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# A Tutorial and Case Study in Propensity Score Analysis: An Application to Estimating the Effect of In-Hospital Smoking Cessation Counseling on Mortality

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Propensity score methods allow investigators to estimate causal treatment effects using observational or nonrandomized data. In this article we provide a practical illustration of the appropriate steps in conducting propensity score analyses. For illustrative purposes, we use a sample of current smokers who were discharged alive after being hospitalized with a diagnosis of acute myocardial infarction. The exposure of interest was receipt of smoking cessation counseling prior to hospital discharge and the outcome was mortality with 3 years of hospital discharge. We illustrate the following concepts: first, how to specify the propensity score model; second, how to match treated and untreated participants on the propensity score; third, how to compare the similarity of baseline characteristics between treated and untreated participants after stratifying on the propensity score, in a sample matched on the propensity score, or in a sample weighted by the inverse probability of treatment; fourth, how to estimate the effect of treatment on outcomes when using propensity score matching, stratification on the propensity score, inverse probability of treatment weighting using the propensity score, or covariate adjustment using the propensity score. Finally, we compare the results of the propensity score analyses with those obtained using conventional regression adjustment.

Propensity score methods allow one to minimize the effects of observed confounding when estimating treatment effects using observational data. An article

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to appear in a special issue on propensity score analysis to be published in *Multivariate Behavioral Research* describes a framework for using propensity scores to estimate causal treatment effects using observational or nonrandomized data (Austin, in press-a). In the review paper, the different methods of using propensity scores to estimate treatment effects are highlighted along with a description of the steps in conducting a propensity score analysis. The objective of the current article is to illustrate the methods described in the overview article using a single data source.

In this article, a propensity score analysis was conducted using four different propensity score methods to estimate the effect of in-patient smoking cessation counseling on mortality in patients hospitalized with a heart attack. The results from the propensity score analyses are compared with those obtained using conventional regression adjustment.

## METHODS

### Data Source

The data consisted of patients hospitalized with acute myocardial infarction (AMI or heart attack) at 103 acute care hospitals in Ontario, Canada, between April 1, 1999, and March 31, 2001. Data on patient history, cardiac risk factors, comorbid conditions and vascular history, vital signs, and laboratory tests were obtained by retrospective chart review by trained cardiovascular research nurses. These data were collected as part of the Enhanced Feedback For Effective Cardiac Treatment (EFFECT) study, an ongoing initiative intended to improve the quality of care for patients with cardiovascular disease in Ontario (Tu et al., 2004; Tu et al., 2009).

The sample was restricted to those patients who survived to hospital discharge and who had documented evidence of being current smokers. For the purposes of the current case study, the treatment or exposure of interest was whether the patient received in-patient smoking cessation counseling. Smokers whose counseling status could not be determined from the medical record were excluded from the current study. Patients with missing data on important baseline clinical covariates were excluded from the sample. Patient records were linked to the Registered Persons Database using encrypted health card numbers, which allowed for determining the vital status of each patient at 3 years following hospital discharge. For the current study, the outcome was survival to 3 years, considered as both a dichotomous and a time-to-event outcome.

### Baseline Comparisons of Treatment Groups

In the overall sample, continuous variables and categorical variables were com-

pared between treatment groups using the standard  $t$  test and chi-square test, respectively. Standardized differences were also used to compare baseline characteristics between the two groups (Austin, 2009a; Flury & Riedwyl, 1986). Furthermore, basic baseline demographic characteristics and the probability of death within 3 years of discharge were compared between participants with complete data on baseline covariates and participants who were excluded from the study sample due to missing data on baseline covariates.

### Estimating the Propensity Score

An initial propensity score model was estimated using the 33 variables described in Table 1. To estimate the propensity score, a logistic regression model was used in which treatment status (receipt of smoking cessation counseling vs. no smoking cessation counseling) was regressed on the baseline characteristics listed in Table 1 (Rosenbaum & Rubin, 1984). The continuous baseline variables were linearly related to the log-odds of receipt of treatment in the initial specification of the propensity score model. Prior research on variable selection for the propensity score suggests that it is preferable to either include those variables that affect the outcome or include those variables that affect both treatment selection and the outcome (Austin, Grootendorst, & Anderson, 2007). The variables listed in Table 1 are plausible predictors of mortality in AMI patients. Because we want to induce balance on variables that are prognostic of mortality, we included these variables in our initial propensity score model.

### Matching on the Propensity Score

Treated and untreated participants were matched on the propensity score. In the data set, there were more treated participants (patients receiving smoking cessation counseling) than there were untreated participants (patients not receiving smoking cessation counseling). For technical reasons when matching, a pool of controls that is at least as large as the number of treated participants was required. Thus, in the context of propensity score matching, we attempted to match a treated participant to each participant who did not receive smoking cessation counseling. Thus, participants who received counseling were used as a pool or reservoir from which to find appropriate participants to match to those participants who did not receive counseling. Because propensity score matching allows one to estimate the average treatment effect for the treated (ATT), this implies that we are estimating the effect of smoking cessation counseling (or the lack thereof) in those patients who ultimately did not receive such therapy (Imbens, 2004).

For reasons described in the forthcoming review, participants were matched on the logit of the propensity score (Rosenbaum & Rubin, 1985) using calipers

TABLE 1  
Baseline Characteristics of the Study Sample

<i>Variable</i>	<i>No Smoking Cessation Counseling (N = 754)</i>	<i>Smoking Cessation Counseling (N = 1,588)</i>	<i>Overall Sample (N = 2,342)</i>	<i>Standardized Difference of the Mean</i>	<i>p Value</i>
Demographic Characteristics					
Age	60.48 ± 13.26	56.24 ± 11.26	57.61 ± 12.10	0.35	< .001
Female	220 (29.2%)	397 (25.0%)	617 (26.3%)	0.09	.032
Presenting Signs and Symptoms					
Acute pulmonary edema	34 (4.5%)	48 (3.0%)	82 (3.5%)	0.08	.067
Vital Signs on Admission					
Systolic blood pressure	146.99 ± 31.82	146.93 ± 29.92	146.95 ± 30.53	0.00	.966
Diastolic blood pressure	84.81 ± 18.99	85.84 ± 18.51	85.50 ± 18.67	0.06	.213
Heart rate	83.28 ± 22.75	81.10 ± 22.54	81.80 ± 22.63	0.10	.029
Respiratory rate	21.18 ± 5.75	20.18 ± 4.64	20.50 ± 5.05	0.20	< .001
Classic Cardiac Risk Factors					
Diabetes	179 (23.7%)	260 (16.4%)	439 (18.7%)	0.19	< .001
Hyperlipidemia	238 (31.6%)	539 (33.9%)	777 (33.2%)	0.05	.254
Hypertension	295 (39.1%)	541 (34.1%)	836 (35.7%)	0.11	.017
Family history of coronary artery disease	253 (33.6%)	754 (47.5%)	1,007 (43.0%)	0.28	< .001
Comorbid Conditions and Vascular History					
Cerebrovascular accident/Transient ischemic attack	62 (8.2%)	67 (4.2%)	129 (5.5%)	0.18	< .001
Angina	198 (26.3%)	412 (25.9%)	610 (26.0%)	0.01	.871
Cancer	22 (2.9%)	20 (1.3%)	42 (1.8%)	0.13	.005
Dementia	21 (2.8%)	6 (0.4%)	27 (1.2%)	0.23	< .001
Previous myocardial infarction	161 (21.4%)	241 (15.2%)	402 (17.2%)	0.16	< .001
Asthma	40 (5.3%)	98 (6.2%)	138 (5.9%)	0.04	.406
Depression	76 (10.1%)	131 (8.2%)	207 (8.8%)	0.06	.145
Peptic ulcer disease	39 (5.2%)	111 (7.0%)	150 (6.4%)	0.07	.093
Peripheral vascular disease	77 (10.2%)	90 (5.7%)	167 (7.1%)	0.18	< .001
Previous coronary revascularization	50 (6.6%)	92 (5.8%)	142 (6.1%)	0.04	.427
Chronic congestive heart failure	24 (3.2%)	24 (1.5%)	48 (2.0%)	0.12	.008
Laboratory Tests					
Glucose	9.35 ± 5.63	8.57 ± 4.79	8.82 ± 5.09	0.15	< .001
White blood count	11.01 ± 4.49	10.77 ± 3.55	10.85 ± 3.88	0.06	.171
Hemoglobin	141.71 ± 19.33	145.83 ± 15.47	144.50 ± 16.92	0.24	< .001
Sodium	138.75 ± 4.54	139.40 ± 3.32	139.19 ± 3.77	0.17	< .001
Potassium	4.10 ± 0.58	4.01 ± 0.49	4.04 ± 0.52	0.16	< .001
Creatinine	99.59 ± 62.86	89.24 ± 30.24	92.57 ± 43.75	0.24	< .001
Prescriptions for Cardiovascular Medications at Hospital Discharge					
Statin	193 (25.6%)	637 (40.1%)	830 (35.4%)	0.31	< .001
Beta-blocker	460 (61.0%)	1,192 (75.1%)	1,652 (70.5%)	0.31	< .001
Angiotensin Converting Enzyme (ACE) inhibitor/Angiotensin receptor blockers	344 (45.6%)	850 (53.5%)	1,194 (51.0%)	0.16	< .001
Plavix	29 (3.8%)	74 (4.7%)	103 (4.4%)	0.04	.37
Acetylsalicylic Acid (ASA)	544 (72.1%)	1,341 (84.4%)	1,885 (80.5%)	0.31	< .001

*Note.* Continuous variables are presented as means ± standard deviation; dichotomous variables are presented as *N* (%).

of width equal to 0.2 of the standard deviation of the logit of the estimated propensity score. This caliper width has been found to result in optimal estimation of risk differences in a variety of settings (Austin, 2010a).

