (18.59%)  | (20.94%)                                      | (20.34%)        |         |
|                     | 1,230  | 4,854   | 17,109  | 23,193          |         |
| 4                   | (20.68%)                                     | (20.09%)  | (22.69%)                                      | (21.98%)        |         |
|                     | 1,340  | 5,148   | 14,718  | 21,206          |         |
| 5                   | (22.53%)                                     | (21.31%)  | (19.52%)                                      | (20.10%)        |         |
| Evaluation in       |  |   |   |                 |         |
| hospitals with      |  |   |   |                 |         |
| cardiac             |  |   |   |                 |         |
| catheterization     | 863  | 7,266   | 30,396  | 38,525          |         |
| capabilities        | (14.51%)                                     | (30.08%)  | (40.31%)                                      | (36.51%)        | < 0.001 |
| Cardiovascular      |  |   |   |                 |         |
| history and risk    |  |   |   |                 |         |
| factors             |  |   |   |                 |         |
| Congestive heart    |  |   |   |                 |         |
| failure             | 40 (0.67%)                                   | 143 (0.59%)   | 413 (0.55%)                                   | 596 (0.56%)     | 0.38    |
| Previous myocardial |  |   | 2,303   | 3,619           |         |
| infarction          | 298 (5.01%)                                  | 1,018 (4.21%)   | (3.05%)                                       | (3.43%)         | < 0.001 |
| Peripheral vascular |  |   | 1,396   | 2,095           |         |
| disease             | 147 (2.47%)                                  | 552 (2.28%)   | (1.85%)                                       | (1.99%)         | < 0.001 |

Table S1. Baseline characteristics of patients who underwent non-invasive testing.

| Chronic renal         |             |             |             |             |         |
|-----------------------|-------------|-------------|-------------|-------------|---------|
| disease               | 36 (0.61%)  | 122 (0.50%) | 271 (0.36%) | 429 (0.41%) | < 0.001 |
| Diabetes              | 1,125       | 4,683       | 15,415      | 21,223      |         |
|                       | (18.92%)    | (19.38%)    | (20.44%)    | (20.12%)    | < 0.001 |
| Dyslipidemia          | 2,842       | 11,735      | 39,283      | 53,860      |         |
|                       | (47.79%)    | (48.57%)    | (52.10%)    | (51.05%)    | < 0.001 |
| Hypertension          | 2,702       | 11,035      | 34,480      | 48,217      |         |
|                       | (45.43%)    | (45.68%)    | (45.73%)    | (45.70%)    | 0.91    |
| Previous              |             |             |             |             |         |
| cerebrovascular       |             |             |             |             |         |
| disease               | 43 (0.72%)  | 151 (0.63%) | 422 (0.56%) | 616 (0.58%) | 0.18    |
| Previous              |             |             |             |             |         |
| revascularization     |             |             | 2,006       | 3,152       |         |
| (PCI or CABG)         | 245 (4.12%) | 901 (3.73%) | (2.66%)     | (2.99%)     | < 0.001 |
| <b>Co-morbidities</b> |             |             |             |             |         |
| Chronic obstructive   |             |             |             |             |         |
| pulmonary disease     | 45 (0.76%)  | 227 (0.94%) | 632 (0.84%) | 904 (0.86%) | 0.23    |
| Cancer                |             |             | 1,850       | 2,667       |         |
|                       | 169 (2.84%) | 648 (2.68%) | (2.45%)     | (2.53%)     | 0.04    |
| Charlson Score        |             |             |             |             |         |
| (mean, standard       |             |             |             |             |         |
| deviation)            | 0.28 (0.83) | 0.27 (0.83) | 0.23 (0.76) | 0.24 (0.78) | < 0.001 |

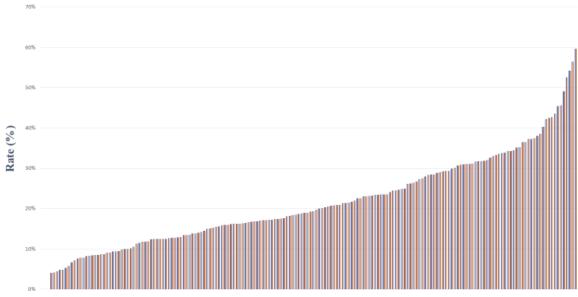


Figure S1. Site specific variation in NIT amongst hospital networks in Ontario.

Hospital Networks