Biostatistics, Epidemiology, and Research Design (BERD) Core

Tabitha Garwe, PhD MPH

Clinical Epidemiology Unit

Propensity Score Analysis in Epidemiologic Research

PART I: May 18th, 2022

Workshop Applied Example: Does an LSI confer a survival advantage?

Use dataset (berdpsa.sas7bdat) and SAS program provided. The primary outcome of interest (DIED) is mortality and the primary exposure of interest is a life-saving intervention (LSI) typically indicated for those at the highest risk of mortality.

Variables in dataset

Variable Name	Description	Additional Info
Died	1=died; 0=survived	**Outcome variable of interest**
LSI	1=Yes ;0=No	**Exposure variable of interest**
AgeP	Patient's age (continuous variable)	Prognostic factor/marker
GE55	1=age >=55 years; 0=age <55 years	Prognostic factor/marker
Male	1=male; 0=female	Prognostic factor/marker
VarPM	1=Yes ;0=No	Prognostic factor/marker
VarLV	1=Yes ;0=No	Prognostic factor/marker
VarINT	1=Yes ;0=No	Prognostic factor/marker
VarHS	1=Yes ;0=No	Prognostic factor/marker
VarCM	1=Yes ;0=No	Prognostic factor/marker
VarCD	1=Yes ;0=No	Prognostic factor/marker
VarSVH	1=Yes ;0=No	Prognostic factor/marker
VarTS	1=Yes ;0=No	Prognostic factor/marker
DSev1	Disease severity score	Prognostic factor/marker
DSev2	Disease severity score (measures different aspect)	Prognostic factor/marker
DSev1F	Disease severity score (post-baseline)	Prognostic factor/marker

PART Ia. Summary Statistics

1634 in the dataset
Outcome: Overall mortality rate was 3.7% (61/1634)
Exposure: 38% (615/1634) had an LSI
Prevalence of risk markers/potentially confounding variables/selection factors
- **33% (543) age 55 years and older**
- **69% (1124) males**
- **62% (1016) VarPM**
- **75% (1220) VarLV**
- **2% (31) VarINT**
- **4% (69) VarHS**
- **18% VarCM**
- **12% VarCD**
- **27% VarSVH**
- **27% VarTS**
- **Age range, 18-98, mean (SD) = 46 (21); median, 43**
- **Disease severity I range, 0-7.84, mean (SD) =7.56 (0.85), median 7.84**
- **Disease severity II range, 1- 75, mean 12.5 (9.6); median 10**

PART Ib. Comparability (of prognostic factors/markers) between LSI groups

Variable	LSI n=615	No LSI n=1019	p-value
Mean Age (SD)	45 (21)	46 (20.4)	0.2284
Age >=55 years , n (%)	195 (32)	348 (34)	0.3096
Male, n (%)	429 (70)	695 (68)	0.5119
VarPM, n (%)	438 (71)	578 (57)	**< 0.0001**
VarLV, n (%)	400 (65)	820 (80)	**<0.0001**
VarINT, n (%)	16 (2.6)	15 (1.5)	0.1049
VarHS, n (%)	45 (7.3)	24 (2.4)	**<0.001**
VarCM, n (%)	124 (20)	176 (17)	0.1437
VarCD, n (%)	90 (15)	107 (11)	**0.0129**
VarSVH n (%)	230 (37)	212 (21)	**< 0.0001**
VarTS, n (%)	245 (40)	195 (19)	**< 0.0001**
Mean Disease severity I (SD)	7.37 (1.1)	7.68 (0.62)	**< 0.0001**
Mean Disease severity II (SD)	16.5 (11)	10 (8)	**< 0.0001**
Mortality, n (%)	44 (7.2)	17 (1.8)	**< 0.0001**

The comparison above supports the existence of confounding by indication in that patients who received an LSI tended to have more severe disease compared to those who did not receive an LSI and the more severe the disease, the higher the risk of mortality.

Part II: Traditional multivariable analysis

One approach to minimizing confounding/selection bias is through multivariable techniques like logistic regression or Cox regression. Using the dataset provided and results from the bivariate comparisons you performed to answer question 2, run a logistic regression model adjusting for covariates to determine the independent effect of the LSI transport on mortality. Retain in the multivariable model only variables that are significantly (p<0.05) associated with the outcome in the bivariate analysis. Report the AUC (and 95% CI) for your final model? What is your overall conclusion regarding the effect of the LSI on mortality based on this analysis?