In those participants who did not receive smoking cessation counseling, differences in baseline covariates between matched and unmatched participants were examined using statistical significance testing and standardized differences.

### Inverse Probability of Treatment Weighting

We weighted the entire study sample by inverse probability of treatment weights derived from the propensity score. Let  $Z$  denote treatment status ( $Z = 1$  denotes treated;  $Z = 0$  denotes untreated) and let  $e$  denote the estimated propensity score. Then the inverse probability of treatment weights are defined by  $\frac{Z}{e} + \frac{1-Z}{1-e}$ .

### Stratification on the Propensity Score

Using the entire study sample, we computed the quintiles of the estimated propensity score. Participants in the overall study sample were stratified into five approximately equal-size groups using the quintiles of the estimated propensity score.

### Balance Diagnostics

As discussed in the forthcoming review article, the true propensity score is a balancing score: conditional on the true propensity score, treated and untreated participants will have the same distribution of measured baseline covariates. However, the true propensity score model is not known in observational studies (unlike randomized experiments in which the true propensity score is often defined by the study design). Thus, balance diagnostics allow one to assess whether the propensity score model has been adequately specified. Appropriate balance diagnostics are highlighted in our forthcoming review and are described in greater detail elsewhere (Austin, 2009b).

*Propensity score matched sample.* We compared the means and prevalences of continuous and dichotomous baseline covariates between treatment groups in the matched sample. The standardized difference was used to quantify differences in means or prevalences between treatment groups. Furthermore, we compared balance between treatment groups in all pairwise interactions of continuous covariates. The variance of continuous variables was compared between treatment groups in the matched sample. Finally, cumulative density plots and quantile-quantile plots were used to compare the distribution of continuous baseline covariates between treatment groups.

The reader should note that statistical significance testing was not used to compare the baseline characteristics of treated and untreated participants in the propensity score matched sample. Such practices have been criticized by different authors. Readers are referred elsewhere for a greater discussion of this practice (Austin, 2007a, 2008a, 2008b; Ho, Imai, King, & Stuart, 2007; Imai, King, & Stuart, 2008).

Diagnostics based on comparing the distribution of the propensity score between treated and untreated participants were not used. Recent research has shown that, in the context of propensity score matching, comparing the distribution of the estimated propensity score between treated and untreated participants does not provide any information as to whether the propensity score model has been adequately specified (Austin, 2009b). For similar reasons, the c statistic (equivalent to the area under the receiver operating characteristic [ROC] curve) of the propensity score model was not reported. The c statistic does not provide information as to whether the propensity score model has been adequately specified (Austin, 2009b; Weitzen, Lapane, Toledano, Hume, & Mor, 2005).

*Stratification on the propensity score.* Within each stratum of the propensity score, standardized differences were used to compare the means and prevalences of measured baseline covariates between treatment groups. Within-quintile standardized differences were computed for each of the 55 pairwise interactions between continuous variables.

*Inverse probability of treatment weighting.* In the sample weighted by the inverse probability of treatment, we computed standardized differences to compare the balance of baseline covariates between treatment groups. We also used standardized differences to compare balance on pairwise interactions between continuous baseline covariates. Empirical cumulative distribution functions and quantile-quantile plots were also used to compare the distribution of continuous baseline covariates between treatment groups in the weighted sample.

*Covariate adjustment using the propensity score.* Austin (2008c) described the weighted conditional absolute standardized difference for comparing balance in baseline covariates after adjusting for the propensity score. Briefly, a given baseline covariate is regressed on the following three variables: the propensity score, an indicator variable denoting treatment assignment, and the interaction between the first two variables. Linear regression is used for continuous covariates, whereas logistic regression is used for dichotomous covariates. From the fitted regression model, for a given value of the propensity score, the mean response is determined assuming a participant was treated and then assuming the participant was untreated. The absolute standardized difference between the mean response for treated participants and the mean response for untreated

participants is then determined. For continuous outcomes, this calculation will also use the estimate of the variance of the error term that was obtained from the linear model. This conditional (on the propensity score) absolute standardized difference is then integrated over the distribution of the propensity score in the study sample.

A second balance diagnostic involves the use of quantile regression (Austin, Tu, Daly, & Alter, 2005). For a given continuous baseline covariate, quantile regression was used to regress the given baseline covariate on the estimated propensity score in treated and untreated participants separately. The use of the 5th, 25th, 50th, 75th, and 95th percentiles has been previously suggested (Austin, 2008c). The model-based estimates of these quantiles in treated and untreated participants can then be displayed graphically.

### Estimating Treatment Effects

As noted earlier, we considered two different outcomes: survival to 3 years post-discharge (a dichotomous outcome) and time to death (a time-to-event outcome) with participants censored at 3 years following hospital discharge.

*Propensity score matching.* The difference in the probability of 3-year mortality between treatment groups was estimated by directly estimating the difference in proportions between treated and untreated participants in the propensity score matched sample. When estimating the statistical significance of treatment effects, the use of methods that account for the matched nature of the sample is recommended (Austin, 2009d, in press-b). Accordingly, McNemar's test was used to assess the statistical significance of the risk difference. Confidence intervals were constructed using a method proposed by Agresti and Min (2004) that accounts for the matched nature of the sample. The number needed to treat (NNT) is the reciprocal of the absolute risk reduction. The relative risk was estimated as the ratio of the probability of 3-year mortality in treated participants compared with that of untreated participants in the matched sample. Methods described by Agresti and Min were used to estimate 95% confidence intervals.

We then estimated the effect of provision of smoking cessation counseling on the time to death. Kaplan-Meier survival curves were estimated separately for treated and untreated participants in the propensity score matched sample. The log-rank test is not appropriate for comparing the Kaplan-Meier survival curves between treatment groups because the test assumes two independent samples (Harrington, 2005; Klein & Moeschberger, 1997). However, the stratified log-rank test is appropriate for matched pairs data (Klein & Moeschberger, 1997).

Finally, we used a Cox proportional hazards model to regress survival time on an indicator variable denoting treatment status (smoking cessation counseling



vs. no counseling). As the propensity score matched sample does not consist of independent observations, we used a marginal survival model with robust standard errors (Lin & Wei, 1989). An alternative to the use of a marginal model with robust variance estimation would be to fit a Cox proportional hazards model that stratified on the matched pairs (Cummings, McKnight, & Greenland, 2003). This approach accounts for the within-pair homogeneity by allowing the baseline hazard function to vary across matched sets.

*Stratification on the propensity score.* We estimated the probability of 3-year mortality for participants in each treatment group in each propensity score strata. The absolute reduction in the probability of 3-year mortality was then determined in each propensity score strata by the difference between the observed probability for treated participants and the observed participants for untreated participants within that stratum. The overall estimated treatment effect was the mean of the stratum-specific risk differences. The standard error of each stratum-specific risk difference can be estimated using standard methods for differences in two binomial proportions. The stratum-specific standard errors can then be pooled to obtain the standard error of the overall risk difference. We also obtained the Mantel-Haenszel estimate of the pooled relative risk across the propensity score strata (Breslow & Day, 1987).

To estimate the effect of counseling on survival, we used a Cox proportional hazards model to regress survival time on treatment status. The model stratified on the propensity score strata, allowing the baseline hazard to vary across the strata.

As a sensitivity analysis, we also stratified the entire study sample into 10 approximately equal-size groups using the deciles of the estimated propensity score.

*Propensity score weighting.* We estimated the absolute reduction in the probability of mortality within 3 years of hospital discharge due to receipt of in-patient smoking cessation counseling using a method described by Lunceford and Davidian (2004). As mentioned earlier, let  $Z_i$  be an indicator variable denoting whether or not the  $i$ th participant was treated; furthermore, let  $e_i$  denote the propensity score for the  $i$ th participant. The weights are defined as  $w_i = \frac{Z_i}{e_i} + \frac{(1-Z_i)}{1-e_i}$ . Assume that  $Y_i$  denotes the outcome variable measured on the  $i$ th participant. The first estimate of the average treatment effect (ATE) is  $\frac{1}{n} \sum_{i=1}^n \frac{Z_i Y_i}{e_i} - \frac{1}{n} \sum_{i=1}^n \frac{(1-Z_i) Y_i}{1-e_i}$ , where  $n$  denotes the number of participants in the full sample. Lunceford and Davidian also provide estimates of the standard error of the estimated treatment effect.

