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ORIGINAL RESEARCH

Graded Coronary Risk Stratification for Emergency Department Patients With Chest Pain: A Controlled Cohort Study

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BACKGROUND: Resource utilization among emergency department (ED) patients with possible coronary chest pain is highly variable.

METHODS AND RESULTS: Controlled cohort study amongst 21 EDs of an integrated healthcare system examining the implementation of a graded coronary risk stratification algorithm (RISTRA-ACS [risk stratification for acute coronary syndrome]). Thirteen EDs had access to RISTRA-ACS within the electronic health record (RISTRA sites) beginning in month 24 of a 48-month study period (January 2016 to December 2019); the remaining 8 EDs served as contemporaneous controls. Study participants had a chief complaint of chest pain and serum troponin measurement in the ED. The primary outcome was index visit resource utilization (observation unit or hospital admission, or 7-day objective cardiac testing). Secondary outcomes were 30-day objective cardiac testing, 60-day major adverse cardiac events (MACE), and 60-day MACE-CR (MACE excluding coronary revascularization). Difference-in-differences analyses controlled for secular trends with stratification by estimated risk and adjustment for risk factors, ED physician and facility. A total of 154 914 encounters were included. Relative to control sites, 30-day objective cardiac testing decreased at RISTRA sites among patients with low (≤2%) estimated 60-day MACE risk (–2.5%, 95% CI –3.7 to –1.2%, $P<0.001$) and increased among patients with non-low (>2%) estimated risk (+2.8%, 95% CI +0.6 to +4.9%, $P=0.014$), without significant overall change (–1.0%, 95% CI –2.1 to 0.1%, $P=0.079$). There were no statistically significant differences in index visit resource utilization, 60-day MACE or 60-day MACE-CR.

CONCLUSIONS: Implementation of RISTRA-ACS was associated with better allocation of 30-day objective cardiac testing and no change in index visit resource utilization or 60-day MACE.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03286179.

Key Words: acute coronary syndrome ■ diagnostic testing ■ prognosis

Patients presenting to the emergency department (ED) with chest pain have large variations in hospital admission rates, mostly driven by guideline recommendations to secure objective cardiac testing for possible acute coronary syndrome (ACS) prior to or within 72 hours of hospital discharge, despite a low overall incidence of acute coronary syndrome.[1–5] However, this practice has not been shown to be associated with improved near-term outcomes,[6–10] with the notable exception of patients with elevated serum

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CLINICAL PERSPECTIVE

What Is New?

- Implementation of a graded coronary risk stratification algorithm in the emergency departments of an integrated healthcare delivery system safely resulted in less objective cardiac testing among patients with chest pain at low risk of major adverse cardiac events while increasing downstream testing among patients at non-low risk.

What Are the Clinical Implications?

- Integration of graded coronary risk scores into clinical practice can help better match resource utilization to observed cardiac risk.

Nonstandard Abbreviations and Acronyms

ACS	acute coronary syndrome
CDS	electronic clinical decision support
CPT	current procedural terminology
DID	difference-in-differences
ECG	electrocardiogram
ED	emergency department
EDACS-ADP	Emergency Department Assessment of Chest pain Score Accelerated Diagnostic Protocol
HEART	History, Electrocardiogram, Age, Risk factors and Troponin
ICD-10	International Classification of Disease, 10th revision
IQR	Interquartile ratio
KPNC	Kaiser Permanente Northern California
LOS	length of stay
MACE	major adverse cardiac event
MACE-CR	major adverse cardiac event, excluding coronary revascularization
MI	myocardial infarction
RISTRA	risk stratification
VF	ventricular fibrillation

troponin levels.[11] Accordingly, a recent clinical policy from the American College of Emergency Physicians recommended against routine objective cardiac testing for patients at low risk for ACS.[12] Accurate identification of chest pain patients at low risk of ACS is essential to this recommendation.

Two well-validated protocols for identifying patients at low risk of ACS are the History, Electrocardiogram, Age, Risk factors, and Troponin Pathway (HEART Pathway) and the Emergency Department Assessment of Chest Pain Score Accelerated Diagnostic Protocol (EDACS-ADP). Both achieve negative predictive values above 99% for 30- to 45-day major adverse cardiac events (MACE) and have specificities ranging between 40% and 60%.[13–15] However, we previously observed that there are subgroups of patients with discordant risk classifications between the 2 protocols (ie, low risk by one and non-low risk by the other) and/or troponin values in the upper range of normal who have marginally higher risks of downstream MACE.[16]

Based on these observations, we designed a risk stratification algorithm risk stratification for acute coronary syndrome (RISTRA-ACS) using both the HEART pathway and EDACS-ADP to predict 60-day MACE risk among ED chest pain patients with possible ACS. We subsequently prospectively validated and evaluated the comparative performance of RISTRA-ACS at 13 of 21 community EDs in an integrated healthcare system using electronic clinical decision support (eCDS) embedded within the electronic health record, finding that RISTRA-ACS demonstrated the best overall performance with a negative likelihood ratio of 0.06 and an area under the receiver operating characteristic curve of 0.92 for 60-day MACE.[17] We hypothesized that the combined availability of and education surrounding RISTRA-ACS at these 13 EDs would lead to (1) a decrease in objective cardiac testing and hospital or observation unit admission among low risk patients and (2) an increase in objective cardiac testing among non-low risk patients. Since the majority of patients presenting with chest pain are at low risk of adverse outcomes,[2] we anticipated that decreases in utilization among low-risk patients would outweigh increases in utilization among non-low risk patients. Thus, an overall decrease in utilization represented our primary hypothesis.

METHODS

Study Design and Setting

We did a controlled cohort study at the 21 EDs within Kaiser Permanente Northern California (KPNC), a private not-for-profit integrated health system of over 4 million members with ≈1.2 million ED visits annually. KPNC members include ≈34% of the region's population and are representative of the demographic and socioeconomic diversity of the surrounding population.[18] All arenas of care (inpatient, outpatient, emergency) within KPNC utilize a single integrated electronic health record (Epic, Verona, WI). This study was approved by the KPNC Institutional Review Board with a waiver

of informed consent. Author JH had full access to the data and takes responsibility for its integrity and data analysis. Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to KPNC at kpnc.irb@kp.org.

The study examined the impact of RISTRA-ACS availability for prospective validation (Clinicaltrials.gov NCT03286179) at 13 exposed EDs (RISTRA sites) versus 8 non-exposed EDs (control sites) during the 24 months following RISTRA-ACS implementation (January 1, 2018 to December 31, 2019) as compared to a 24-month pre-implementation period (January 1, 2016 to December 31, 2017). A time-interrupted approach was planned to allow for a 12-month run-in period (January 1, 2018 to December 31, 2018) such that only the second post-implementation year was used to assess the impact of RISTRA-ACS availability. We chose a 12-month run-in period to maximize physician familiarity with RISTRA-ACS, particularly among late-adopters. Encounter inclusion criteria were age ≥18 years, chief complaint of chest pain or chest discomfort, serum troponin measurement within 6 hours of ED arrival, and active health plan membership defined as 9 out of 12 months prior and two continuous months following the encounter, except in cases of death, to ensure complete follow-up for the outcome period. Encounters were excluded if there was an ED diagnosis of ST-elevation myocardial infarction, a discharge from the ED against medical advice, or if the patient had an included encounter in the prior 60 days (owing to a 60-day outcome period). We estimated a study cohort size of 150 000 encounters over the 36-month analytic period based on the size of a prior retrospective study of coronary risk score performance in the same setting.[16]

Serum troponin values at all sites were obtained using a fourth-generation troponin I assay, the Access AccuTnI+3 (Beckman-Coulter, Brea, California). The 99th percentile for this assay is 0.04 ng/mL per local institutional reporting guidelines and reference literature.[19] The coefficient of variation at the 99th percentile is <10%, and the limits of blank, detection and quantitation are <0.01 ng/mL, 0.01 ng/mL, and 0.02 ng/mL, respectively.

RISTRA-ACS

RISTRA-ACS was incorporated as a module in a web-based eCDS interface referred to as RISTRA (risk stratification) which is nested within the electronic health record, as previously described for several other use cases.[20,21] RISTRA-ACS eCDS was made available at all RISTRA sites beginning on January 1, 2018. RISTRA-ACS automatically imported relevant structured data from the electronic health record (eg, past medical history), which was modified and/or validated by the clinician, followed by user input of subjective elements from the clinical history. Details of RISTRA-ACS data collection, troponin testing protocol, risk estimate algorithm and screen shots of the eCDS interface are available in Data S1, Figure S1, and Figure S2. Once no further serum troponin measurements were recommended, users were given one of four possible recommendations for disposition based on estimated risk, including an option for no further testing among patients with a low (2% or less) estimated 60-day MACE risk (Figure 1).

Since a previous study employing the RISTRA eCDS platform suggested that availability of the eCDS without accompanying education was insufficient to influence practice change, ED physicians were educated about RISTRA-ACS in advance of eCDS availability during the last quarter of 2017.[20] Specific attention was given to internal and external findings regarding the predictive value of low versus high-normal range troponin values for downstream MACE,[16,22] the validated test characteristics of the HEART pathway and EDACS-ADP,[23–25] and literature questioning the utility of routine non-invasive cardiac testing and/or hospital admission among low-risk patients.[26–28] Real-time prompts were available via automated text messages to ED physicians whenever serum troponin results became available for an adult patient under their care with a chief complaint of chest pain or discomfort.[29] All ED physicians were able to place orders for objective cardiac testing, including outpatient appointments, though specific test availability varied by facility and day of the week.

Variables

Since this study concerned both RISTRA-exposed and control sites, and included encounters from both pre- and post-implementation periods irrespective of RISTRA-ACS use or access, we ascertained component variables for RISTRA-ACS risk determination for all study encounters using a standardized and previously validated automated retrospective methodology.[30] In brief, variables needed to calculate HEART and EDACS scores were electronically extracted from the electronic health record using structured data (eg, past medical history from the problem list, smoking status, troponin values) supplemented with free text extraction and processing of both unstructured clinical notes (for presenting symptoms) and the finalized expert interpretation of electrocardiograms (ECGs) obtained during the index ED encounter. The history component of the HEART score was calculated in a standardized fashion by considering the net balance of any higher risk symptoms (eg, pain radiating to the

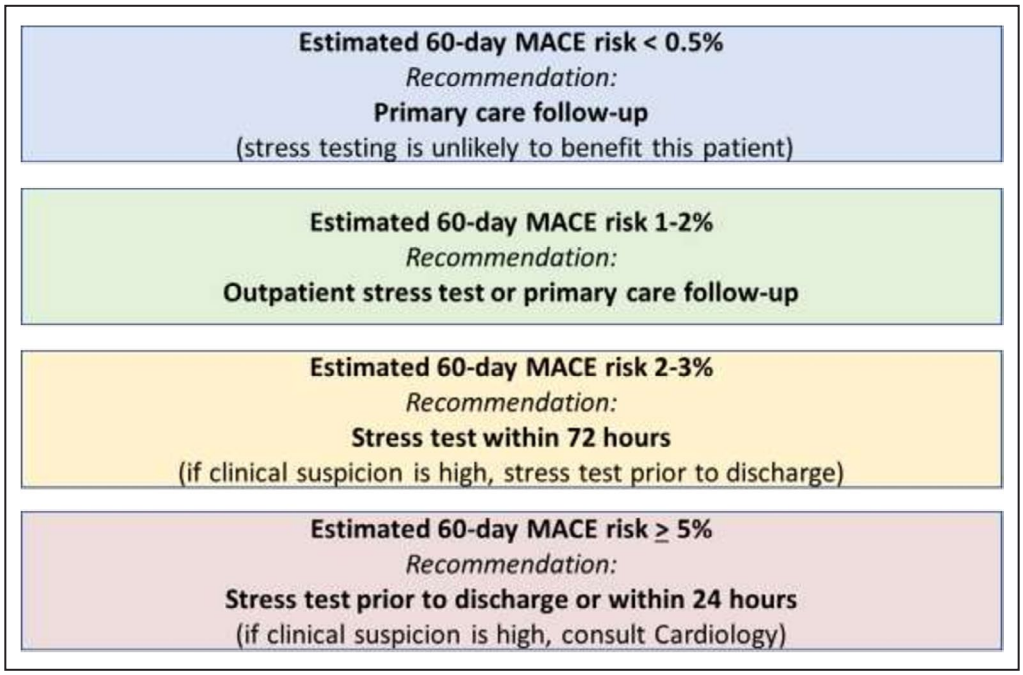


Figure 1. Risk stratification for acute coronary syndrome-ACS estimated risk prediction categories and accompanying recommendations.
MACE indicates major adverse cardiac event. RISTRA-ACS, risk stratification for acute coronary syndrome.

arm) against any lower risk symptoms (eg, pain reproduced with inspiration). Only crescendo angina (an independent non-low risk criterion in EDACS-ADP) was not assessed retrospectively. Troponin values used for retrospective risk estimate determination were restricted to those obtained within 6 hours of ED arrival. Further details regarding retrospective risk score elements and determination are provided in Data S2, Table S1, and Table S2.