Odds Ratio Estimates and Wald Confidence Intervals				
Effect	**Unit**	**Estimate**	**95% Confidence Limits**	
LSI 1 vs 0	1.0000	2.100	1.061	4.155
VarCM 1 vs 0	1.0000	2.618	1.303	5.264
VarSVH 1 vs 0	1.0000	3.682	1.685	8.043
AgeP	1.0000	1.037	1.019	1.055
DSev1	1.0000	0.450	0.362	0.559
DSev2	1.0000	1.062	1.030	1.095

AUC (95% CI), 0.95 (0.93-0.7), HL- GOF p=0.6307

Part III: Propensity Score Analysis

Now, instead of performing multivariable adjustment, we will create propensity scores that quantify the predicted probability of receiving an LSI and then use the propensity scores in a second logistic regression model (if appropriate)

   a. Perform multivariable logistic regression that models LSI as a function of the following variables: *VarPM GE55 Male VarLV VarINT VarHS VarCM VarCD VarSVH VarTS AgeP DSev1 DSev2*. Retain in the logistsic regression model only variables with a p-value < 0.20. ***I did not include interaction terms in this model, but one should definitely consider including such terms if it improves treatment assignment prediction.*** What is the AUC (95% CI) for the propensity score model?

Odds Ratio Estimates and Wald Confidence Intervals				
Effect	**Unit**	**Estimate**	**95% Confidence Limits**	
VarPM 1 vs 0	1.0000	1.313	1.040	1.657
VarLV 1 vs 0	1.0000	0.546	0.427	0.698
VarINT 1 vs 0	1.0000	0.446	0.164	1.214
VarHS 1 vs 0	1.0000	1.737	0.967	3.123

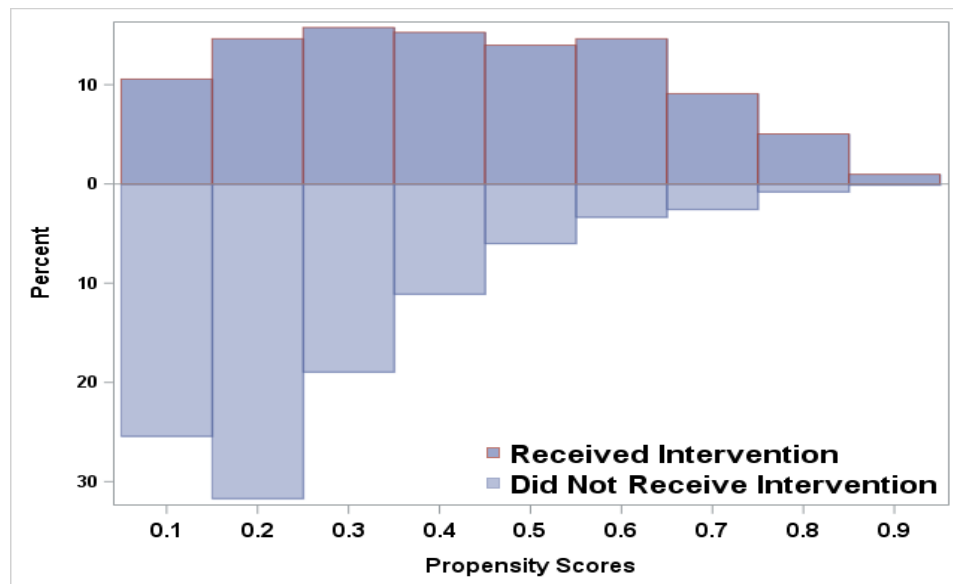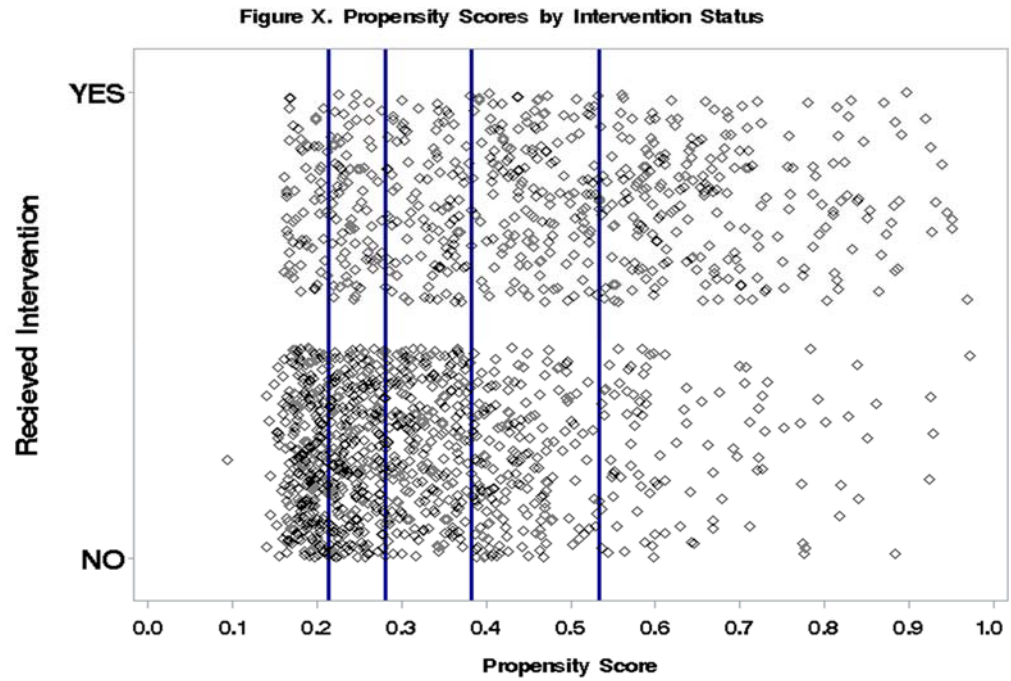| Odds Ratio Estimates and Wald Confidence Intervals				
Effect	Unit	Estimate	95% Confidence Limits	
VarSVH 1 vs 0	1.0000	1.409	1.031	1.925
VarTS 1 vs 0	1.0000	1.678	1.221	2.307
AgeP	1.0000	0.996	0.990	1.001
DSev1	1.0000	0.773	0.643	0.929
DSev2	1.0000	1.041	1.021	1.061