We used a second weighted estimator, also described by Lunceford and Davidian (2004), from the family of doubly robust estimators. This estimator requires specifying the propensity score model and regression models relating

the expected outcome to baseline covariates in treated and untreated subjects separately. Let  $m_z(\mathbf{X}, \alpha_z) = E(Y|Z = z, \mathbf{X})$ . Then

$$\hat{\Delta}_{DR} = \frac{1}{N} \sum_{i=1}^N \frac{Z_i Y_i - (Z_i - \hat{e}_i) m_1(\mathbf{X}_i, \hat{\alpha})}{\hat{e}_i} - \frac{1}{N} \sum_{i=1}^N \frac{(1 - Z_i) Y_i - (Z_i - \hat{e}_i) m_0(\mathbf{X}_i, \hat{\alpha})}{1 - \hat{e}_i}.$$

$\hat{\Delta}_{DR}$  has a “double-robustness” property in that the estimator remains consistent if either the propensity score model is correctly specified or if both the outcomes regression models are correctly specified (Lunceford & Davidian, 2004). For the outcomes-regression models, we used logistic regression models in which the dichotomous outcome was regressed on the 33 baseline covariates described in Table 1.

We then used an approach similar to the aforementioned to estimate the relative reduction in the probability of mortality within 3 years. Each of the estimators described by Lunceford and Davidian (2004) were modified to estimate the relative risk rather than the difference in risks. Confidence intervals were estimated using nonparametric bootstrap methods with 1,000 bootstrap samples.

We then used logistic regression to regress survival to 3 years (a dichotomous outcome) on an indicator variable denoting receipt of in-patient smoking cessation counseling in the weighted sample. Standard errors were obtained using a robust variance estimate (Joffe, Ten Have, Feldman, & Kimmell, 2004). The logistic regression model was then modified by adjusting for the 33 variables in Table 1.

Our second outcome was time to death with participants censored at 3 years after hospital discharge. We used two different methods to estimate the effect of smoking cessation counseling on time to death in the weighted sample. First, we fit a Cox proportional hazards model with counseling as the only predictor variable. We used the inverse probability of treatment weights. Furthermore, we used a robust sandwich variance estimator to account for the weighted nature of the sample. Our second approach was based on the method of Xie and Liu (2005) to estimate adjusted Kaplan-Meier estimates of survival curves in a sample weighted by the inverse probability of treatment. Xie and Liu proposed a weighted version of the log-rank test to test the null hypothesis that the two survival curves are equal to one another.

*Covariate adjustment using the propensity score.* We considered two different approaches to using covariate adjustment using the propensity score. The first approach is based on regressing the outcome on two independent

variables: an indicator variable denoting treatment assignment and the estimated propensity score. For the binary outcome (survival to 3 years postdischarge) a logistic regression model was used, whereas for the time-to-event outcome, a Cox proportional hazards regression model was used.

The aforementioned two approaches, although common in the medical literature, have been shown to result in biased estimates of conditional odds ratios and hazards ratios (Austin, Grootendorst, Normand, & Anderson, 2007). Furthermore, the aforementioned approach for binary outcomes has also been shown to result in biased estimation of marginal odds ratios (Austin, 2007b). Thus, we implemented an approach based on one described by Imbens (2004). This approach is similar to one described by Austin (2010b) for estimating marginal treatment effects using logistic regression models. The aforementioned logistic regression model was fit to the sample. Then for each participant, two predicted probabilities were obtained: the probability of the outcome if the participant had been treated and the probability of the outcome if the participant had been untreated. The average probability of the outcome if untreated can then be determined over all participants in the full study sample. Similarly, the average probability of the outcome if treated can then be determined over all participants in the sample. The difference between these two probabilities is the average treatment effect (Imbens, 2004). Confidence intervals were obtained using non-parametric bootstrap techniques (Efron & Tibshirani, 1993). A similar approach can be used to estimate the relative reduction in death due to smoking cessation counseling. The aforementioned approach can be replicated for the time-to-event outcome (Austin, 2010c). Using this approach, one can determine the absolute reduction in the probability of an event occurring within a specified duration of follow-up.

## Regression Adjustment

For comparative purposes, we used regression adjustment to estimate the effect of smoking cessation counseling on mortality. First, logistic regression was used to regress an indicator variable denoting survival to 3 years postdischarge on an indicator variable denoting receipt of smoking cessation counseling and the 33 baseline covariates listed in Table 1. The logistic regression model was then modified by using restricted cubic smoothing splines to model the relationship between continuous baseline covariates and the log-odds of mortality.

We then used a Cox proportional hazards model to regress survival time on treatment status and the 33 baseline covariates listed in Table 1. We then modified the Cox proportional hazards model by using restricted cubic smoothing splines to model the relationship between continuous baseline covariates and the log-hazard of mortality.

## RESULTS

### Sample Description

The study sample for this case study consisted of 2,342 participants, of whom 1,588 received in-patient smoking cessation counseling and 754 did not. The baseline characteristics of exposed and unexposed participants are described in Table 1. Patients receiving smoking cessation counseling tended to be younger ( $p < .001$ ), were less likely to be female ( $p = .032$ ), tended to have a lower burden of comorbid conditions, and were more likely to receive prescriptions for cardiac medications at hospital discharge compared with patients who did not receive in-patient smoking cessation counseling. There were statistically significant differences in 22 of the 33 baseline characteristics between exposed and unexposed participants in the study sample. Twenty of the variables had standardized differences that exceeded 0.10. Thus, as is typical in observational studies, there were systematic differences in baseline characteristics between treated and untreated patients.

There were no statistically significant differences in basic demographic characteristics (age and sex) and in the probability of death within 3 years of discharge between participants with complete data on baseline covariates and participants who were excluded due to missing data on baseline covariates.

### Matching on the Propensity Score

The standard deviation of the logit of the propensity score was equal to 0.7013542. Thus, 0.2 of the standard deviation of the logit of the propensity score was equal to 0.14027084. Therefore, matched treated and untreated participants were required to have logits of the propensity score that differed by at most 0.14027084.

When participants who received in-patient smoking cessation counseling were matched with participants who did not receive smoking cessation counseling on the logit of the initially specified propensity score model, 682 matched pairs were formed. Thus, 90% of patients who did not receive in-patient smoking cessation counseling were successfully matched to a patient who did receive in-patient smoking cessation counseling.

### Balance Diagnostics

*Propensity score matching.* The baseline characteristics of patients receiving in-patient smoking cessation counseling and those not receiving counseling in the initial propensity score matched sample are described in Table 2. Across the 33 baseline covariates, the absolute standardized differences ranged

TABLE 2  
Baseline Characteristics of Treated and Untreated Participants  
in the First Propensity Score Matched Sample

<i>Variable</i>	<i>No Smoking Cessation Counseling (N = 682)</i>	<i>Smoking Cessation Counseling (N = 682)</i>	<i>Standardized Difference of the Mean</i>	<i>Variance Ratio</i>
Demographic Characteristics				
Age	59.3 ± 11.8	59.5 ± 13.1	0.012	1.235
Female	176 (25.8%)	188 (27.6%)	0.040	1.043
Presenting Signs and Symptoms				
Acute pulmonary edema	28 (4.1%)	29 (4.3%)	0.007	1.034
Vital Signs on Admission				
Systolic blood pressure	148.8 ± 31.2	147.7 ± 31.2	0.036	1.002
Diastolic blood pressure	86.4 ± 18.9	85.7 ± 18.5	0.036	0.952
Heart rate	83.2 ± 24.4	82.5 ± 21.9	0.029	0.808
Respiratory rate	20.9 ± 5.3	21.0 ± 5.7	0.027	1.130
Classic Cardiac Risk Factors				
Diabetes	149 (21.8%)	148 (21.7%)	0.004	0.995
Hyperlipidemia	217 (31.8%)	218 (32.0%)	0.003	1.002
Hypertension	276 (40.5%)	260 (38.1%)	0.048	0.979
Family history of coronary artery disease	229 (33.6%)	244 (35.8%)	0.046	1.030
Comorbid Conditions and Vascular History				
Cerebrovascular accident/Transient ischemic attack	47 (6.9%)	45 (6.6%)	0.012	0.960
Angina	174 (25.5%)	174 (25.5%)	0.000	1.000
Cancer	15 (2.2%)	14 (2.1%)	0.010	0.935
Dementia	6 (0.9%)	9 (1.3%)	0.042	1.493
Previous myocardial infarction	143 (21.0%)	138 (20.2%)	0.018	0.974
Asthma	42 (6.2%)	35 (5.1%)	0.044	0.842
Depression	64 (9.4%)	64 (9.4%)	0.000	1.000
Peptic ulcer disease	36 (5.3%)	35 (5.1%)	0.007	0.974
Peripheral vascular disease	64 (9.4%)	54 (7.9%)	0.052	0.857
Previous coronary revascularization	45 (6.6%)	45 (6.6%)	0.000	1.000
Chronic congestive heart failure	20 (2.9%)	14 (2.1%)	0.056	0.706
Laboratory Tests				
Glucose	9.1 ± 5.4	9.2 ± 5.6	0.019	1.095
White blood count	10.7 ± 3.8	10.8 ± 4.1	0.024	1.154
Hemoglobin	144.2 ± 16.4	143.1 ± 18.4	0.064	1.249
Sodium	139.0 ± 3.4	139.0 ± 3.9	0.002	1.364
Potassium	4.1 ± 0.5	4.1 ± 0.5	0.014	1.166
Creatinine	93.2 ± 38.3	93.2 ± 43.9	0.001	1.310
Prescriptions for Cardiovascular Medications at Hospital Discharge				
Statin	184 (27.0%)	188 (27.6%)	0.013	1.014
Beta-blocker	425 (62.3%)	437 (64.1%)	0.036	0.980
Angiotensin Converting Enzyme (ACE) inhibitor/Angiotensin receptor blockers	335 (49.1%)	322 (47.2%)	0.038	0.997
Plavix	30 (4.4%)	29 (4.3%)	0.007	0.968
Acetylsalicylic Acid (ASA)	513 (75.2%)	514 (75.4%)	0.003	0.996

*Note.* Continuous variables are presented as means ± standard deviation; dichotomous variables are presented as *N* (%).

from a low of 0 to a high of 0.064, with a median of 0.018, indicating that the means and prevalences of continuous and dichotomous variables were very similar between treatment groups in the matched sample. The variance ratios ranged from a low of 0.81 (admission heart rate) to a high of 1.36 (sodium), indicating that the variance of some continuous variables was different between the two treatment groups in the initial propensity score matched sample.