Outcomes

The primary study outcome was index visit resource utilization (defined as hospital or observation unit admission, or 7-day objective cardiac testing). Objective cardiac testing included exercise electrocardiography, myocardial perfusion imaging, stress echocardiography, computed tomographic coronary angiography, or coronary catheterization. Secondary outcomes included 60-day MACE (defined as the composite outcome of acute myocardial infarction, cardiac arrest, cardiogenic shock, coronary revascularization, or all-cause mortality), 60-day MACE excluding coronary revascularization (MACE-CR), and 30-day objective cardiac testing. MACE-CR was included as a secondary outcome due to a lack of reliable methodology, specifically following an ED visit,[31] to categorize coronary revascularization procedures as either elective or non-elective based on diagnostic and/or billing codes, and because inclusion of elective coronary revascularization procedures is inconsistent with consensus agreements on appropriate MACE endpoints.[32]

Acute myocardial infarction, cardiac arrest or cardiogenic shock was considered to have occurred if a corresponding *International Classification of Disease, 10th revision* (ICD-10) code was the first or second diagnosis listed at an inpatient or ED encounter within the integrated healthcare system, or was used in a coded claim for services provided at facilities outside of the system (any coding position). For coronary revascularization, any corresponding ICD-10 procedure or current procedural terminology (CPT) code during a hospitalization within or outside of the integrated healthcare system was counted. All-cause mortality was determined using a composite death database comprised of KPNC mortality records, California Department of Public Health Vital Records, and Social Security Death Index data. Objective cardiac testing and hospital or observation admissions were tracked using internal procedure codes and patient care encounters, respectively. ICD-10 and CPT codes used to define outcomes above are available in Data S3.

Data Analysis

Difference-in-differences analyses were used to compare changes in primary and secondary outcomes between RISTRA and control sites during the 12-month

post-implementation period (beyond the 12-month run-in period) in comparison to the 24-month pre-implementation period. This analytic approach controls for secular trends and is not directly affected by imbalances in baseline variables between comparator groups, assuming those imbalances remain relatively constant over time within those groups.[33] We analyzed all study eligible encounters from both pre- and post-implementation periods, as opposed to focusing on encounters in which RISTRA-ACS was employed, both because we anticipated that practice change would eventually develop independent of RISTRA-ACS use (owing to intuitive familiarity with the algorithm) and due to concern for uncontrolled bias if we attempted to identify matched controls (due to unmeasured confounding of clinical concern for ACS and the physician's perceived utility of clinical decision support for a given patient).

The difference-in-differences was determined from the coefficient of the interaction term between study

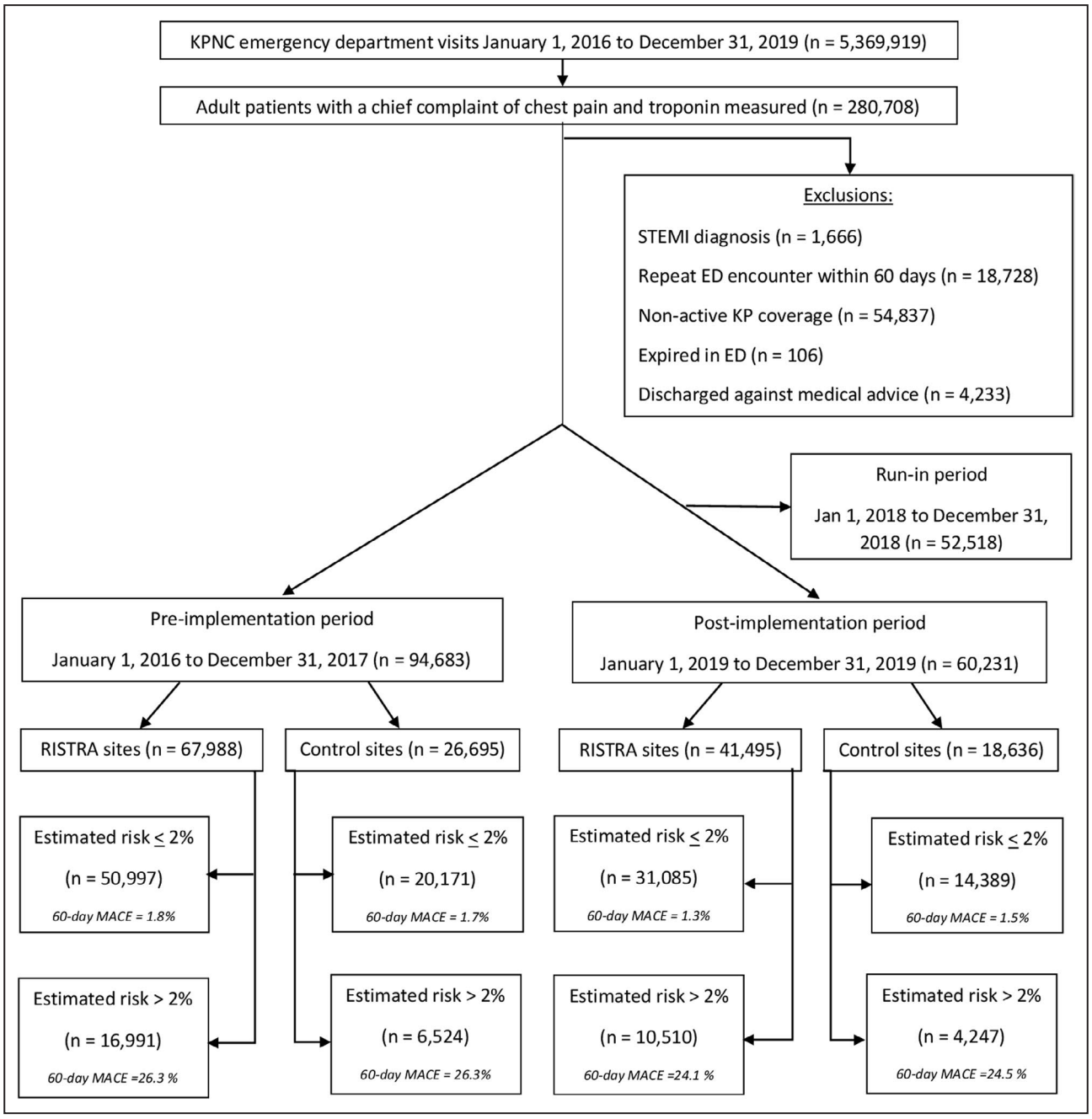


Figure 2. Study cohort selection and stratification.
ED, emergency department; KP, Kaiser Permanente, KPNC, Kaiser Permanente Northern California; MACE, major adverse cardiac event; RISTRA, risk stratification; STEMI, ST-elevation myocardial infarction.

site and implementation period in a mixed-effects regression model, adjusted for patient-level variables (age, sex, past medial history [diabetes, myocardial infarction, coronary revascularization], RISTRA-ACS estimated 60-day MACE risk, and peak troponin value within 6 hours of ED arrival) with random effects for initial treating ED physician and facility. These additional patient level variables were chosen de novo to account for underweighting or lack of representation within the risk scores, as well as to account for any key changes in patient risk within comparator groups over time. Stratified analyses for encounters with low (≤2%) and non-low (>2%) estimated 60-day MACE risk were performed to assess the hypotheses that RISTRA-ACS implementation would be associated with (1) a decrease in objective cardiac testing and hospital or observation unit admission among low-risk patients and (2) an increase in 30-day objective cardiac testing among non-low risk patients. This cut-point was chosen given that RISTRA-ACS recommended against (<0.5% estimated risk) or gave the option of deferring (1%–2% estimated risk) further objective cardiac testing for patients at 2% or lower estimated 60-day MACE risk.

Sensitivity analyses included: (1) exclusion of patients with index visit diagnoses of MACE (to assess for impact of RISTRA-ACS exposure on the incidence of delayed MACE diagnoses), (2) exclusion of patients seen by physicians in the lowest quartile of study eligible encounters (to enrich for physicians with greater patient contact during the study period), (3) exclusion of low-adopting RISTRA sites (those sites with below median RISTRA-ACS eCDS use among patients with a chief complaint of chest pain who underwent serum troponin testing, treating eCDS use as a proxy for facility-level adoption of the RISTRA-ACS algorithm), (4) use of a truncated 6-month run-in period with an 18-month post-implementation period, and (5) using fixed effects instead of random effects in the primary difference-in-differences model (to assess for bias from unmeasured variables). All hypotheses were two-sided with significance set at α=0.05. Data analyses were performed using Stata 14.2 (StataCorp, College Station, Texas).

RESULTS

There were 5 369 919 total ED encounters during the 48-month study period, of which 154 914 were study eligible during the 36-month analytic period (94 683 in the pre-implementation period and 60 231 in the post-implementation period, Figure 2). Of these eligible encounters, 109 583 (70.7%) presented to the 13 RISTRA sites. The overall median age was 60 years, 45.1% were male, 26.3% had a history of diabetes, 19.7% had coronary artery disease, and 12.5% had prior coronary revascularization, with similar prevalence of these risk factors and distribution of estimated 60-day MACE risk between RISTRA and control sites (Table 1). RISTRA-ACS was accessed during 14% of study eligible encounters at RISTRA sites in the post-implementation period with interfacility variation ranging between

Table 1. Patient Characteristics

	All sites	RISTRA sites (n=13)	Control sites (n=8)
Number of encounters	154 914	109 583	45 331
Age, y, median (IQR)	60 (48–72)	60 (48–72)	59 (47–71)
Male (%)	45.1	44.9	45.5
White (%)	51.1	50.8	51.6
Black (%)	12.3	13.4	9.7
Asian (%)	15.1	16.3	11.9
Hispanic (%)	19.8	17.6	24.9
Other (%)	1.9	1.9	1.9
Past medical history			
Hypertension (%)	52.6	52.7	52.5
Hypercholesteremia (%)	52.0	52.2	51.8
Diabetes (%)	26.3	26.0	26.9
Coronary artery disease (%)	19.7	19.8	19.5
Coronary revascularization (%)	12.5	12.5	12.6
Myocardial infarction (%)	13.8	14.0	13.5
Stroke (%)	9.5	9.3	10.0
Peripheral artery disease (%)	3.7	3.7	3.7
Smoker (%)	9.5	9.4	9.8
Family history (%)*	4.6	4.4	5.2
Obesity (%)	42.1	41.0	44.6
Risk estimates			
HEART score (median, IQR)	4 (3–5)	4 (3–5)	4 (3–5)
EDACS (median, IQR)	12 (7–17)	12 (8–18)	12 (6–16)
<0.5% 60-d MACE risk (%)	36.1	35.5	37.7
1%–2% 60-d MACE risk (%)	39.1	39.4	38.5
2%–3% 60-d MACE risk (%)	7.4	7.4	7.4
5%–7% 60-d MACE risk (%)	4.8	4.9	4.6
>7% 60-d MACE risk (%)	12.5	12.8	11.8
Low (<2%) risk for 60-d MACE (%)†,†	75.3	74.9	76.2
Non-low (>2%) risk for 60-d MACE (%)‡	24.7	25.1	23.8

Data are presented for all sites and stratified by site designation (RISTRA versus control) and are inclusive of the pre-implementation period (January 1, 2016 to December 31, 2017) and the post-implementation period (January 1, 2019 to December 31, 2019). ECG indicates electrocardiogram; EDACS, Emergency Department Assessment of Chest pain Score; HEART, History, Electrocardiogram, Age, Risk factors, Troponin; IQR, interquartile ratio; MACE, major adverse cardiac event; RISTRA, risk stratification.

*Family history of premature coronary artery disease in a first degree relative aged 55 or younger.

†Estimated 60-d MACE risk of 2% or less.

‡Estimated 60-d MACE risk of >2%.

8% to 24%. Quarterly averages of RISTRA-ACS use among study eligible encounters during the run-in and post-implementation periods are shown in Figure 3.

Frequencies of observed outcomes are reported in Table 2, with stratification by study period and site, and are summarized using unadjusted difference-in-differences statistics. Adjusted difference-in-differences analyses comparing post- and pre-implementation periods at RISTRA versus control sites are shown in Table 3. For the primary outcome of index visit resource utilization, there were no statistically significant adjusted difference-in-differences at RISTRA sites overall (–0.3%, 95% CI –1.4% to +0.8%, *P*=0.62) or among patients with either low (–1.1%, 95% CI –2.3% to +0.2%, *P*=0.10) or non-low estimated 60-day MACE risks (+1.5%, 95% CI –0.6% to +3.5%, *P*=0.15). Likewise, there were no statistically significant changes in 60-day MACE or 60-day MACE-CR outcomes overall in either risk strata. There was however a statistically significant decrease in 30-day objective cardiac testing at RISTRA sites among patients at low estimated 60-day MACE risk (–2.5%, 95% CI –3.7 to –1.2%, *P*<0.001) as well as an increase among patients at non-low estimated risk (+2.8%, 95% CI +0.6 to +4.9%, *P*=0.014). Time-trend graphs for the outcomes are shown in Figure 4 (index visit resource utilization), Figure 5 (30-day objective cardiac testing), Figure 6 (60-day MACE), and Figure 7 (60-day MACE-CR).