AUC (95% CI): 0.72 (0.69-0.75); H-L Goodness-of-Fit Test, p=0.1014

Note on using ROC (AUC) analysis - Some suggest propensity score models are best assessed with standardized difference and balance of the covariants. There have been several studies, including a well-regarded study by Brookhart et al. (Brookhart MA, et al. Variable selection for propensity score models. American Journal of Epidemiology. 2006 Apr 19; 163 (12):1149-56.), that suggest that AUCs are not the best way to characterize the performance of a propensity model as they are meant to control confounders and not necessarily to predict treatment.

b. Use SAS PROC RANK to establish quintiles for the propensity scores or probabilities, and then compare the distribution of propensity scores across quintiles, between the LSI=1 and LSI=0 groups.

Table of quintile by LSI			
quintile(Rank for Variable pscore)	LSI		
Frequency Col Pct	0	1	Total
0	267 26.20	59 9.59	326
1	248 24.34	78 12.68	326
2	227 22.28	101 16.42	328
3	175 17.17	152 24.72	327
4	102 10.01	225 36.59	327
Total	1019	615	1634

c. Graphically assess distribution of propensity score across LSI groups

Figure X. Propensity Scores by Intervention Status

d. Assess effectiveness of propensity score as a balancing score – significance testing

Variable	LSI n=615	No LSI n=1019	p-value	p-value ps-adjusted
Mean Age (SD)	45 (21)	46 (20.4)	0.2284	0.8116
Age >=55 years , n (%)	195 (32)	348 (34)	0.3096	0.6697
Male, n (%)	429 (70)	695 (68)	0.5119	0.4343
VarPM, n (%)	438 (71)	578 (57)	**< 0.0001**	0.8171
VarLV, n (%)	400 (65)	820 (80)	**<0.0001**	0.9407
VarINT, n (%)	16 (2.6)	15 (1.5)	0.1049	0.6667
VarHS, n (%)	45 (7.3)	24 (2.4)	**<0.001**	0.2625
VarCM, n (%)	124 (20)	176 (17)	0.1437	0.9296
VarCD, n (%)	90 (15)	107 (11)	**0.0129**	0.1968
VarSVH n (%)	230 (37)	212 (21)	**< 0.0001**	0.6714
VarTS, n (%)	245 (40)	195 (19)	**< 0.0001**	0.5999
Mean Disease severity I (SD)	7.37 (1.1)	7.68 (0.62)	**< 0.0001**	**0.0207**
Mean Disease severity II (SD)	16.5 (11)	10 (8)	**< 0.0001**	**0.0130**

Note – severity scores (both DSev1 and DSev2) not balanced between treatment groups