In an attempt to further minimize some of the residual differences in the distribution of the baseline covariates between treatment groups, the original specification of the propensity score model was modified. The first modification was to relax the assumption that the continuous variables were each linearly related to the log-odds of exposure. The propensity score model was modified so that restricted cubic smoothing splines with five knots were used to model the relationship between continuous baseline variable and the log-odds of exposure (Harrell, 2001). The matching process described earlier was repeated and the similarity of the distribution of treated and untreated participants in the resultant matched sample was assessed. Despite modifications of the propensity score model, there remained continuous variables whose variances were greater in one group than in the other group (variance ratios ranging from 0.91 to 1.34). The highest variance ratio was for glucose. The current specification of the propensity score model was then further modified by including interactions between glucose (and the variables required for modeling glucose using restricted cubic smoothing splines) and several of the dichotomous variables.

The resultant matched sample consisted of 646 matched pairs (85.7% of patients not receiving smoking cessation counseling were successfully matched to a patient receiving counseling with a similar value of the logit of the propensity score). The baseline characteristics of treated and untreated participants are described in Table 3. The standardized differences ranged from a low of 0 to a high of 0.055 with a median of 0.014 (25th and 75th percentiles: 0.006 and 0.038, respectively). The variance ratios for continuous variables ranged from 0.86 to 1.15. The absolute standardized differences for all 55 two-way interactions between continuous baseline covariates ranged from 0.001 to 0.076 with a median of 0.016.

The aforementioned analyses indicate that the means and variances of continuous variables were similar between treatment groups in the matched sample. Similarly, the prevalence of dichotomous variables was similar between treatment groups. In addition, the mean of two-way interactions between continuous baseline covariates was similar between treatment groups in the propensity score matched sample.

Figure 1 reports empirical cumulative distribution plots and quantile-quantile plots for four continuous baseline covariates: age, systolic blood pressure, creatinine, and glucose. These plots indicate that the distribution of each of these four continuous variables was very similar between treatment groups in the

TABLE 3  
Baseline Characteristics of Treated and Untreated Participants  
in the Final Propensity Score Matched Sample

<i>Variable</i>	<i>No Smoking Cessation Counseling (N = 646)</i>	<i>Smoking Cessation Counseling (N = 646)</i>	<i>Standardized Difference of the Mean</i>	<i>Variance Ratio</i>
Demographic Characteristics				
Age	59.1 ± 12.4	58.7 ± 12.4	0.026	0.998
Female	178 (27.6%)	175 (27.1%)	0.010	0.989
Presenting Signs and Symptoms				
Acute pulmonary edema	31 (4.8%)	25 (3.9%)	0.046	0.814
Vital Signs on Admission				
Systolic blood pressure	147.7 ± 30.5	147.8 ± 31.3	0.002	1.055
Diastolic blood pressure	85.5 ± 17.7	85.7 ± 18.5	0.015	1.092
Heart rate	82.1 ± 22.4	82.4 ± 22.3	0.013	0.993
Respiratory rate	20.8 ± 5.5	20.9 ± 5.7	0.012	1.046
Classic Cardiac Risk Factors				
Diabetes	130 (20.1%)	140 (21.7%)	0.038	1.056
Hyperlipidemia	216 (33.4%)	214 (33.1%)	0.007	0.995
Hypertension	247 (38.2%)	247 (38.2%)	0.000	1.000
Family history of coronary artery disease	218 (33.7%)	235 (36.4%)	0.055	1.035
Comorbid Conditions and Vascular History				
Cerebrovascular accident/Transient ischemic attack	39 (6.0%)	46 (7.1%)	0.044	1.166
Angina	165 (25.5%)	166 (25.7%)	0.004	1.004
Cancer	15 (2.3%)	13 (2.0%)	0.021	0.869
Dementia	5 (0.8%)	8 (1.2%)	0.047	1.593
Previous myocardial infarction	131 (20.3%)	131 (20.3%)	0.000	1.000
Asthma	33 (5.1%)	35 (5.4%)	0.014	1.057
Depression	63 (9.8%)	63 (9.8%)	0.000	1.000
Peptic ulcer disease	30 (4.6%)	30 (4.6%)	0.000	1.000
Peripheral vascular disease	57 (8.8%)	57 (8.8%)	0.000	1.000
Previous coronary revascularization	44 (6.8%)	43 (6.7%)	0.006	0.979
Chronic congestive heart failure	13 (2.0%)	14 (2.2%)	0.011	1.075
Laboratory Tests				
Glucose	9.0 ± 5.3	9.1 ± 5.5	0.011	1.075
White blood count	10.9 ± 3.9	10.7 ± 3.6	0.038	0.863
Hemoglobin	143.2 ± 16.7	143.9 ± 17.6	0.041	1.117
Sodium	139.1 ± 3.5	139.0 ± 3.3	0.025	0.920
Potassium	4.0 ± 0.5	4.1 ± 0.5	0.004	1.151
Creatinine	93.8 ± 39.6	92.1 ± 40.2	0.045	1.033
Prescriptions for Cardiovascular Medications at Hospital Discharge				
Statin	189 (29.3%)	185 (28.6%)	0.014	0.987
Beta-blocker	424 (65.6%)	427 (66.1%)	0.010	0.993
Angiotensin Converting Enzyme (ACE) inhibitor/Angiotensin receptor blockers	302 (46.7%)	309 (47.8%)	0.022	1.002
Plavix	24 (3.7%)	28 (4.3%)	0.031	1.159
Acetylsalicylic Acid (ASA)	476 (73.7%)	488 (75.5%)	0.043	0.953

*Note.* Continuous variables are presented as means ± standard deviation; dichotomous variables are presented as *N* (%).

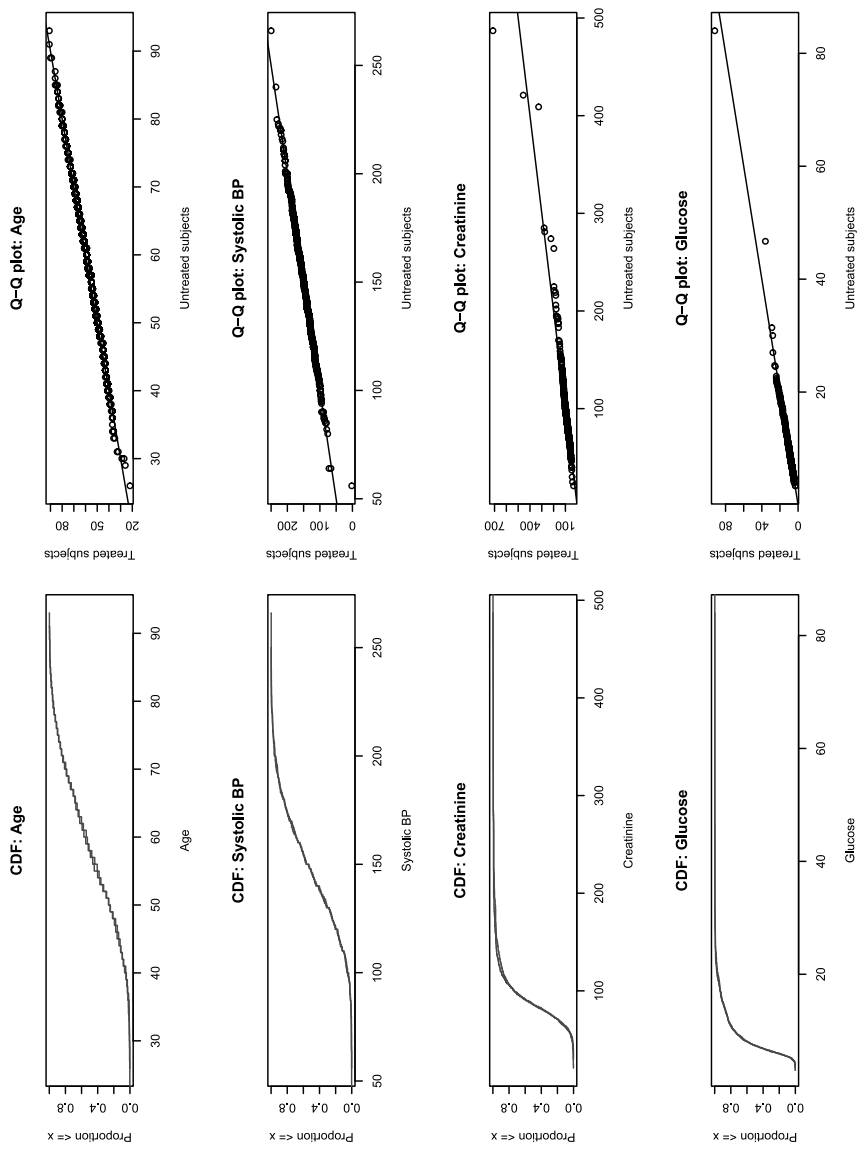


FIGURE 1 Comparing distribution of continuous covariates in propensity-score matched sample.



propensity score matched sample. Similar plots could be produced for the remaining continuous baseline covariates.