Sensitivity analyses (Tables S3, S4, S5, S6 and S7) were supportive of the primary analysis, with the additional statistically significant findings at RISTRA sites of (1) a decrease in 30-day objective cardiac testing among all patients without an index encounter diagnosis of MACE (–1.3%, 95% CI –2.5% to –0.2%, *P*=0.026) and (2) a decrease in all outcomes among patients at low estimated risk of 60-day MACE following exclusion of RISTRA sites with below median eCDS use during the post-implementation period.

DISCUSSION

In this controlled cohort study of the impact of RISTRA-ACS availability, while there was no statistically significant adjusted difference-in-differences in the primary outcome of index visit resource utilization, there was a statistically significant redistribution of 30-day objective cardiac testing at RISTRA sites during the post-implementation period, with a 2.5% absolute decrease among patients at low (≤2%) estimated 60-day MACE risk and a 2.8% absolute increase among patients at non-low (>2%) estimated risk. While relatively modest, the decrease in objective cardiac testing among patients at low estimated risk of 60-day MACE appeared safe in that there was no associated increase in 60-day MACE or MACE-CR outcome incidence (upper 95% CI for adjusted MACE and MACE-CR difference-in-differences of 0.0% and +0.1%, respectively). These results remained robust in sensitivity analyses.

Prior studies have demonstrated decreases in objective cardiac testing following implementation

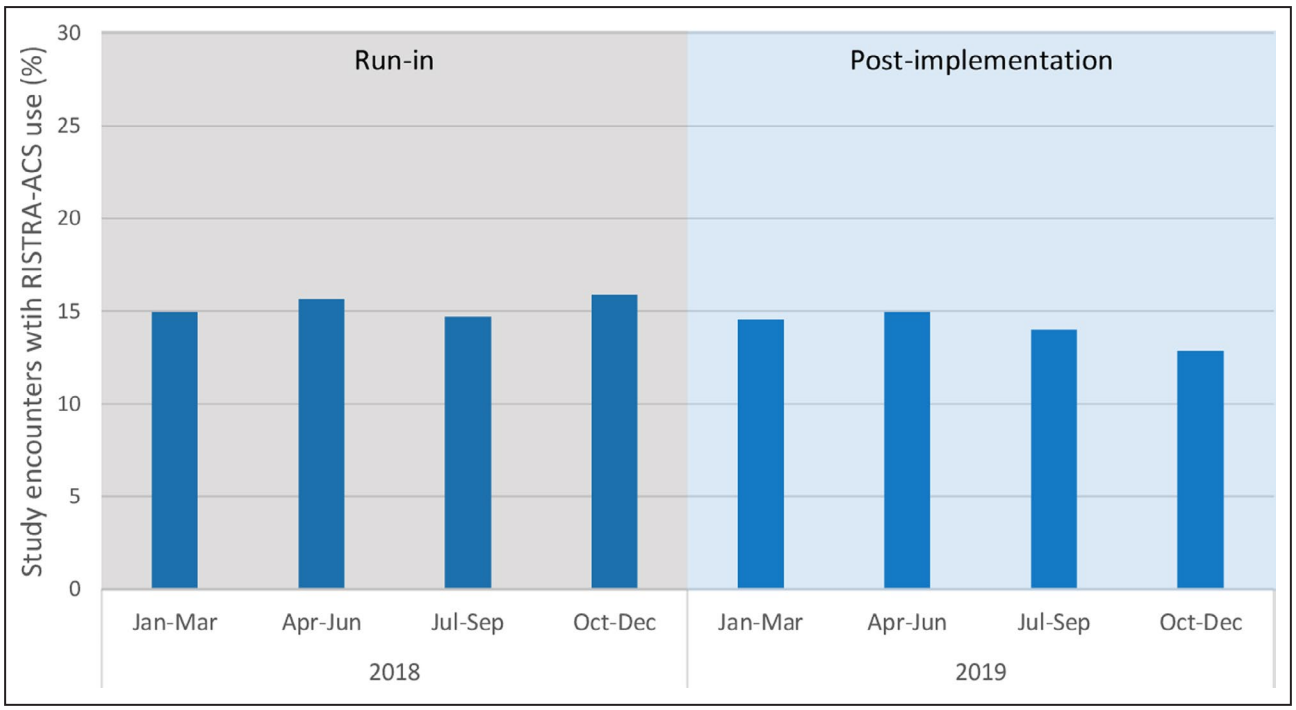


Figure 3. Quarterly averages of RISTRA-ACS use among study eligible patient encounters (RISTRA sites only).
RISTRA-ACS, risk stratification for acute coronary syndrome.

Table 2. Study Outcomes and Index Encounter Findings

	All sites (n=21)		RISTRA sites (n=13)		Control sites (n=8)		RISTRA - control
Implementation period	Pre	Post	Pre	Post	Pre	Post	Unadjusted difference in differences (95% CI)
Study subjects (n)	94 683	60 231	67 988	41 595	26 695	18 636	
Index encounter							
Multiple troponin tests within 6 h of ED arrival (%)	27.1	29.3	29.3	33.0	21.7	21.0	+4.4 (+3.5 to +5.2)
ED LOS, hours (mean, SD)	4.6 (2.9)	4.7 (3.3)	4.6 (2.9)	4.7 (3.4)	4.7 (2.9)	4.5 (3.1)	+0.3 (+0.2 to +0.3)
ED LOS, hours (median, IQR)	4 (3–6)	4 (3–6)	4 (3–6)	4 (3–6)	4 (3–6)	4 (3–5)	+0.3 (+0.2 to +0.3)
Total LOS, hours (mean, SD)	16.5 (39.3)	15.8 (37.4)	17.2 (41.2)	16.5 (37.8)	14.8 (34.0)	14.4 (36.5)	−0.3 (−1.2 to +0.6)
Total LOS, hours (median, IQR)	5 (3–14)	5 (3–9)	5 (3–17)	5 (3–12)	5 (3–8)	4 (3–7)	+0.1 (−0.1 to +0.2)
Initial troponin >99th percentile (%)	7.9	7.4	7.8	7.6	8.0	7.0	+0.8 (+0.2 to +1.4)
Troponin >99th percentile within 6 h of ED arrival (%)	8.9	8.4	8.9	8.7	9.0	7.7	+1.1 (+0.2 to +2.0)
MACE (%)	4.6	4.2	4.7	4.4	4.3	3.6	+0.4 (−0.1 to +0.9)
MACE-CR (%)	3.9	3.6	3.9	3.8	3.9	3.2	+0.5 (0.0 to +0.9)
Acute MI (%)	3.7	3.3	3.7	3.5	3.6	3.0	+0.5 (0.0 to +0.9)
Index visit resource utilization							
Admission (%)	10.2	9.4	10.4	9.5	9.8	9.1	−0.1 (−0.8 to +0.5)
Observation unit (%)	17.0	14.4	19.2	16.5	11.6	9.8	−0.9 (−1.7 to 0.0)
7-d exercise electrocardiography (%)	24.3	15.4	26.2	16.1	19.3	14.0	−4.8 (−5.7 to −3.9)
7-d myocardial perfusion imaging (%)	10.2	9.2	11.2	10.4	7.5	6.6	+0.2 (−0.5 to +0.8)
7-d stress echocardiography (%)	0.3	0.1	0.2	0.2	0.4	0.1	+0.3 (+0.2 to +0.4)
7-d CT coronary angiography (%)	0.2	0.3	0.2	0.3	0.4	0.3	+0.2 (0.0 to +0.3)
7-d coronary catheterization (%)	7.4	6.4	7.5	6.6	7.2	6.1	+0.3 (−0.3 to +0.8)
Any 7-d objective cardiac test (%)	35.6	27.7	37.5	29.8	30.6	23.1	−0.2 (−1.2 to +0.9)
Index visit resource utilization (%)	46.9	38.3	49.2	40.8	40.9	32.8	−0.3 (−1.4 to +0.8)
30-d objective cardiac testing							
Exercise electrocardiography (%)	28.4	19.9	30.2	20.0	23.9	19.7	−6.0 (−7.0 to −5.1)
Myocardial perfusion imaging (%)	12.3	11.8	13.4	12.9	9.4	9.3	−0.4 (−1.1 to +0.3)
Stress echocardiography (%)	0.8	0.5	0.7	0.5	0.9	0.3	+0.4 (+0.2 to +0.6)
CT coronary angiography (%)	0.4	0.6	0.4	0.6	0.6	0.7	+0.1 (−0.1 to +0.2)
Coronary catheterization (%)	8.4	7.3	8.4	7.4	8.2	7.1	+0.1 (−0.5 to +0.7)
Any objective cardiac test (%)	40.7	33.7	42.4	35.1	36.3	30.7	−1.8 (−2.8 to −0.7)
60-d outcomes							
MACE (%)	8.0	6.9	8.0	7.0	8.1	6.7	+0.5 (−0.1 to +1.1)
MACE-CR (%)	7.0	6.3	6.9	6.4	7.1	6.1	+0.5 (0.0 to +1.1)
Acute MI (%)	5.9	5.1	5.8	5.2	6.0	4.8	+0.6 (+0.1 to +1.1)
Cardiac arrest/VF (%)	0.2	0.2	0.2	0.2	0.2	0.2	0.0 (−0.1 to +0.1)
Cardiogenic shock (%)	0.2	0.2	0.2	0.2	0.2	0.2	0.0 (−0.1 to +0.1)
Coronary revascularization (%)	3.6	2.8	3.5	2.7	3.9	3.0	+0.2 (−0.2 to +0.6)
All-cause mortality (%)	1.3	1.3	1.3	1.3	1.3	1.4	0.0 (−0.3 to +0.2)

Unadjusted difference in differences represent the change in percentage of outcomes at RISTRA sites relative to control sites in the post-implementation period (January 1, 2019 to December 31, 2019) as compared to the pre-implementation period (January 1, 2016 to December 31, 2017). CT, computed tomography; ED, emergency department; LOS, length of stay; MACE, major adverse cardiac event; MACE-CR, major adverse cardiac event excluding coronary revascularization; MI, myocardial infarction; RISTRA, risk stratification; VF, ventricular fibrillation.

of standardized coronary risk scores in the ED. In their stepped-wedge multicenter randomized trial of a HEART score care pathway, Poldervaart et al reported an unadjusted 8% decrease (65% to 57%) in diagnostic procedures within 3 months following an ED chest pain visit.[34] Mahler et al, analyzing a

Table 3. Difference-in-Differences (DID) Analysis

	Unadjusted DID (95% CI)	*P* value	Adjusted DID (95% CI)	*P* value
Low risk subgroups				
Index visit resource utilization*	−1.9% (−3.1 to −0.7)	0.003	−1.1% (−2.3 to +0.2)	0.10
30-d objective cardiac testing	−3.8% (−5.0 to −2.6)	<0.001	−2.5% (−3.7 to −1.2)	<0.001
60-d MACE	−0.3% (−0.7 to 0.0)	0.041	−0.3% (−0.6 to 0.0)	0.051
60-d MACE-CR	−0.2% (−0.4 to +0.1)	0.13	−0.2% (−0.4 to +0.1)	0.16
Non-low risk subgroups				
Index visit resource utilization*	+1.7% (−0.5 to +3.8)	0.13	+1.5% (−0.6 to +3.5)	0.15
30-d objective cardiac testing	+3.4% (+1.1 to +5.7)	0.004	+2.8% (+0.6 to +4.9)	0.014
60-d MACE	+1.2% (−0.8 to +3.2)	0.24	+0.4% (−1.2 to +2.1)	0.62
60-d MACE-CR	+1.1% (−0.9 to +3.0)	0.29	+0.2% (−1.4 to +1.8)	0.83
Overall				
Index visit resource utilization*	−0.3% (−1.4 to +0.8)	0.56	−0.3% (−1.4 to +0.8)	0.62
30-d objective cardiac testing	−1.8% (−2.8 to −0.7)	0.001	−1.0% (−2.1 to +0.1)	0.079
60-d MACE	+0.5% (−0.1 to +1.1)	0.12	−0.2% (−0.6 to +0.3)	0.49
60-d MACE-CR	+0.5% (0.0 to +1.1)	0.062	−0.1% (−0.6 to +0.3)	0.52

