Supplemental Online Content

Kawatkar AA, Sharp AL, Baecker A, Natsui S, Redberg RF, Lee M-S, Ferencik M, et al. Early Noninvasive Cardiac Testing After Emergency Department Evaluation for Suspected Acute Coronary Syndrome. *JAMA Intern Med*. Published online October 5, 2020. doi:10.1001/jamainternmed.2020.4325

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eTable 1. Logistic Regression of First Stage IV Model Predicting Early NIT

	Odds Ratio	Lower 95% CI	Upper 95% CI
Medical Center Practice Pattern	**1·06**	**1·06**	**1·07**
Day of the Week IV			
Weekday	Reference		
Weekend	**0·82**	**0·78**	**0·88**
Age Categories			
18-49	Reference		
50-69	**3·0**	**2·84**	**3·16**
70 and Above	**3·34**	**3·12**	**3·56**
Sex Female	Reference		
Male	**1·19**	**1·15**	**1·24**
Race Categories			
White	Reference		
Black	**0·90**	**0·85**	**0·95**
Asian	**1·66**	**1·0003**	**1·13**
All Other Race	0·96	0·91	1·005
Smoking Status			
Never Smoked	Reference		
Quit Smoking	0·98	0·94	1·02
Active/Passive Smoker	1·02	0·95	1·10
Body Mass Index (BMI)			
Normal BMI	Reference		
Under Weight	**0·76**	**0·62**	**0·93**
Overweight	**1·15**	**1·10**	**1·20**
Obese	**1·30**	**1·23**	**1·36**
Elevated Troponin (0·04-0·5)	**1·37**	**1·25**	**1·50**
Coronary Artery Disease (CAD)	**0·84**	**0·80**	**0·89**
Stroke	0·93	0·83	1·05
Percutaneous transluminal coronary angioplasty (PTCA) or Coronary artery bypass graft (CABG) in prior year	**0·64**	**0·53**	**0·77**
Family history of CAD	**1·13**	**1·08**	**1·17**

Family history of Stroke	0·98	0·93	1·03
Antidiabetic medications in past 90 days	**1·24**	**1·17**	**1·31**
Anticoagulant medications in past 90 days	**0·89**	**0·84**	**0·95**
Anti-hyperlipidemic medications in past 90 days	**1·13**	**1·08**	**1·18**
Anti- hypertension medications in past 90 days	**1·17**	**1·12**	**1·23**
Elixhauser Comorbidity Index	**0·93**	**0·92**	**0·94**

Bold Font Indicates Statistically Significant Estimates
Logit model estimates are only presented for ease of interpretability of the odds ratio. Actual estimation used a probit model specification instead of logit model.

eTable 2. Overall Diagnostic Test for the IV Model Assumptions

Model Assumption	Diagnostic test type	**Death/Acute MI** Test statistic (*P value*) or Stock-Yogo (2005) Critical Value*	**Death** Test statistic (*P value*) or Stock-Yogo (2005) Critical Value*	**Acute MI** Test statistic (*P value*) or Stock-Yogo (2005) Critical Value*	**Coronary Revascularization** Test statistic (*P value*) or Stock-Yogo (2005) Critical Value*	**MACE** Test statistic (*P value*) or Stock-Yogo (2005) Critical Value*
Instrument Strength	First Stage F	1531 (p<0·0001)	1531 (p<0·0001)	1531 (p<0·0001)	1531 (p<0·0001)	1531 (p<0·0001)
Weak Instrument	Cragg-Donald Wald F statistic	1475 (8·7)*	1475 (8·7)*	1475 (8·7)*	1475 (8·7)*	1475 (8·7)*
Rank Test/Under-identification test	Kleibergen-Paap rk LM statistic	2816 (p<0·0001)	2816 (p<0·0001)	2816 (p<0·0001)	2816 (p<0·0001)	2816 (p<0·0001)
Overidentification	Sargan–Hansen test *J*-statistic	0·902 (p=0·34)	0·144 (p=0·70)	0·42 (p= 0·52)	0.05 (p=0.82)	0·76 (p=0·38)
Instrument redundancy	LM test of redundancy	2747 (p<0·0001)	2747 (p<0·0001)	2747 (p<0·0001)	2747 (p<0·0001)	2747 (p<0·0001)
Testing is based on linear additive specification. Actual estimation used a probit model for the treatment choice (early NIT vs not) as well as probit model for the binary outcomes associated with death, acute myocardial infarction, coronary revascularization and major adverse cardiovascular events						

The order condition for identification of an IV model is a necessary condition and generally easy to check. The order condition however is not a sufficient condition. To ensure that the necessary and sufficient rank condition was satisfied, we checked the Kleibergen–Paap Lagrange multiplier (LM) statistic.[1,2] The precision of IVs parameters is generally lower and in the presence of weak instruments, the loss of precision will be severe.[2,3] The problem with weak instruments arises when the strength of the correlation between the endogenous regressors and the excluded instruments is statistically significant but small in magnitude.[4,5] We evaluated the validity of our IV approach to the weak instruments problem on the basis of the individual first-stage F-statistic and also the Angrist–Pischke first-stage F-statistic.[6]

To check if the excluded instruments are uncorrelated to the error we performed overidentification test. This orthogonality condition is generally not confirmed statistically. However, in the overidentified case, if we maintain the hypothesis that the model is identified, a rejection of the hypothesis implies rejecting the orthogonality conditions. Given these assumptions, an overidentification test was performed for all excluded instruments on the basis of the Hansen J-statistic to ensure that the excluded instruments are uncorrelated to the error.[2,3,7-9] Lastly, because our model was overidentified, it is important to ensure that the excluded instruments are not redundant and that each adds to the efficiency of the estimator. On the basis of the LM test, we checked the redundancy of the IV medical center practice pattern conditional on the weekend IV as the excluded instrument.[10-12] Most of the test statistics were made robust to arbitrary heteroskedasticity.[13]

The IV specification testing presented in supplemental table 2 indicated that the two excluded instruments: 1. Medical Center Practice Pattern and 2. Day of the Week were a) strongly correlated to the treatment (i.e. NIT within 3 days); b) were not weak instruments; c) satisfy the order as well as rank condition; d) were not redundant and lastly were orthogonal to the outcome error and appropriately excluded from the outcome model since they only acted through the exposure of early NIT. The IV models satisfied all assumption necessary for consistent estimate of the parameters.

The average treatment effect parameter identified by our IV models maybe sensitive to our covariate or functional form specification.[6] Additionally, it could be the case that medical centers with higher NIT preference may have increased adoption of other ACC/AHA guidelines and/or protocols that may improve outcomes. To mitigate these concerns, we estimated the local average treatment effect (LATE) as the ratio of the expected death/MI risk reduction to the probit model estimate of day of the week IV.[6] This LATE estimate was a 3.7% reduction in risk of the primary outcome. Though LATE is based on weaker assumption compared to the IV models, it only applies to compliers i.e. those patients who are influenced to undertake treatment only by change in value of the IV and not otherwise.[14] Some non-compliers could be unusually sick and/or maybe persistent in obtaining NIT even on weekends or at medical centers with low preferences due to being unusually organized and aware. Non-compliers also include a portion that could really benefit from NIT and are strongly advised to have these tests performed, yet they leave without testing, against medical advice. LATE filters out some of these non-compliers and hence it's estimate is higher compared to the estimated average treatment effect.

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