Taken together, the aforementioned analyses indicate that the modified propensity score model appears to have been adequately specified. After matching on the estimated propensity score, observed systematic differences between treated and untreated participants appear to have been greatly reduced or eliminated.

The final specification of the propensity score model is used for the remainder of the case study. In a particular application of propensity score methods, one would typically optimize the specification of the propensity score to the particular propensity score method that is being employed. We have elected to use the current specification of the propensity score for all four propensity score methods for two reasons. First, it allows readers to compare the relative performance of different propensity score methods with a uniform specification of the propensity score model. Second, modifying the specification of the propensity score model across different propensity score methods appears to be at odds with the conceptual perspective that there is one true propensity score model.

Among the 754 participants in the study sample who did not receive smoking cessation counseling, there were substantial differences in baseline characteristics between the 646 participants included in the matched sample and the 108 participants who were not included in the matched sample (due to no appropriate participant who did receive smoking cessation counseling being identified). There existed statistically significant differences in 24 of the 33 baseline covariates between matched and unmatched participants. Furthermore, 29 of the baseline covariates had standardized differences that exceeded 0.10 between matched and unmatched participants. For instance, the mean of age matched and unmatched participants were 58.7 years and 70.9 years, respectively.

*Stratification on the propensity score.* The quintiles of the estimated propensity score were 0.55243, 0.67427, 0.75205, and 0.82271, respectively. The proportion of participants within each stratum who received smoking cessation counseling ranged from a low of 39.1% in the stratum with the lowest propensity score to a high of 86.1% in the stratum with the highest propensity score. In the stratum of participants with the lowest propensity score, the minimum, 25th percentile, median, 75th percentile, and maximum propensity score for participants who did not receive smoking cessation counseling were 0.005, 0.294, 0.415, 0.484, and 0.551, respectively. In participants who did receive smoking cessation counseling, these statistics were 0.081, 0.381, 0.475, 0.519, and 0.552, respectively. Thus, in this lower stratum, the distribution of the propensity score was shifted modestly lower in untreated participants compared with treated participants. However, overall, there was reasonable overlap in the propensity score between treated and untreated participants. In each of the middle three strata, the distribution of the propensity score was very similar

between treated and untreated participants. In the fifth stratum, the maximum propensity score in treated participants was 0.981, whereas it was 0.944 in untreated participants. In some settings, inadequate overlap in the propensity score may be observed between treated and untreated participants within a given propensity score stratum (if this occurs, it often occurs in either the lowest or highest strata). If this occurs, some applied investigators may choose to exclude untreated participants with very low propensity scores or treated participants with very high propensity scores. However, when this is done, one needs to be aware that one is changing the population to which the estimated treatment effect applies.

For the 33 variables described in Table 1, the minimum absolute standardized differences were 0, 0.007, 0.012, 0.002, and 0.008 across the five propensity score strata. The maximum absolute standardized differences were 0.213, 0.221, 0.210, 0.253, and 0.220 across the five strata. The median absolute standardized differences were 0.074, 0.062, 0.077, 0.069, and 0.074 across the five strata. Within-quintile standardized differences were computed for each of the 55 pairwise interactions between continuous variables. The minimum standardized differences were 0.003, 0.001, 0.004, 0.001, and 0.003 across the five propensity score strata. The maximum standardized differences were 0.202, 0.159, 0.230, 0.166, and 0.228 across the five strata. The median standardized differences were 0.090, 0.044, 0.082, 0.082, and 0.072 across the five strata.

The aforementioned sets of balance diagnostics suggest that, on average, treated and untreated participants have similar distributions of measured baseline covariates within strata of the propensity score. One could complement the aforementioned quantitative analyses by graphical analyses comparing the distribution of continuous covariates between treatment groups within each stratum of the propensity score. For instance, one could use within-stratum empirical cumulative distribution plots or quantile-quantile plots to compare the distribution of continuous covariates between treatment groups. Due to space constraints, we omit these analyses from this article.

In comparing the within-quintile balance with that observed in the propensity score matched sample described earlier, one notes that modestly greater imbalance persists when stratifying on the propensity score compared with when matching on the propensity score (e.g., compare the median standardized differences). This is consistent with prior empirical observations (Austin & Mamdani, 2006; Austin, 2009c) and with the results from prior Monte Carlo simulations (Austin, 2009c; Austin, Grootendorst, & Anderson, 2007). Greater residual imbalance tends to be eliminated by matching on the propensity score than by stratifying on the quintiles of the propensity score.

*Propensity score weighting.* The individual inverse probability of treatment weights ranged from 1.0 to 18.0. The weighted standardized differences

were computed for the 33 variables listed in Table 1. The absolute standardized differences ranged from 0.001 to 0.031 with a median of 0.010 (the 25th and 75th percentiles were 0.007 and 0.015, respectively). The variance ratios for the continuous variables ranged from 0.36 to 0.50. The absolute standardized differences for the 55 two-way interactions between continuous variables ranged from 0.001 to 0.031 with a median of 0.012 (the 25th and 75th percentiles were 0.007 and 0.018, respectively). Thus, although the means and prevalences of continuous and dichotomous variables were well balanced between treatment groups in the weighted sample, there is some evidence of greater dispersion in untreated patients compared with treated patients.

Figure 2 describes empirical cumulative distribution functions and nonparametric estimates of the density functions for four continuous covariates in treated and untreated participants separately in the sample weighted by the inverse probability of treatment. In examining the eight panels in Figure 2, one observes that the distribution of each of the four continuous variables was very similar between treated and untreated participants in the weighted sample.

The evidence provided by the empirical cumulative distribution functions and the nonparametric density plots appears to be in conflict with that provided by the ratios of the variances of the continuous variables. The former suggests that the distributions are comparable between treatment groups, whereas the latter suggests that greater variability is found in untreated participants than in treated participants. Upon further examination, it was found that the inverse probability of treatment weights were systematically higher in untreated participants than in treated participants. We hypothesize that a few large weights in the untreated participants may have resulted in inflated variance estimates in this population, resulting in shrunken variance ratios.

*Covariate adjustment using the propensity score.* In the full study sample, the weighted conditional absolute standardized differences ranged from 0.001 to 0.194 for the 33 variables listed in Table 1. The median weighted conditional absolute standardized difference was 0.062, whereas the first and third quartiles were 0.024 and 0.093, respectively.

Figure 3 displays the graphical balance diagnostics based on quantile regression for age, systolic blood pressure, creatinine, and glucose. The relationship between the quantiles of the baseline variable and the propensity score in treated participants is described using the five solid lines, whereas the relationship between the quantiles of the baseline variable and the propensity score in untreated participants is described using the five dashed lines. In examining Figure 3, one notes that the distribution of each of the four baseline covariates is approximately similar between treatment groups across the range of the propensity score. However, there was some evidence of differences in the 95th percentile of the

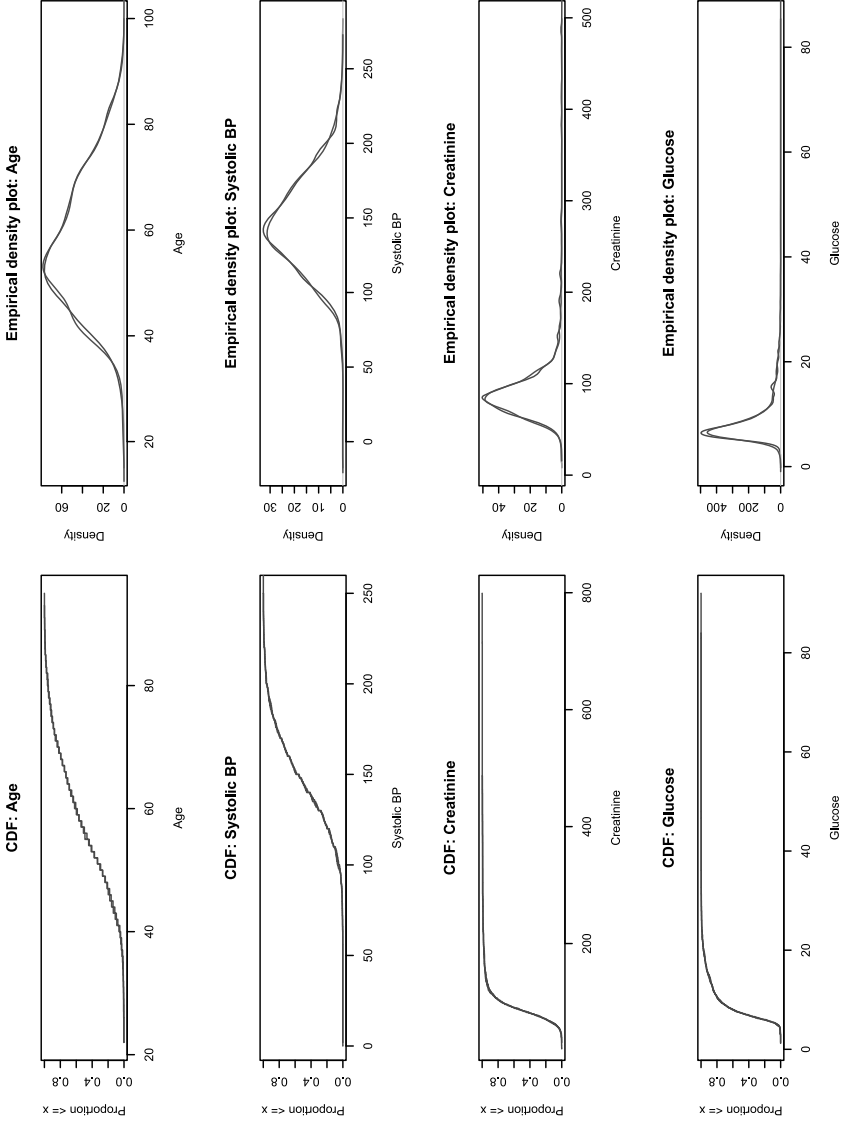


FIGURE 2 Comparing distribution of continuous covariates in inverse probability of treatment weighted sample.