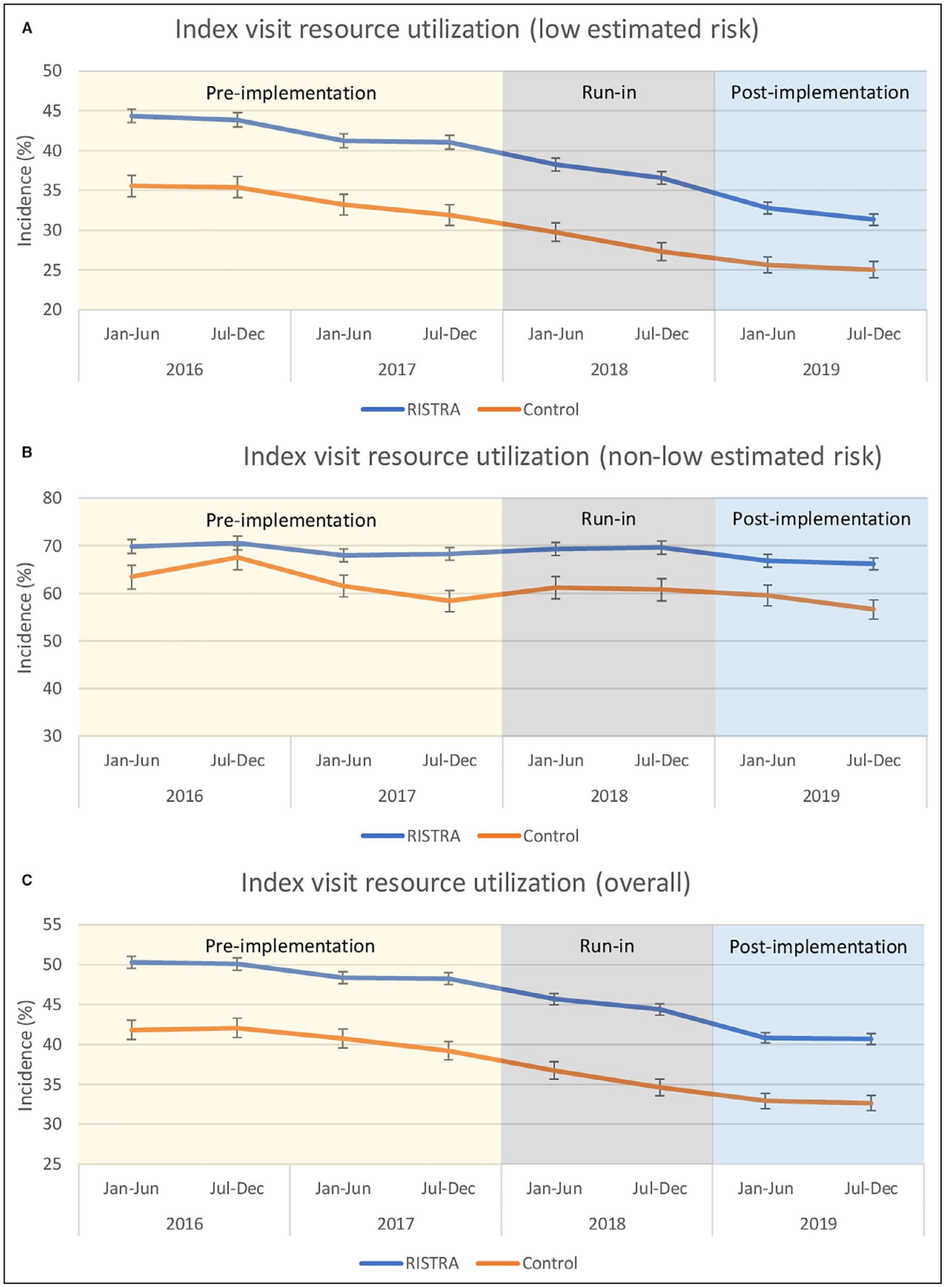
Percentages represent the observed differences in outcomes at RISTRA sites relative to control sites in the post-implementation period (January 1, 2019 to December 31, 2019) as compared to the pre-implementation period (January 1, 2016 to December 31, 2017). Results are presented both with and without adjustment for age, sex, past medical history, estimated RISTRA risk, and troponin, with random effects at both facility and provider levels. The low-risk subgroup includes patient encounters with an estimated 60-day MACE risk of ≤2%, and the non-low risk subgroup represents the remainder of encounters with >2% estimated 60-day MACE risk. DID indicates difference-in-differences; MACE, major adverse cardiac event; MACE-CR, major adverse cardiac event excluding coronary revascularization; RISTRA, risk stratification.

*A composite of observation unit or hospital admission during the index ED visit, or objective cardiac testing within the following 7 days.

multicenter implementation of the HEART Pathway, observed a 6% decrease in 30-day hospitalizations (61.6% to 55.6%) and a 3.8% decrease in 30-day objective cardiac testing (34.5% to 30.7%).[35] After implementation of the HEART score in 13 EDs of an integrated health system, Sharp et al noted a 4.4% adjusted decrease (accounting for pre-implementation trends) in the composite of hospitalization or objective cardiac testing within 30 days.[36] However, the latter two studies lacked concurrent controls to account for unanticipated time trends, and Poldervaart et al did not observe significant differences in utilization when controlling for clustering and time steps. This potential for confounding by time trends is apparent in the current study by the steady decrease in 30-day objective cardiac testing at control sites noted in the time-trend graphs (Figure 3). As such, the 2.5% absolute decrease in objective cardiac testing observed in the low-risk subgroup arguably represents a more certain association between ED coronary risk score availability and utilization than previous reports, as does the 1.3% overall adjusted reduction in 30-day objective cardiac testing among patients without an index encounter MACE diagnosis, who arguably better represent the population of interest (ie, patients without overt evidence of ACS).

We also observed a time-dependence in the impact of RISTRA-ACS availability among RISTRA sites, reflected by a gradual steepening of the downward slope for 30-day cardiac testing at RISTRA sites during the post-implementation period (Figure 3). One possible reason for this apparent incremental adoption of practice change at RISTRA sites relates to the notion that physicians are more comfortable engaging in risk-averse behavior (eg, increased testing of patients identified as non-low risk), as opposed to deferring objective testing for low risk patients.[37] This is also suggested by the slight increase in 30-day objective cardiac testing among non-low risk patients at the end of the pre-implementation period, corresponding to the beginning of physician education regarding the predictive value of low versus high-normal range troponin values. It is thus conceivable that a longer observation period would have been revealing as physicians became increasingly comfortable with the notion of forgoing observation and deferring objective cardiac testing for low risk patients.

Figure 4. Time trends in index visit resource utilization.
Outcomes are stratified by RISTRA sites (blue lines) and control sites (orange lines). Error bars represent 95% confidence intervals. Figures are presented by estimated risk of 60-day major adverse cardiac events: (**A**) patients with low (≤2%) estimated risk; (**B**) patients with non-low (>2%) estimated risk; (**C**) overall (any risk).


A
Index visit resource utilization (low estimated risk)
Incidence (%)
50
45
40
35
30
25
20
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control
B
Index visit resource utilization (non-low estimated risk)
Incidence (%)
80
70
60
50
40
30
Pre-implementation
Run-in
Post-implementation
RISTRA
Control
C
Index visit resource utilization (overall)
Incidence (%)
55
50
45
40
35
30
25
Pre-implementation
Run-in
Post-implementation
RISTRA
Control

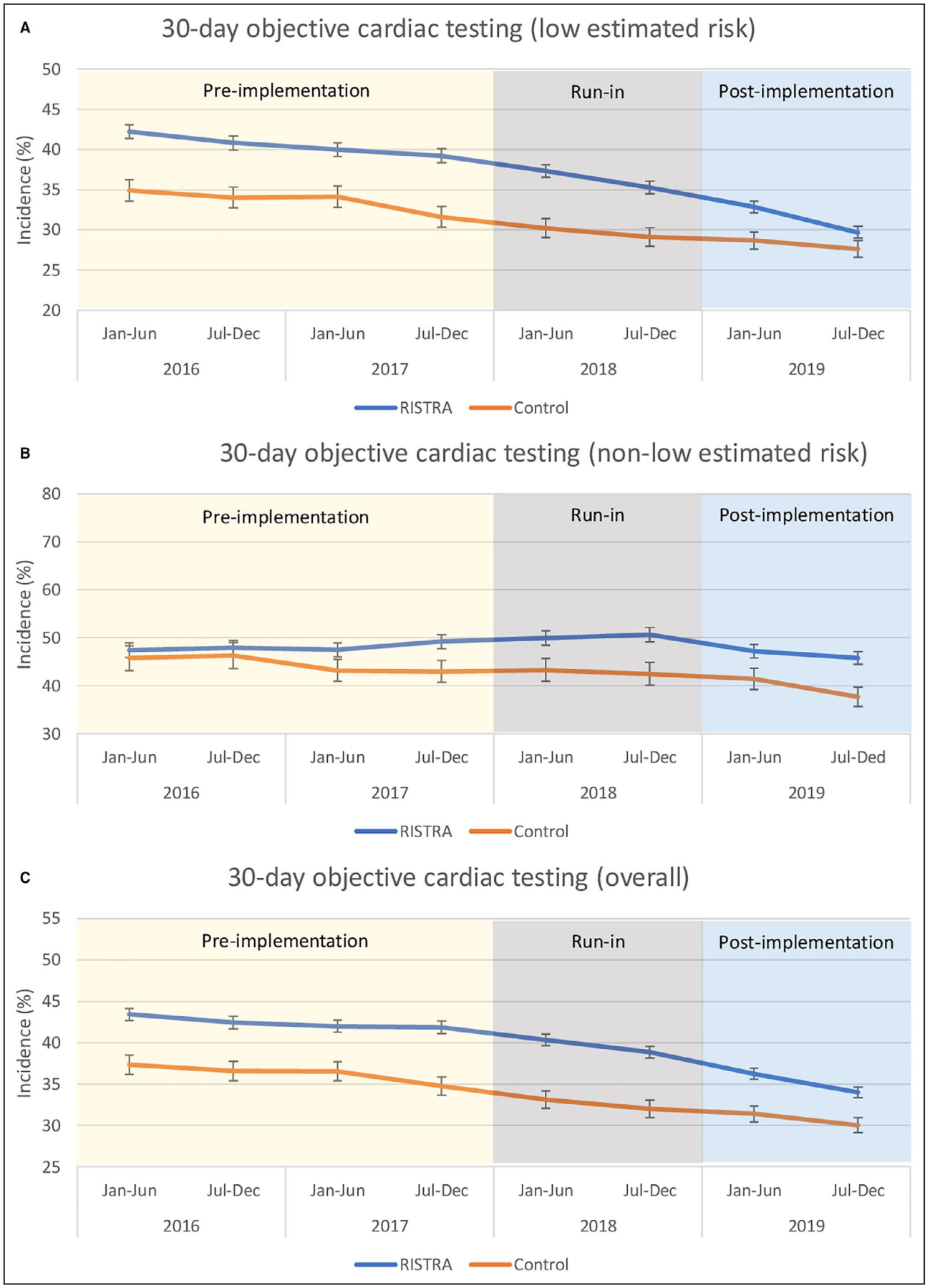

A
30-day objective cardiac testing (low estimated risk)
Incidence (%)
50
45
40
35
30
25
20
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control
B
30-day objective cardiac testing (non-low estimated risk)
Incidence (%)
80
70
60
50
40
30
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
Jul-Ded
2016
2017
2018
2019
RISTRA
Control
C
30-day objective cardiac testing (overall)
Incidence (%)
55
50
45
40
35
30
25
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control

Figure 5. Time trends in 30-day objective cardiac testing.
Outcomes are stratified by RISTRA sites (blue lines) and control sites (orange lines). Error bars represent 95% confidence intervals. Figures are presented by estimated risk of 60-day major adverse cardiac events: (**A**) patients with low (≤2%) estimated risk; (**B**) patients with non-low (>2%) estimated risk; (**C**) overall (any risk).

It is also notable that, on average, RISTRA-ACS use among study eligible patients was relatively low (averaging 14% during the post-implementation period). There was however a good deal of variability in RISTRA-ACS use between facilities, with facility-level averages ranging from 8% to 24%. While the drivers of this variability are likely complex (pre-existing physician biases, perceived lack of proven utility and/or safety) and beyond the scope of this study, it is notable that sensitivity analysis following exclusion of RISTRA sites with below median RISTRA-ACS eCDS use supported the study hypothesis in showing a statistically significant decrease in the primary outcome of index visit resource utilization among patients at low estimated risk of 60-day MACE, in addition to the forementioned impacts on 30-day objective cardiac testing. Thus, in treating the proportion of study eligible encounters with RISTRA-ACS use as proxy for facility-level adoption of the RISTRA-ACS algorithm, this finding supports a potential for greater impact on resource utilization with higher overall adoption of the RISTRA-ACS algorithm, such as might be realized in the wake of demonstrated safety and utility herein.