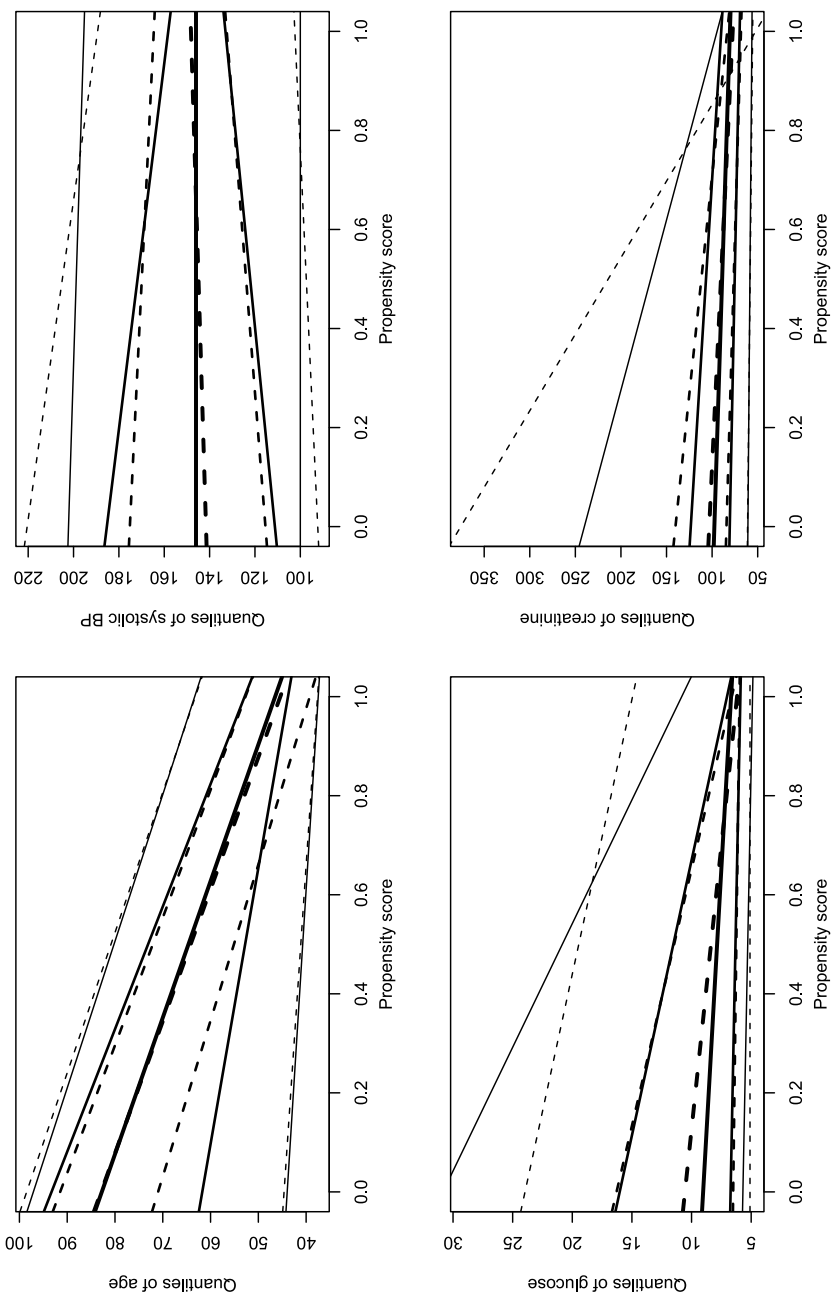


FIGURE 3 Quantile regression to compare conditional distribution of baseline covariates between treatment groups.

conditional distributions between treated and untreated participants for three of the four continuous covariates.

Based on the results of the balance diagnostics described in the preceding sections, we were satisfied that our specification of the propensity score was adequate. Having satisfied ourselves that the propensity score model was adequately specified, we proceeded to estimate the effect of treatment on outcomes using the four different propensity score methods.

### Estimated Treatment Effects

*Propensity score matching.* The matched sample consisted of 646 matched pairs. In this matched sample, 91 treated participants and 103 untreated participants died within 3 years of hospital discharge. The probabilities of death within 3 years of discharge were 0.141 (91/646) and 0.159 (103/646) for treated and untreated participants, respectively. The absolute reduction in the probability of 3-year mortality was 0.0185 (95% confidence interval [-0.018, 0.055]). There was no significant difference in the probability of 3-year mortality between treatment groups ( $p = .3173$ ). The NNT, the reciprocal of the absolute risk reduction, was 54. Thus, one would need to provide in-patient counseling to 54 smokers in order to avoid one death within 3 years of hospital discharge. The relative risk of death in treated participants compared with untreated participants was  $91/103 = 0.88$  (95% confidence interval: [0.69, 1.13]). Thus, in-patient smoking cessation counseling reduced the risk of 3-year mortality by 12%. However, the relative risk was not statistically significantly different from unity ( $p = .3176$ ). Thus, there was no evidence that the provision of smoking cessation counseling reduced the risk of death in current smokers within 3 years of hospital discharge.

The left panel of Figure 4 depicts the Kaplan-Meier survival curves in treated and untreated participants in the propensity score matched sample. The two survival curves were not significantly different from one another ( $p = .2486$ ). Using a Cox proportional hazards model, the estimated hazard ratio was 0.874 (95% confidence interval: [0.672, 1.136]). Thus, provision of smoking cessation counseling prior to hospital discharge reduced the hazard of subsequent death by 12.6%. However, this effect was not statistically different from the null effect ( $p = .3130$ ).

*Stratification on the propensity score.* The probability of 3-year mortality in participants not receiving in-patient smoking cessation counseling was 0.37, 0.16, 0.10, 0.05, and 0.05 in the first through fifth strata of the propensity score, respectively. The probability of 3-year mortality in participants receiving in-patient smoking cessation counseling was 0.25, 0.14, 0.09, 0.04, and 0.04 in the first through fifth strata, respectively. Thus, the absolute reduction in 3-year

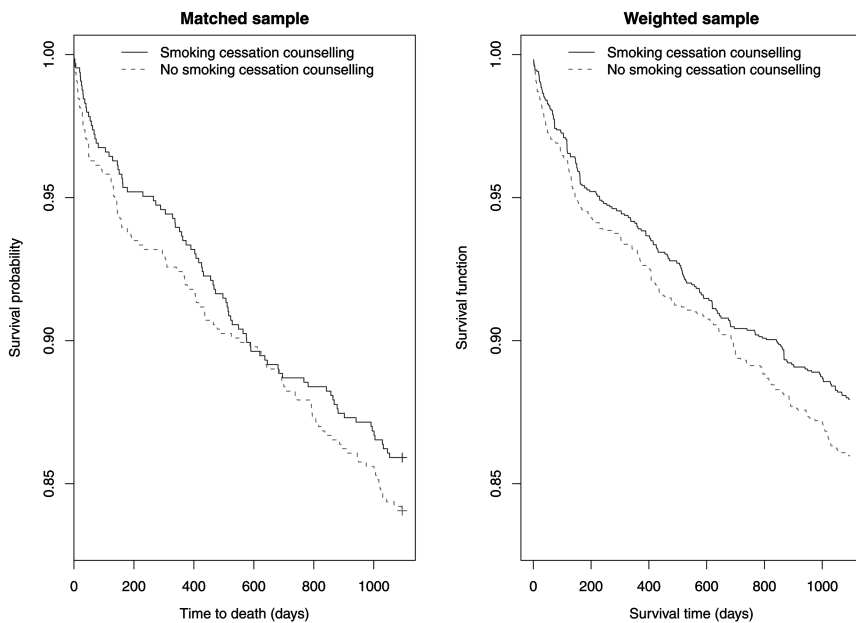


FIGURE 4 Kaplan-Meier survival curves in matched and weighted samples.

mortality was 0.126, 0.023, 0.015, 0.007, and 0.001, in the first through fifth propensity score strata, respectively. The mean of these five stratum-specific absolute risk reductions is 0.034. Thus, if all current smokers received in-patient smoking cessation counseling, the probability of 3-year mortality would be reduced by 0.034. The standard error of the pooled risk difference was 0.015. Thus, a 95% confidence interval for the absolute reduction in the probability of mortality within 3 years is (0.006, 0.063). The Mantel-Haenszel estimate of the pooled relative risk across the propensity score strata was 0.75 (95% confidence interval: 0.59–0.96). Provision of smoking cessation counseling significantly reduced the risk of death within 3 years by 25% ( $p = .0236$ ).

Figure 5 depicts the stratum-specific Kaplan-Meier survival curves for treated and untreated subjects across the five propensity-score strata. When using a Cox proportional hazards model that stratified on the five propensity score strata, the estimated hazard ratio was 0.72 (95% confidence interval: 0.57–0.91). Thus, receipt of in-patient smoking cessation counseling reduced the hazard of death by 28%. This effect was statistically significant ( $p = .0065$ ).

As a sensitivity analysis, we repeated the aforementioned analyses using 10 strata rather than 5 strata. The estimated absolute risk reduction was 0.027 (95% confidence interval: [−0.002, 0.056]), whereas the pooled relative risk was 0.805

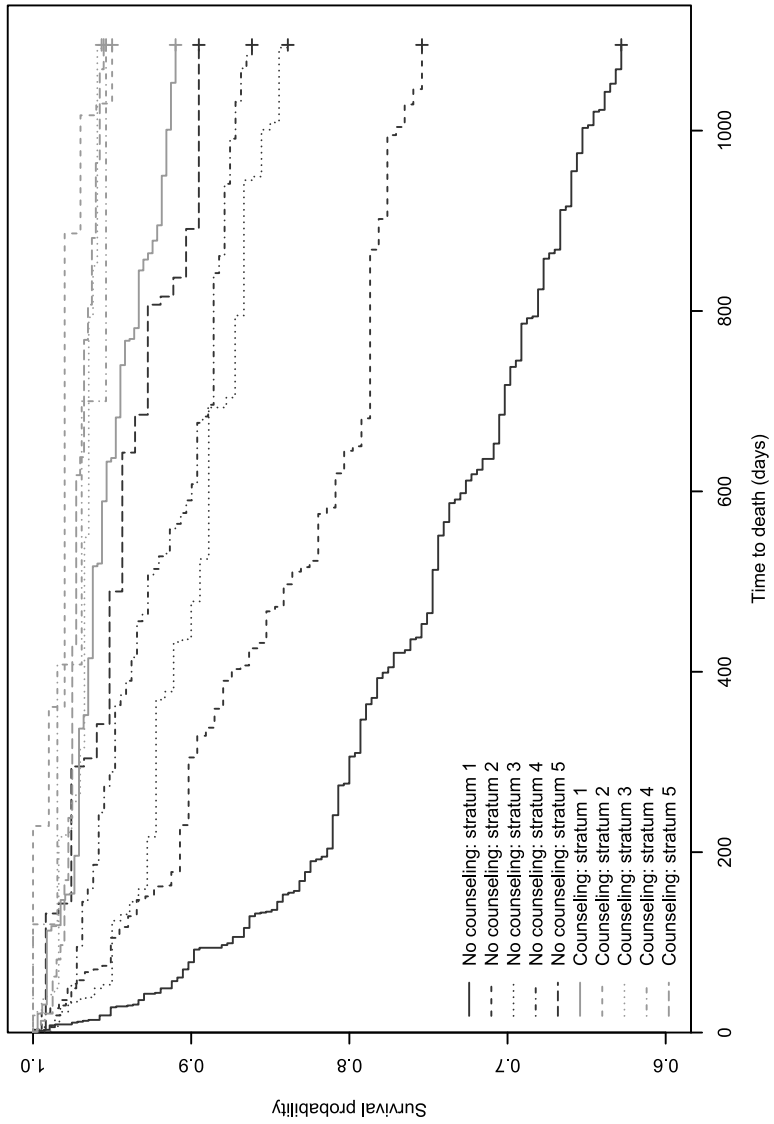


FIGURE 5 Kaplan-Meier survival curves in PS strata.



(95% confidence interval: 0.628–1.031). For time to death, the estimated hazard ratio was 0.775 (95% confidence interval: 0.608–0.989). Thus, smoking cessation counseling decreased the hazard of death by 22.5% ( $p = .04$ ).

*Propensity score weighting.* Using the first weighted estimate, counseling reduced the probability of death within 3 years by 0.020 (95% confidence interval:  $-0.008$  to  $0.047$ ), which was not statistically significantly different from 0 ( $p = .1558$ ). The  $\hat{\Delta}_{DR}$  estimate of the absolute reduction in the probability of mortality due to counseling was 0.025 (95% confidence interval:  $-0.002$  to  $0.052$ ). Counseling did not reduce the probability of mortality within 3 years of discharge ( $p = .0689$ ).

Using the first weighted estimator, the relative risk of death within 3 years in treated patients compared with untreated patients was 0.86 (95% confidence interval: 0.66–1.10). Using the doubly robust estimator, the relative risk was 0.82 (95% confidence interval: 0.66–1.03).

Using logistic regression in the weighted sample, the resultant odds ratio was 0.84 (95% confidence interval: 0.63–1.11). When the logistic regression model was modified by adjusting for the 33 variables in Table 1, the estimated odds ratio was attenuated to 0.98 (95% confidence interval: 0.95–1.00). In neither case was the estimated odds ratio statistically significantly different from 1 ( $p = .2193$  and  $.0998$ , respectively).

When a Cox proportional hazards model was used in the weighted sample, the estimated hazard ratio for counseling was 0.850 (95% confidence interval: 0.655 to 1.102). Thus, counseling did not reduce the hazard of subsequent death ( $p = .2203$ ). The right panel of Figure 4 displays the estimates of the Kaplan-Meier survival curves in the sample weighted by the inverse probability of treatment. One observes that in-patient smoking cessation counseling improved survival postdischarge. At 3 years, the probability of death was 0.880 and 0.860 in those who did and did not receive counseling, respectively. The absolute reduction in the probability of death within 3 years due to smoking cessation counseling was 0.020. However, there was no evidence that the two survival curves were different from one another ( $p = .2107$ ).

*Covariate adjustment using the propensity score.* When we used logistic regression to regress the odds of survival to 3 years on an indicator variable for treatment status and the propensity score, one inferred that receipt of in-patient smoking cessation counseling reduced the odds of death within 3 years of discharge by 20.8% (odds ratio: 0.792; 95% confidence interval: 0.600–1.046). Similarly, treatment reduced the hazard of postdischarge mortality by 20.2% (hazard ratio: 0.798; 95% confidence interval: 0.624–1.022). Neither the odds ratio nor the hazard ratio were statistical significantly different from the null treatment effect ( $p = .100$  and  $.074$ , respectively). As noted in the Methods

section, use of these approaches is discouraged as they have been shown to lead to biased estimation of odds ratios and hazard ratios.

When using the method based on that described by Imbens (2004), we estimated that the probability of death within 3 years if all participants were untreated was 0.144, whereas the probability of death if all participants were treated was 0.121. Thus, treatment reduced the population probability of death within 3 years by 0.023 (95% confidence interval was  $[-0.005, 0.052]$ ). Similarly, the relative risk was 0.84 (16% relative reduction in the probability of death within 3 years of hospital discharge; 95% confidence interval: 0.68–1.04). Thus, using covariate adjustment using the propensity score, neither the effect of counseling on the absolute or relative reduction in the probability of mortality was statistically significant from the null effect.

*Regression adjustment.* When logistic regression was used to regress an indicator variable denoting survival to 3 years postdischarge on an indicator variable denoting receipt of smoking cessation counseling and the 33 baseline covariates listed in Table 1, the adjusted odds ratio for smoking cessation counseling was 0.73 (95% confidence interval: 0.54–0.98). Thus, smoking cessation counseling reduced the odds of mortality ( $p = .0371$ ). When the logistic regression model was modified by using restricted cubic smoothing splines to model the relationship between continuous baseline covariates and the log-odds of mortality, the resultant odds ratio for counseling was 0.77 (95% confidence interval: 0.56–1.05). Thus, smoking cessation counseling did not significantly reduce the odds of mortality ( $p = .0942$ ).

When we used a Cox proportional hazards model to regress survival time on treatment status and the 33 baseline covariates listed in Table 1, the adjusted hazard ratio for smoking cessation counseling was 0.72 (95% confidence interval: 0.57–0.92). Thus, smoking cessation counseling reduced the hazard of postdischarge mortality ( $p = .0080$ ). When we modified the Cox proportional hazards model by using restricted cubic smoothing splines to model the relationship between continuous baseline covariates and the log-hazard of mortality, the resultant hazard ratio for counseling was 0.78 (95% confidence interval: 0.61–0.99). Thus, counseling significantly reduced the hazard of death ( $p = .0441$ ).

## DISCUSSION

In this case study and tutorial on propensity score methods, we have illustrated the use of different propensity score methods for estimating treatment effects when using observational data. Several observations merit highlighting and discussion.

First, we highlight that specifying the propensity score model was an iterative process that involved several iterations of model specification and assessing the balance of measured baseline covariates between treated and untreated participants in the propensity score matched sample. In this case study, we required three steps before we were satisfied that the propensity score model had been adequately specified. Balance assessment plays a critical role in any propensity score analysis.

Second, different propensity score methods eliminated systematic differences between treated and untreated participants to differing degrees. Propensity score matching and inverse probability of treatment weighting using the propensity score reduced systematic differences between treated and untreated participants to a greater extent than did stratification on the propensity score or covariate adjustment using the propensity score. These observations are similar to prior empirical observations and to the results of Monte Carlo simulations (Austin, 2009c).