The potential for coronary risk stratification to decrease downstream resource utilization has important cost saving implications. Using a bottom-up inventory-based cost calculation methodology, investigators from the PROMISE trial placed the median cost of exercise electrocardiography at $174 and pharmacologic myocardial perfusion imaging at $1132.[38] From that vantage, exercise electrocardiography appears to be a relatively low-cost strategy with little potential for cost savings from resource stewardship. However, the total direct health care costs at 90 days were more similar between the two strategies, being $1770 for exercise electrocardiography and $2274 for myocardial perfusion imaging, likely owing to higher downstream costs due to false positive or indeterminate test results among patients undergoing exercise electrocardiography. Accordingly, an economic analysis of a randomized controlled trial of the HEART pathway in the ED estimated a median cost savings of $1785 at 30 days for every additional patient who did not undergo objective cardiac testing in the intervention arm.[39] Thus, even a 1% absolute decrease in objective cardiac testing, as observed in this study, could yield savings upwards of 5 billion dollars annually when extrapolated to the 7.6 million patients evaluated annually for chest pain in U.S. EDs.[40]

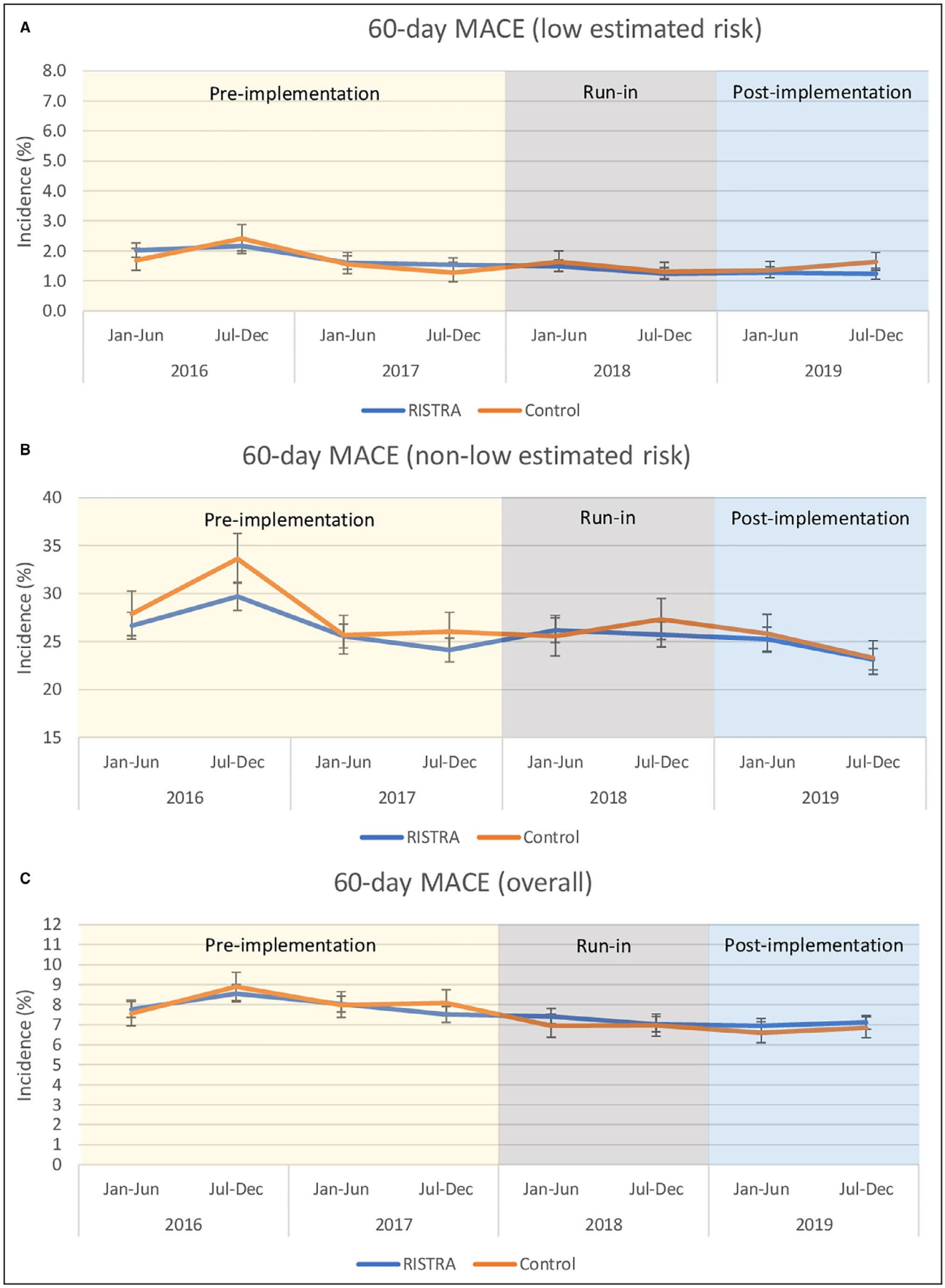
In terms of associations between RISTRA-ACS implementation and ED operations, we observed increases at RISTRA sites in the unadjusted difference-in-differences for ED length of stay (+0.3 hours) and the proportion of patients with multiple troponin tests within 6 hours of ED arrival (+4.4%). While some increase in troponin testing was anticipated due to RISTRA-ACS's emphasis on early repeat measurement of troponin values above the level of quantitation (to establish whether values were rising), it is more difficult to attribute increases in ED length of stay to RISTRA-ACS availability given competing factors such as ED boarding times among admitted patients. Regardless, the increase in ED length of stay was relatively small.

Finally, we observed an increase in the proportion of patients at RISTRA sites diagnosed with acute myocardial infarction during the index encounter (unadjusted difference-in-differences of +0.5%, 95% CI 0.1% to 0.9%). A similar increase in index diagnoses of myocardial infarction was noted in the HEART Pathway implementation trial.[35] However, as RISTRA sites also saw an increase in patients with initial troponin values over the 99th percentile (+0.8%, 95% CI +0.2% to +1.4%) and a nearly identical increase in 60-day acute myocardial infarction diagnoses, inclusive of the index encounter (+0.6%, 95% CI +0.1% to 1.1%), it is less likely that the increase in index acute myocardial infarction diagnoses represented detection of otherwise "missed" events as opposed to variations in disease incidence among ED populations over time. This highlights the importance of using both risk-adjustment and contemporaneous controls in measuring implementation-associated impacts.

Limitations

Limitations include the retrospective determination of risk scores, outcome ascertainment using diagnostic and procedural codes, non-randomized assignment of implementation (RISTRA) sites, the opt-in nature of the RISTRA eCDS interface, and a study setting within an integrated healthcare system. Regarding

Figure 6. Time trends in 60-day major adverse cardiac events (MACE).
Outcomes are stratified by RISTRA sites (blue lines) and control sites (orange lines). Error bars represent 95% confidence intervals. Figures are presented by estimated risk of 60-day major adverse cardiac events: (**A**) patients with low (≤2%) estimated risk; (**B**) patients with non-low (>2%) estimated risk; (**C**) overall (any risk).


A
60-day MACE (low estimated risk)
Incidence (%)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control
B
60-day MACE (non-low estimated risk)
Incidence (%)
40
35
30
25
20
15
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control
C
60-day MACE (overall)
Incidence (%)
12
11
10
9
8
7
6
5
4
3
2
1
0
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control

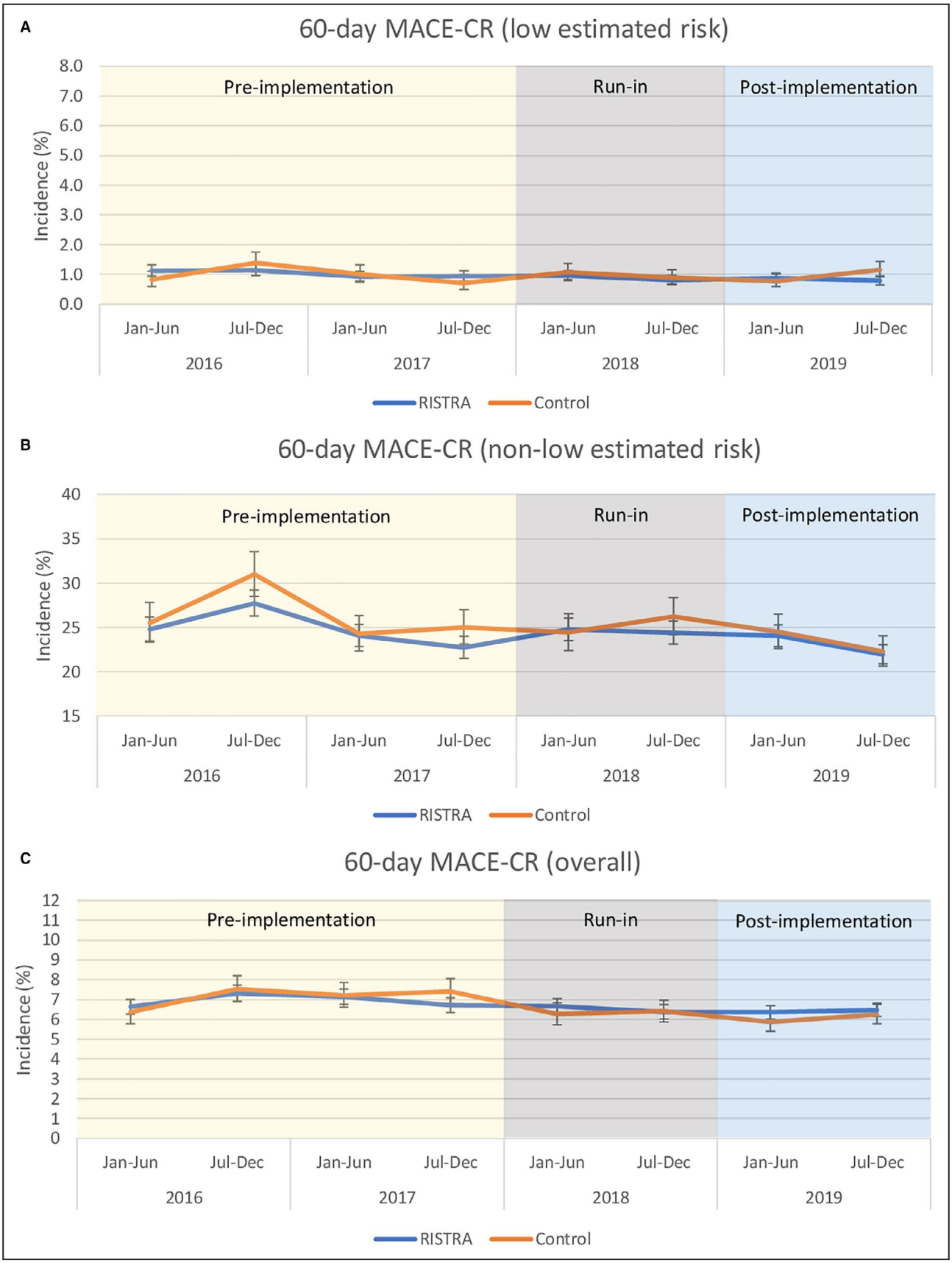

A
60-day MACE-CR (low estimated risk)
Incidence (%)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control
B
60-day MACE-CR (non-low estimated risk)
Incidence (%)
40
35
30
25
20
15
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control
C
60-day MACE-CR (overall)
Incidence (%)
12
11
10
9
8
7
6
5
4
3
2
1
0
Pre-implementation
Run-in
Post-implementation
Jan-Jun
Jul-Dec
2016
2017
2018
2019
RISTRA
Control

Figure 7. Time trends in 60-day major cardiac adverse events except coronary revascularization (MACE-CR).
Outcomes are stratified by RISTRA sites (blue lines) and control sites (orange lines). Error bars represent 95% confidence intervals Figures are presented by estimated risk of 60-day major adverse cardiac events: (**A**) patients with low (≤2%) estimated risk; (**B**) patients with non-low (>2%) estimated risk; (**C**) overall (any risk).

the retrospective risk score methodology, given that we have previously shown it to have similar reliability as compared to prospective score calculations,[30] and since the methodology was applied uniformly across all sites and study periods, we expect this carried minimal potential bias. However, the retrospective risk determination was dependent on troponin values, and we observed a 4.4% increase in patients undergoing repeat troponin testing at RISTRA sites. Thus, it is possible that risk was underestimated at control sites in the post-implementation period. However, even assuming a 15% prevalence of acute myocardial infarction and a 15% gain in sensitivity with repeat troponin testing, any resulting bias would be expected to be exceedingly small (ie, <0.1% absolute difference).[41,42]

While outcomes were determined based on diagnostic and procedural codes, there was no expected outcome ascertainment bias between control and RISTRA sites as all are overseen by a centralized health information management department. Furthermore, by restricting the study population to patients with continuous health plan coverage during the follow-up period we were able to obtain a full accounting of healthcare encounters both within and external to the integrated healthcare system. However, it is conceivable that the follow-up window was too short to detect changes in outcomes from differing acute management strategies. For example, in the SCOT-HEART randomized trial of computed tomographic coronary angiography, clear statistically supported differences in follow-up MACE were not evident until nearly 2 years later.[43,44] Thus further study including long-term follow-up is thus warranted.

Since RISTRA site designation was not randomized but rather driven by the availability of local clinical champions and study investigators, it is possible that RISTRA sites were more amenable to practice change than control sites. However, the degree of variance in RISTRA-ACS use amongst RISTRA sites (range 8% to 24% of possibly eligible encounters) at least demonstrates non-uniform facility-level uptake, though we cannot exclude unmeasured confounding from local practice initiatives during the study period (we are unaware of any). Additionally, though there was some occasional crossover of physicians from RISTRA to control sites due to intermittent staffing shortages, these instances represented <0.2% of study encounters. Regardless, such crossover would be expected to bias results towards the null.

From an eCDS implementation standpoint, the potential impact of RISTRA-ACS may have been limited due to the opt-in structure of the interface. However, there are a variety of potential clinical scenarios and diagnostic considerations encapsulated by a chief complaint of chest pain and/or the use of troponin testing. As such, an assistive, clinician-selected portal within the electronic health record was deemed the most pragmatic solution to achieve the five "rights" of clinical decision support for a complex decision: the right information, to the right recipients, on the right platform, in the right format and at the right time.[45] Finally, as the study was performed within an integrated healthcare system, external generalizability cannot be assumed.

CONCLUSION

Implementation of a coronary risk stratification algorithm in EDs of an integrated health system appeared safe in the short-term. While RISTRA-ACS availability was not associated with a change in index visit resource utilization, 30-day objective cardiac testing did safely decrease among patients with a low estimated risk of 60-day MACE, and appropriately increased among the remainder of patients with non-low estimated risk.

APPENDIX

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Disclosures

None.

Supplementary Material

Data S1–S3
Tables S1–S7
Figures S1–S2

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Supplemental Material

Data S1. Supplemental Methods: RISTRA-ACS data collection and troponin testing protocol

RISTRA-ACS imported relevant structured data from the electronic health record (e.g. past medical history), which was modified and/or validated by the clinician, followed by user input of subjective elements from the clinical history. These included the timing of pain onset and the presence or absence of following symptoms: 1) pain on inspiration, 2) sharp or stabbing pain, 3) nausea or vomiting, 4) exertional symptoms, 6) radiation of pain to arm, shoulder, neck or jaw 7) diaphoresis 8) pain reproduced by palpation and 9) crescendo angina (pain which is recurrent and worsening, lasts at least 5-10 minutes, and occurs at rest or with minimal exertion). As in recent studies of the HEART pathway, the history component of the HEART score (range 0 to 2 points) was determined in a standardized fashion by considering the net balance of any "high risk" symptoms (e.g. pain radiating to the arm) against any "low risk" symptoms (e.g. pain reproduced with inspiration).[35] Physicians also provided a structured ECG interpretation as either 1) normal, 2) abnormal/non-diagnostic (defined as any repolarization abnormalities, bundle branch blocks, paced rhythms, old or non-specific T wave or ST-segment changes, or evidence of prior infarction) or 3) new ischemic change (new ST-segment depressions of at least 0.05 mV in 2 contiguous leads or T-wave inversions > 1 mV in depth). Following initial data entry, RISTRA-ACS calculated both EDACS and HEART scores to determine a binary classifier for each (low risk versus non-low risk) based on the corresponding protocols (EDACS-ADP and HEART pathway, Tables e1 and e2). One key difference was that a history of coronary artery disease was not considered an independent non-low risk criterion for the HEART score component of RISTRA-ACS, in contrast to the HEART pathway.[35]

Serum troponin measurements were then imported from the electronic health record and further troponin testing in 2 hours intervals[41] was recommended unless one of two criteria was met: 1) serial troponin values were unchanged or decreasing over a minimum 2 hour interval, with the last troponin

being measured at least 4.5 hours from pain onset, or 2) a troponin value below the level of quantitation (LOQ) was obtained at least 3 hours (if both EDACS and HEART indicated low risk) or 4.5 hours (all others) from pain onset. The 4.5-hour cut-off represents the midpoint of the guideline recommended 3 to 6-hour window from pain onset for troponin testing, while a 3-hour cut-off was reserved for those at very low risk.[4] Both cut-offs were further justified based on a plateau in diagnostic performance of fourth generation troponin assays within 2 to 4 hours from chest pain onset.[42]

Data S2. Supplemental Methods: Retrospective determination of risk score variables

Text extraction and processing from unstructured clinical notes

To obtain data needed for the present illness aspects of each risk score, we developed several algorithms based on text string searches using parsed segments of the unstructured clinical notes written during the ED encounter, refined through an iterative process, to categorize key elements of the presenting symptoms as either "present", "absent" or "missing data". Specifically, we developed algorithms to identify six categorical symptoms (pain or dyspnea with exertion; diaphoresis; radiation of pain to the arm, neck, shoulder, or jaw; pain worse with inspiration; pain reproduced by palpation, sharp or stabbing pain). Text string searches were also used to supplement categorization of smoking status and family history of premature coronary artery disease if missing from the social and family history fields of the EHR. Lastly, we applied text string searches to categorize the final written electrocardiogram (ECG) interpretations based on the risk score criteria (i.e. ischemic, nonspecific, normal).

As an example, for identification of diaphoresis, we extracted text strings, parsed by word groups, sentence breaks or paragraph break punctuations encompassing a keyword. For diaphoresis, we used the keywords "diapho", "sweat" or "clammy". Specific positive or negative indicators were tailored to the specific symptom category, with corresponding hierarchical categorization schemes, following iterative text string and electronic chart review process by the study investigators. In general, "present" text indicators included: has, have, had, with, worse, y, +. Similarly, "absent" text indicators included: absent, nowhere, non, not, none, w/o, without, negative, denies, never, or, -, lack, normal. In addition, the first word of a sentence string was taken into account to categorize lists of symptoms that were present or absent (e.g. "Associated" being an indicator of symptom presence, while "Denie" or "No" being indicators of symptom absence).

General rules:

Negative indicators

no |(no)|absent|nowhere|non|not|none|w\/\o|without|chronic|negative|denie|never| or | -|lack|normal|(-)| appears among 4 words prior to the keyword OR
|no|(no)|absent|nowhere|none|negative|never| or | n |(-)| appears among 4 words after the keyword OR |non(keyword)|, |non-(keyword)| present OR

Text fragment starting with |no|not|denie| or text fragment with |no and or| or text fragment with |negative for|, except if |but| in the fragment

Positive indicators (only if no negative indicators found) and:

|Has |have |had |with |worse| y |+ | appears in the text fragment, or text fragment beginning with |associated| (except for radiation) OR
with |positive for| in text fragment or |+| immediately before or after the keyword

<u>Condition specific criteria for text string searches (in addition to the overall positive words):</u>

Diaphoresis

Keywords = “diapho”, “sweat”, “clammy”
Positive if no negative criteria and |diaphoretic|diaphoresis|sweating|clammy|

Nausea or vomiting
Keywords = “nausea” or “vomit” or “nauseous”
Exclude if “needed” or “PRN” appears among 4 words prior to the keyword or if keyword in all CAPS
Positive if any positive crtieria, otherwise classify as negative

Pain with inspiration

Keywords = “pleurit”, “inspir”, “respirop” or “deep bre”

Positive if no negative and |pleuritic|exacerbate|reproduce| in 4 words before or after keyword

Pain with palpation

Keywords = “palpate”, “chest wall tenderness”
Positive only if |chest|reproduc|worse|tender| within 4 words of “palpate”
Negative if |nontender| within 4 words before or after keyword
Exclude phrases with |abd|abdomen|lumbar|back

Sharp or stabbing pain

Keywords “sharp”, “stabbing”, excluding “sharps”

Radiation of pain to the arm, neck, shoulder, or jaw

Positive if combination of keyword "radia" and either |neck|arm|shoulder|jaw|elbow|ear|head|face| within 4 words of keyword
Positive if no negative criteria met and combination of keyword “pain” and
|arm|shoulder|jaw|elbow|ear|head|face|
Exclude if “radiation concern”, “risk of radiation” or text fragment begins with “return”

Pain or dyspnea with exertion

Keywords “exert”, “activity” or “DOE”
Exclude if “motor activity”

Smoking status

Positive if presence of keywords “smoker” or “smoking” and no information on smoking status available in EHR social history fields (otherwise social history overrides text)

Family history of premature coronary artery disease

Keywords “FH”, “FamHx” or “family history” AND |MI|CAD| if no positive family history found in EHR family history fields (otherwise family history overrides text)

Electrocardiograph (ECG) interpretation text

2 point for HEART risk score, or automatic non-low risk criteria if text contains “Ischemia”; “depression”; “acute”; “injury”
1 point for HEART or EDACS risk score if any of the following: QRS 120 or greater, “left bundle”; “right bundle”,; “pace...”; “hypertrophy”; “LVH”; “repol...”; “digoxin”; “hypertrophy”; “non-specific”; “nonspecific”; “infarct”; “Q-waves”
0 points if none of the above

Data S3. Supplemental Methods: International Classification of Disease, 10th edition (ICD-10) and Current Procedural Terminology (CPT) codes for major adverse cardiac event (MACE) and coronary revascularization outcomes.

MACE outcome	ICD-10 code
Acute myocardial infarction	I21.0x, I21.1x, I21.2x, I21.3x, I21.4x, I21.9
Cardiac arrest	I49.0x, I46.x
Cardiogenic shock	R57.0, R57.9

Coronary revascularization outcome	ICD-10 procedure coding system	CPT code
Percutaneous coronary intervention*	0270xx, 0271xx, 2072xx, 0273xx	92920-92934, 92937, 92938, 92941, 92943, 92944, 92973
Coronary artery bypass grafting	0210xx	33510-33516, 33533-33536

* CPT codes from AHRQ QI™ ICD-10-CM/PCS Specification version 2018

Table S1. The Emergency Department Assessment of Chest pain Score (EDACS)

- Age in years
  - 18-45 (add 2 points)
  - 46-50 (add 4 points)
  - 51-55 (add 6 points)
  - 56-60 (add 8 points)
  - 61-65 (add 10 points)
  - 66-70 (add 12 points)
  - 71-75 (add 14 points)
  - 76-80 (add 16 points)
  - 81-85 (add 18 points)
  - 86+ (add 20 points)
- Known coronary artery disease (previous myocardial infarction, coronary bypass surgery or percutaneous coronary intervention) OR ≥ 3 cardiac risk factors (hypertension, hyperlipidemia, diabetes, smoking in past 90 days, or family history of premature coronary artery disease in 1st degree relative age under 55 years) in patients aged 18-50 years old (add 4 points)
- Male sex (add 6 points)
- Typical symptoms
  - Diaphoresis (add 3 points)
  - Pain radiating to arm, shoulder, neck or jaw (add 5 points)
- Atypical symptoms
  - Pain with inspiration (subtract 4 points)
  - Pain reproduced by palpation (subtract 6 points)

For EDACS accelerated diagnostic protocol (EDACS-ADP) classification, patients with any of the following were considered non-low risk: 1) EDACS score ≥ 16, 2) new ischemic electrocardiogram, 3) positive troponin (> 99th percentile) or 4) presence of crescendo angina (pain which is recurrent and worsening, lasts at least 5-10 minutes, and occurs at rest or with minimal exertion

Table S2 - The History, Electrocardiogram, Age, Risk factors and Troponin (HEART) score

- History (standardized as the net number of higher-risk minus lower-risk symptoms)*
  - ≥ 2 net symptoms (highly suspicious, 2 points)
  - 0-1 net symptoms (moderately suspicious, 1 point)
  - < 0 net symptoms (slightly suspicious, 0 points)
- Electrocardiogram findings (E)
  - New ischemic changes (ST-segment depressions ≥ 0.05 mV in 2 contiguous leads or T-wave inversions ≥ 1 mV; 2 points)
  - Repolarization abnormalities, bundle branch blocks, paced rhythms, non-specific T wave or ST-changes, or evidence of prior infarction (1 point)
  - Normal (0 points)
- Age
  - ≥ 65 (2 points)
  - 45-64 (1 point)
  - < 45 (0 points)
- Risk Factors (hypercholesterolemia, hypertension, diabetes, smoking in past 90 days, premature family history of premature coronary artery disease in 1st degree relative aged < 55 years, body mass index $\underline{\geq}$ 30)
  - 3 risk factors OR known atherosclerotic disease (coronary revascularization, stroke, myocardial infarction, peripheral artery disease; 2 points)
  - 1-2 risk factors (1 point)
  - 0 risk factors (0 points)
- Troponin
  - Less than or equal to the normal limit (0 points)
  - 1 to 3 times the normal limit (1 point)
  - > 3 times the normal limit (2 points)

For HEART risk classification, patients with any of the following were considered non-low risk: 1) HEART score ≥ 4, 2) new ischemic electrocardiogram or 3) positive troponin (> 99th percentile).