Third, when outcomes were binary, propensity score methods allowed estimation of absolute risk reductions (or differences in proportions) and relative risks. In contrast, conventional logistic regression only allowed estimation of odds ratios. Many authors have suggested that relative risks and risk differences are preferable to odds ratios for quantifying the magnitude of treatment effects (Sackett, 1996; Sinclair & Bracken, 1994). The reader is referred elsewhere for a more detailed discussion of propensity score methods for estimating risk differences and relative risks (Austin, 2008d, 2010e; Austin & Laupacis, 2011).

Fourth, when estimating absolute and relative reductions in the probability of mortality within 3 years of hospital discharge, the magnitude of estimated treatment effects varied across the different propensity score methods. Table 4 summarizes the estimated absolute risk reductions and relative risks across the four propensity score methods. The estimated relative risks varied from 0.75 (stratification on the propensity score with five strata) to 0.88 (propensity score matching). Furthermore, in only one instance (stratification with five strata) did the associated 95% confidence interval exclude unity. Stratification on the quin-

TABLE 4  
Comparison of Effect Sizes Across Different Propensity Score Methods

<i>Propensity Score Method</i>	<i>Absolute Risk Difference (95% Confidence Interval)</i>	<i>Relative Risk (95% Confidence Interval)</i>
Propensity score matching	0.0185 (−0.018, 0.055)	0.88 (0.69, 1.13)
Stratification on the propensity score—5 strata	0.035 (0.006, 0.063)	0.75 (0.59, 0.96)
Stratification on the propensity score—10 strata	0.027 (−0.002, 0.056)	0.80 (0.63, 1.03)
Weighting—first estimator	0.020 (−0.008, 0.047)	0.86 (0.66, 1.01)
Weighting—doubly robust estimator	0.025 (−0.002, 0.052)	0.82 (0.66, 1.03)
Covariate adjustment using the propensity score	0.023 (−0.005, 0.052)	0.84 (0.68, 1.04)

tiles of the propensity score removed less of the systematic differences between treated and untreated participants than did matching or weighting using the propensity score. Thus, the greater effect size obtained using stratification may reflect a greater amount of residual bias. In our comparison of treated and untreated participants in the original sample, we observed that treated participants tended to be younger and healthier than untreated participants. Furthermore, they were more likely to receive discharge prescriptions for medications that reduce cardiac mortality and morbidity. Thus, some of the difference between the stratified estimate and those obtained using weighting or matching may reflect persistent residual differences between treated and untreated participants with the treated participants being healthier than the untreated participants. Similarly, when estimating absolute risk reductions, the greatest reduction in mortality was observed when stratification was used, whereas the smallest absolute reduction was observed when matching was used. As with relative risks, stratification was the only propensity score method that resulted in a 95% confidence interval for the absolute risk reduction that excluded the null value.

Fifth, we highlight that propensity score matching allows one to estimate the ATT, whereas the other three methods allow one to estimate the ATE (Imbens, 2004, although we note that the other methods can be adapted to estimate the ATT as well). The latter three methods allow one to estimate the effect on average mortality in the population if one shifted the *entire* population from receiving no counseling to receiving smoking cessation counseling. Because of how matching was done, the matching estimator is estimating the effect of smoking cessation counseling in those participants who ultimately did not receive counseling. We have already noted that participants who did not receive smoking cessation counseling tended to be older and sicker than patients who received counseling. Thus, the populations to which each estimate applies are qualitatively and quantitatively different from one another. In comparing the two panels of Figure 4, one should note that the probability of survival to 3 years is different in the untreated population (matched analysis) compared with survival in the overall population if all participants were untreated (weighted analysis). Complicating the interpretation of the matched estimator is the fact that of those patients who did not receive in-patient smoking cessation counseling, only 86% were successfully matched to a patient who did receive smoking cessation counseling. Ideally, each participant who did not receive counseling would be matched to a participant who received counseling. Then, the estimated treatment effect would apply to the population of participants who did not receive counseling. However, we have noted that, of those participants who did not receive counseling, unmatched participants were systematically different from those who were matched. In particular, unmatched participants were substantially older. Due to incomplete matching, it is not clear how to describe the population to which the matched estimator applies. Incomplete matching appears to occur

frequently in applied applications, complicating the interpretation of the matched estimator. Applied investigators need to decide which of the ATE or the ATT is more meaningful in their research context. In the context of smoking cessation counseling offered to patients hospitalized with an AMI, the choice may depend in part on the intensity of counseling and the degree to which patients' commitment is required.

Sixth, we contrast the different odds ratios that were obtained using different methods. In the sample weighted by the inverse probability of treatment, we obtained two odds ratios: 0.84 and 0.98. The first was obtained by regressing survival on treatment status, whereas the second was obtained after additional adjustment for baseline covariates. Neither odds ratio was statistically significantly different from one ( $p > .09$ ). In contrast, conventional logistic regression in the original unweighted sample resulted in an odds ratio of 0.73 (this was attenuated to 0.77 when cubic smoothing splines were used to model the relationship between continuous baseline covariates and the log-odds of mortality). The first two odds ratios are estimates of the marginal odds ratio for the reduction in mortality due to counseling, whereas the latter two odds ratios are estimates of the conditional odds ratio (Rosenbaum, 2005). Differences between these two sets of estimates reflect the fact that propensity score methods allow for estimation of marginal treatment effects, whereas regression adjustment allows for estimation of conditional treatment effects (Rosenbaum, 2005). For odds ratios, marginal and conditional effects do not coincide (Gail, Wieand, & Piantadosi, 1984; Greenland, 1987).

Seventh, we highlight that there are well-developed methods for assessing the similarity of treated and untreated participants conditional on the propensity score. These methods allow one to assess whether the propensity score model has been adequately specified. Having removed or reduced systematic differences between treatment groups, one can then directly compare outcomes in the resultant matched, stratified, or weighted sample. In contrast, when using regression adjustment it is more difficult to assess whether the regression model relating outcomes to treatment and baseline covariates has been correctly specified. In our initial conventional logistic regression model, the odds ratio for counseling was 0.73 ( $p = .0371$ ). However, this was attenuated to 0.77 ( $p = .0942$ ) when cubic smoothing splines were used to model the relationship between continuous baseline variables and the log-odds of mortality. However, uncertainty persists as to whether this second model had been adequately specified.

Eighth, we remind the reader that propensity score methods only allow one to account for measured baseline variables. Estimates using each of the estimates of treatment effect may be susceptible to bias due to unmeasured confounding variables. The reader is referred elsewhere for an illustration of this (Austin, Mamdani, Stukel, Anderson, & Tu, 2005). Rosenbaum and Rubin (1983) described sensitivity analyses to assess the sensitivity of the study conclu-

sions to unmeasured covariates when propensity score methods are used. These sensitivity analyses allow one to assess how strongly an unmeasured confounder would have to be associated with treatment selection in order for a previously statistically significant treatment effect to become statistically nonsignificant if the unmeasured confounder had been accounted for. However, in our case study, the large majority of estimated effects were not statistically significant. Thus, we did not employ these sensitivity analyses in this case study.

Ninth, we highlight that the question of whether providing smoking cessation counseling reduces postdischarge mortality in AMI patients is a complex clinical question Readers are referred elsewhere for an examination of this clinical question (Van Spall, Chong, & Tu, 2007). The analyses presented in the current case study were merely intended to illustrate the use of different statistical methods and were not intended to address this clinical question. However, to underline the importance of the clinical question, we note that a prior study found that approximately 31% of patients who were discharged alive from the hospital with a diagnosis of AMI were current smokers at the time of the infarction, whereas 36% were former smokers (Rea et al., 2002). A meta-analysis of 12 cohort studies found that smoking cessation following AMI reduced the odds of subsequent mortality by 46% (Wilson, Gibson, Willan, & Cook, 2000). It is important to note that this mortality benefit was consistent across a range of factors. Given the large number of patients hospitalized with acute myocardial infarction, the high prevalence of current smokers among these patients, the high mortality rate in this patient population, and the potential benefit of smoking cessation in these patients, it is critical that effective means of successfully encouraging smoking cessation be developed. A systematic review of 33 randomized and quasi-randomized controlled trials found that smoking cessation counseling in hospitalized smokers increased the odds of smoking cessation at 6 and 12 months by 65% if the counseling began during hospitalization and included supportive contacts for more than 1 month after hospital discharge (Rigotti, Munafo, & Stead, 2008). However, interventions with less postdischarge contact were not found to be effective. In the context of patients hospitalized with AMI, a randomized controlled trial found that bedside smoking cessation counseling followed by seven telephone calls over the first 6 months after discharge had a substantial effect on smoking cessation 1 year after discharge (Dornelas, Sampson, Gray, Waters, & Thompson, 2000). In an analysis of a multicenter registry of patients hospitalized with an AMI, a multivariable analysis found that, although individual smoking cessation counseling did not influence the odds of smoking cessation, being treated at a facility that offered an in-patient smoking cessation program increased the odds of smoking cessation (Dawood et al., 2008). Finally, a meta-analysis found that, when comparing different health care providers, smoking cessation was most effective when provided by physicians (Gorin & Heck, 2004).

In summary, we have illustrated the appropriate steps in conducting analyses using different propensity score methods. Increased use of these methods may allow for more transparent estimation of causal treatment effects using observational data.

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