** Higher-risk symptoms =* exertional chest pain or dyspnea; pain radiating to arm, shoulder, neck or jaw; diaphoresis; nausea or vomiting*; Lower-risk symptoms =* pain worse with inspiration; pain reproduced by palpation; sharp or stabbing pain

Table S3. Sensitivity analysis: Excluding patients with index encounter diagnosis of major adverse cardiac event (MACE).

		Unadjusted DID (95% CI)	p-value	Adjusted DID (95% CI)	p-value
Low risk subgroups	Index visit resource utilization*	-1.9% (-3.1 to -0.6)	0.003	-1.1% (-2.4 to +0.2)	0.092
	30-day objective cardiac testing	-3.7% (-5.0 to -2.6)	<0.001	-2.5% (-3.8 to -1.2)	**<0.001**
	60-day MACE	-0.3% (-0.5 to +0.0)	0.051	-0.3% (-0.6 to 0.0)	0.061
	60-day MACE-CR	-0.2% (-0.4 to +0.1)	0.16	-0.2% (-0.4 to +0.1)	0.17
Non-low risk subgroups	Index visit resource utilization*	+1.1% (-1.4 to +3.6)	0.39	+1.5% (-1.0 to +4.0)	0.24
	30-day objective cardiac testing	+2.3% (-0.1 to +4.8)	0.064	+2.5% (0.0 to +5.0)	**0.05**
	60-day MACE	0.0% (-1.5 to +1.4)	0.98	+0.1% (-1.3 to +1.5)	0.92
	60-day MACE-CR	-0.2% (-1.5 to +1.1)	0.78	-0.2% (-1.4 to +1.1)	0.81
Overall	Index visit resource utilization*	-0.9% (-2.0 to +0.2)	0.13	-0.4% (-1.6 to +0.7)	0.47
	30-day objective cardiac testing	-2.4% (-3.5 to -1.4)	<0.001	-1.3% (-2.5 to -0.2)	**0.026**
	60-day MACE	-0.1% (-0.5 to +0.3)	0.51	-0.2% (-0.6 to +0.2)	0.27
	60-day MACE-CR	-0.1% (-0.4 to +0.3)	0.71	-0.2% (-0.5 to +0.1)	0.31

Difference-in-differences represent the difference between the 12-month post-implementation period (January 1, 2019 to December 31, 2019) and the 24-month pre-implementation period (January 1, 2016 and December 31, 2017) at RISTRA compared to control sites.

Abbreviations: DID = difference-in-differences; MACE = major adverse cardiac event; MACE-CR = MACE excluding coronary revascularization

Table S4. Sensitivity analysis: Excluding patients seen by emergency medicine physicians in the lowest quartile of chest pain encounters.

		Unadjusted DID (95% CI)	p-value	Adjusted DID (95% CI)	p-value
Low risk subgroups	Index visit resource utilization*	-2.4% (-3.6 to -1.1)	<0.001	-1.0% (-2.3 to +0.3)	0.12
	30-day objective cardiac testing	-4.2% (-5.5 to -2.9)	<0.001	-2.4% (-3.7 to -1.0)	**<0.001**
	60-day MACE	-0.3% (-0.7 to 0.0)	0.048	-0.3% (-0.7 to 0.0)	0.064
	60-day MACE-CR	-0.2% (-0.4 to +0.1)	0.20	-0.2% (-0.4 to +0.1)	0.23
Non-low risk subgroups	Index visit resource utilization*	+1.4% (-0.9 to +3.6)	0.23	+1.4% (-0.7 to +3.5)	0.20
	30-day objective cardiac testing	+2.9% (+0.5 to +5.2)	0.018	+2.4% (+0.1 to +4.7)	**0.041**
	60-day MACE	+1.3% (-0.8 to +3.4)	0.22	+0.5% (-1.3 to +2.2)	0.61
	60-day MACE-CR	+1.1% (-0.9 to +3.2)	0.28	+0.2% (-1.5 to +1.8)	0.84
Overall	Index visit resource utilization*	-0.8% (-1.9 to +0.4)	0.20	-0.2% (-1.4 to +0.9)	0.69
	30-day objective cardiac testing	-2.2% (-3.3 to -1.1)	<0.001	-1.0% (-2.1 to +0.2)	0.10
	60-day MACE	+0.5% (-0.1 to +1.1)	0.097	-0.2% (-0.6 to +0.3)	0.54
	60-day MACE-CR	+0.6% (0.0 to +1.2)	0.046	-0.1% (-0.6 to +0.3)	0.60

Difference-in-differences represent the difference between the 12-month post-implementation period (January 1, 2019 to December 31, 2019) and the 24-month pre-implementation period (January 1, 2016 and December 31, 2017) at RISTRA compared to control sites.

Abbreviations: DID = difference-in-differences; MACE = major adverse cardiac event; MACE-CR = MACE excluding coronary revascularization

Table S5. Sensitivity analysis: Excluding RISTRA sites with below median use of RISTRA-ACS. Median facility-level use of RISTRA-ACS among study patients was 17% (range 8 to 24%).

		Unadjusted DID (95% CI)	p-value	Adjusted DID (95% CI)	p-value
Low risk subgroups	Index visit resource utilization*	-2.2% (-3.6 to -0.7)	0.003	-1.5% (-3.0 to 0.0)	**0.047**
	30-day objective cardiac testing	-3.8% (-5.2 to -2.3)	<0.001	-2.4% (-3.9 to -0.9)	**0.002**
	60-day MACE	-0.4% (-0.8 to 0.0)	0.036	-0.4% (-0.8 to 0.0)	**0.033**
	60-day MACE-CR	-0.3% (-0.6 to 0.0)	0.041	-0.3% (-0.6 to 0.0)	**0.042**
Non-low risk subgroups	Index visit resource utilization*	+2.2% (-0.3 to +4.7)	0.09	+1.9% (-0.4 to +4.3)	0.11
	30-day objective cardiac testing	+4.1% (+1.4 to +6.8)	0.003	+3.5% (+0.9 to +6.0)	**0.008**
	60-day MACE	+1.7% (-0.7 to +4.1)	0.16	+0.8% (-1.1 to +2.8)	0.40
	60-day MACE-CR	+1.5% (-0.8 to +3.8)	0.21	+0.5% (-1.4 to +2.4)	0.58
Overall	Index visit resource utilization*	-0.6% (-1.9 to +0.7)	0.33	-0.5% (-1.8 to +0.8)	0.45
	30-day objective cardiac testing	-1.6% (-2.9 to -0.3)	0.013	-0.7% (-2.0 to +0.6)	0.27
	60-day MACE	+0.3% (-0.4 to +1.0)	0.39	-0.1% (-0.7 to +0.4)	0.66
	60-day MACE-CR	+0.3% (-0.3 to +1.0)	0.33	-0.1% (-0.7 to +0.4)	0.58

Difference-in-differences represent the difference between the 12-month post-implementation period (January 1, 2019 to December 31, 2019) and the 24-month pre-implementation period (January 1, 2016 and December 31, 2017) at RISTRA compared to control sites.

Abbreviations: DID = difference-in-differences; MACE = major adverse cardiac event; MACE-CR = MACE excluding coronary revascularization

Table S6. Sensitivity analysis: Using a truncated 6-month run-in period and an extended 18-month post-implementation period.

		Unadjusted DID (95% CI)	p-value	Adjusted DID (95% CI)	p-value
Low risk subgroups	Index visit resource utilization*	-1.1% (-2.2 to 0.0)	0.058	-0.3% (-1.4 to +0.8)	0.61
	30-day objective cardiac testing	-2.8% (-3.9 to -1.7)	<0.001	-1.7% (-2.9 to -0.6)	**0.003**
	60-day MACE	-0.3% (-0.6 to 0.0)	0.053	-0.3% (-0.6 to 0.0)	0.058
	60-day MACE-CR	-0.2% (-0.4 to 0.0)	0.13	-0.2% (-0.4 to +0.1)	0.14
Non-low risk subgroups	Index visit resource utilization*	+1.8% (-0.2 to +3.7)	0.073	+1.7% (-0.2 to +3.5)	0.077
	30-day objective cardiac testing	+3.7% (+1.6 to +5.8)	<0.001	+3.2% (+1.2 to +5.2)	**0.002**
	60-day MACE	+0.8% (-1.0 to +2.7)	0.36	+0.2% (-1.3 to +1.7)	0.78
	60-day MACE-CR	+0.6% (-1.2 to +2.4)	0.49	-0.1% (-1.5 to +1.4)	0.91
Overall	Index visit resource utilization*	+0.2% (-0.8 to +1.2)	0.65	+0.3% (-0.6 to +1.3)	0.50
	30-day objective cardiac testing	-1.0% (-2.0 to 0.0)	0.047	-0.4% (-1.4 to +0.6)	0.48
	60-day MACE	+0.4% (-0.1 to +0.9)	0.15	-0.2% (-0.6 to +0.3)	0.44
	60-day MACE-CR	+0.4% (-0.1 to +0.9)	0.11	-0.2% (-0.6 to +0.2)	0.39

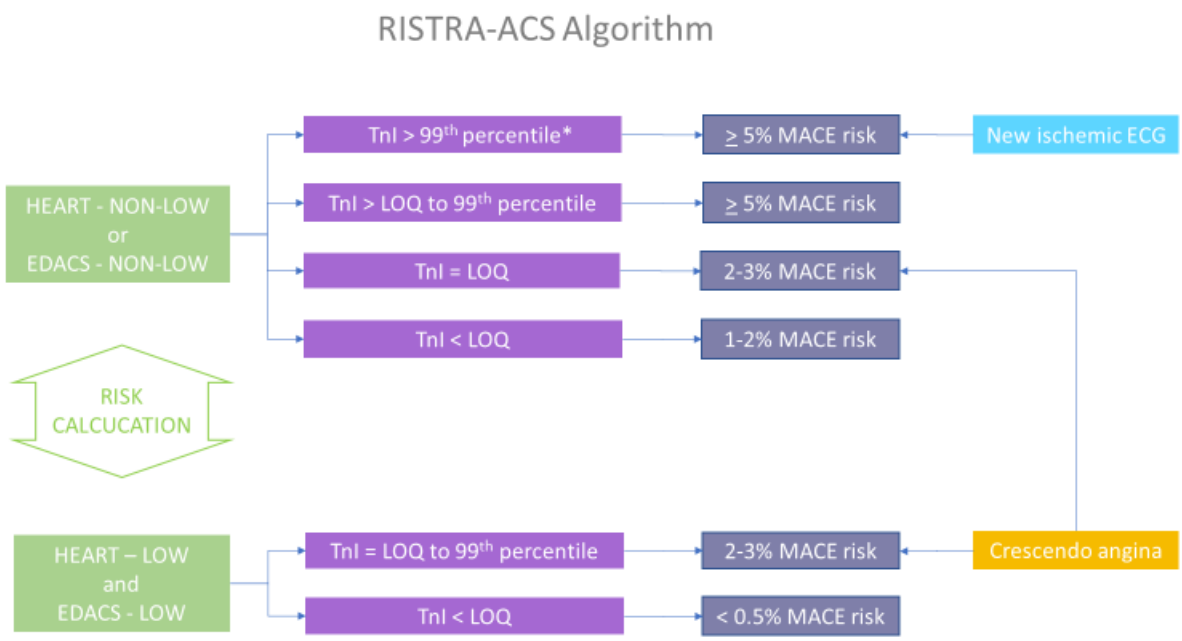
Difference-in-differences represent the difference between an 18-month post-implementation period (July 1, 2018 to December 31, 2019) and the 24-month pre-implementation period (January 1, 2016 and December 31, 2017) at RISTRA compared to control sites.

Abbreviations: DID = difference-in-differences; MACE = major adverse cardiac event; MACE-CR = MACE excluding coronary revascularization

Table S7. Sensitivity analysis: Modeling the primary difference-in-differences analysis using fixed effects in place of random effects

		Unadjusted DID (95% CI)	p-value	Adjusted DID (95% CI)	p-value
Low risk subgroups	Index visit resource utilization*	-1.9% (-3.1 to -0.7)	0.003	-0.8% (-2.0 to +0.4)	0.17
	30-day objective cardiac testing	-3.8% (-5.0 to -2.6)	<0.001	-2.7% (-3.9 to -1.5)	<0.001
	60-day MACE	-0.3% (-0.7 to 0.0)	0.041	-0.3% (-0.6 to 0.0)	0.061
	60-day MACE-CR	-0.2% (-0.4 to +0.1)	0.13	-0.2% (-0.5 to +0.0)	0.085
Non-low risk subgroups	Index visit resource utilization*	+1.7% (-0.5 to +3.8)	0.13	+1.8% (-0.2 to +3.8)	0.08
	30-day objective cardiac testing	+3.4% (+1.1 to +5.7)	0.004	+2.8% (+0.7 to +5.0)	0.01
	60-day MACE	+1.2% (-0.8 to +3.2)	0.24	+0.4% (-1.2 to +2.1)	0.60
	60-day MACE-CR	+1.1% (-0.9 to +3.0)	0.29	+0.1% (-1.5 to +1.7)	0.87
Overall	Index visit resource utilization*	-0.3% (-1.4 to +0.8)	0.56	0.0% (-1.1 to +1.0)	0.96
	30-day objective cardiac testing	-1.8% (-2.8 to -0.7)	0.001	-1.2% (-2.2 to -0.1)	0.031
	60-day MACE	+0.5% (-0.1 to +1.1)	0.12	-0.2% (-0.6 to +0.3)	0.51
	60-day MACE-CR	+0.5% (0.0 to +1.1)	0.062	-0.2% (-0.6 to +0.3)	0.45

Figure S1. RISTRA-ACS Algorithm. Estimated 60-day major adverse cardiac event (MACE) risk prediction based on risk scores and peak troponin value.

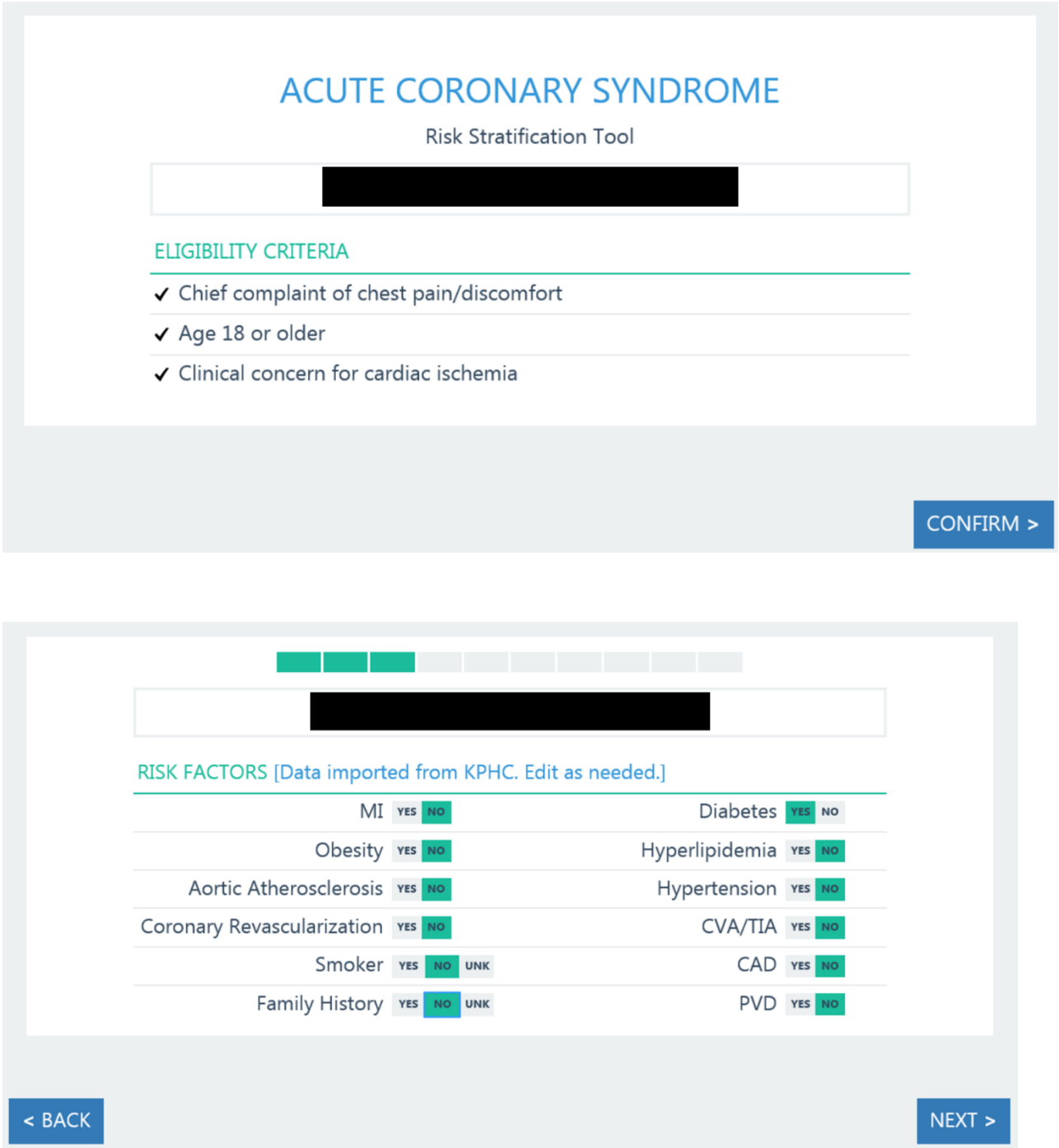


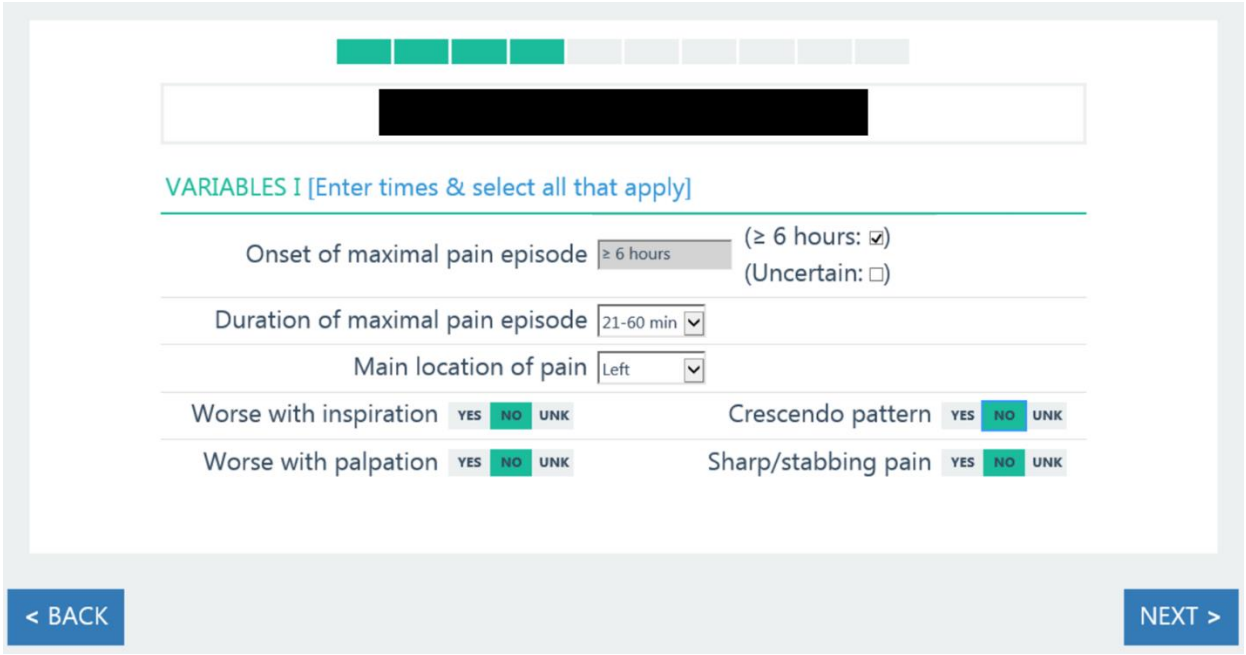
Troponin measurement timing guidance was provided within the electronic clinical decision support (see supplemental methods 2). Note that for retrospective risk determination, only the peak troponin value within 6 hours of ED arrival was used and crescendo angina was not captured.

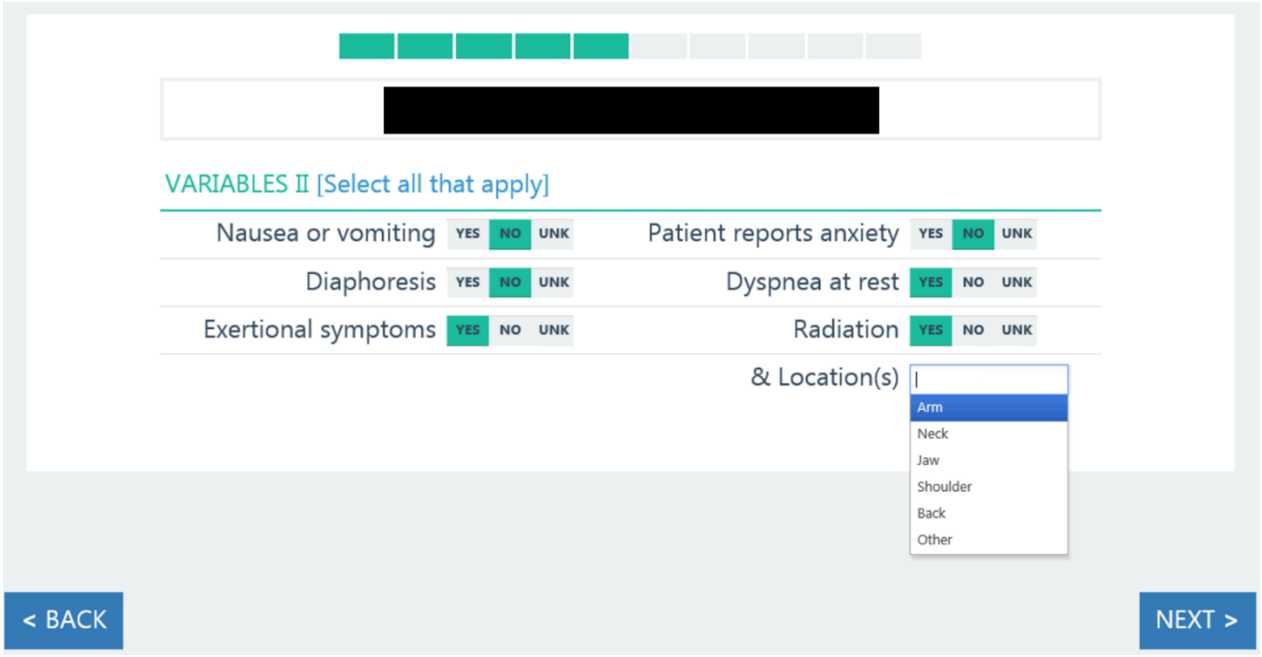
* Troponin (TnI) above the 99th percentile was considered an automatic non-low risk criterion for both HEART and EDACS characterizations.

Abbreviations: ECG = electrocardiogram; HEART = History, Electrocardiogram, Age, Risk factors and Troponin score; EDACS = Emergency Department Assessment of Chest pain Score; LOQ = level of quantification; MACE = major adverse cardiac event at 60-days; TnI = serum troponin I.

Figure S2. Sample screenshots of the RISTRA-ACS electronic clinical decision support interface




[redacted]
VARIABLES I [Enter times & select all that apply]
Onset of maximal pain episode
≥ 6 hours
(≥ 6 hours: ☑)
(Uncertain: ☐)
Duration of maximal pain episode
21-60 min
Main location of pain
Left
Worse with inspiration YES NO UNK
Crescendo pattern YES NO UNK
Worse with palpation YES NO UNK
Sharp/stabbing pain YES NO UNK
< BACK
NEXT >


[redacted]
VARIABLES II [Select all that apply]
Nausea or vomiting YES NO UNK
Patient reports anxiety YES NO UNK
Diaphoresis YES NO UNK
Dyspnea at rest YES NO UNK
Exertional symptoms YES NO UNK
Radiation YES NO UNK
& Location(s)
Arm
Neck
Jaw
Shoulder
Back
Other
< BACK
NEXT >

[redacted]

PAST EKGs	1st	2nd	3rd
	11/21/2019	-	-

TODAY'S EKGs	1st	2nd	3rd
Use the most abnormal	09:16	11:44	-

Normal ○ Abnl/nondiagnostic ○ New ischemic change ○

TROPONIN	1st	2nd	3rd
Time from symptom onset:	6h: 23m	-	-
Value:	<0.02	-	-

< BACK REFRESH NEXT >

[redacted]

ESTIMATED RISK EDACS: LOW HEART: LOW

Risk of a Major Adverse Cardiac Event in the next 60 days
(based on internal validation study of 118,822 KPNC patients):

<0.5%

RECOMMENDATION

Primary Care follow-up
(Stress testing is unlikely to benefit this patient)

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