

BIAS REDUCTION IN OBSERVATIONAL COHORT STUDIES

- using Propensity scores

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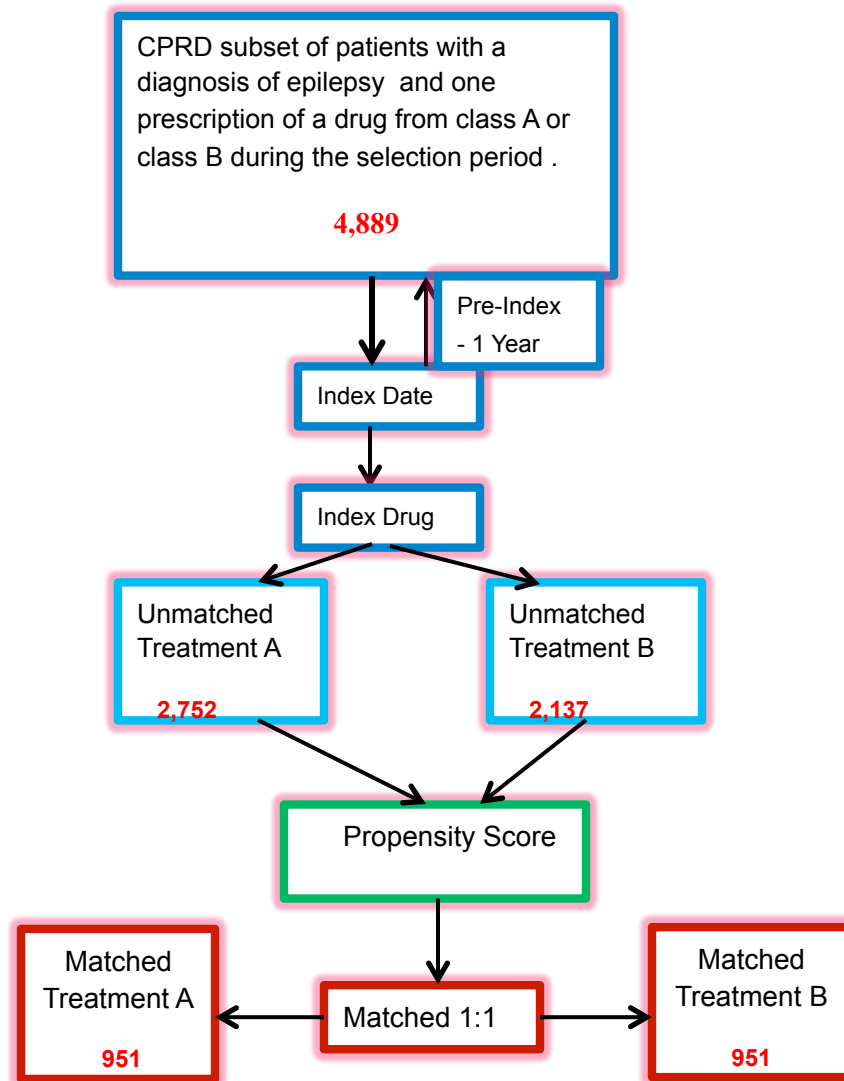
AGENDA

- ◉ Introduction - Matching and Propensity Scores
- ◉ Study Design
- ◉ How it was done - Variable Selection and PROC LOGISTIC
- ◉ Matching approach
- ◉ Results of matching
- ◉ Conclusion
- ◉ Acknowledgements

INTRODUCTION

- ◉ The aim of this study was to compare the direct healthcare cost of treating patients with epilepsy on a particular class of drugs from treatment A against another class of drugs from treatment B, using the propensity score-matched cohort methodology on a 1:1 basis.
- ◉ Matching
 - is where exposed subjects are matched to unexposed based on their baseline characteristics
 - limitations : large sample size, large number of confounders
 - advantages: reduce confounding
- ◉ Propensity Score: the probability of the patient being prescribed treatment B on the basis of the selected covariates at baseline

STUDY DESIGN



VARIABLE SELECTION FOR THE PROPENSITY SCORE MODEL

- Selection of the baseline Characteristics including the epilepsy related clinical variables.
 - All of the Baseline Characteristics variables were selected.
- Selection of the Comorbidities and Concomitant medication
 - If either the treatment differences were statistically different with a p-value of <0.05 or if the comorbidity or the medication had an incidence of $>1\%$ in either treatment .
 - 318 variables used for matching

MATCHING APPROACH

- ◉ Propensity Score Creation using PROC LOGISTIC

```
proc logistic data=fullbase;  
class &varlistc/order=freq param=ref ref=first;  
model indextype (event="TRTB")=&varlist;  
output out=prop_score p=prop_score;  
run;
```

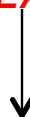
PROC LOGISTIC

- fits the linear logistic regression models for binary (Y's , N's) or ordinal response data by the method of maximum likelihood
- modelled the likelihood of a patient receiving treatment B using '(event=TRTB)' and the numeric and character confounding variables in the &varlist, the character variables are specified in the class statement
- param= option defines the parameterisation and uses the variable ref which specifies the baseline variable in 'ref=first'
- prop_score is the output dataset and p= names the variable containing the predicted probabilities i.e. the propensity score.

MATCHING APPROACH (CONT'D)

- Propensity Score was transformed to $\text{logit(PS)} = \log(\text{prop_score} / (1 - \text{prop_score}))$;
- Caliper = $0.2 * \text{std}(\text{logitps})$
- Matching carried out using a validated in-house macro which applied the Caliper method without replacement.
- Within each age range subjects were matched on their $\text{logit(PS)} \pm \text{caliper}$

TREATED LOGIT(PS) (21-30 YRS)



$\pm \text{CALIPER}$

CONTROL LOGIT(PS) (21-30 YRS)

RESULTS

- Matching was successful as there was a good overlap of the logit(PS) :

Figure 1 Bar Chart of propensity scores by Cohort by 0.1 score range and Histogram of Logit PS

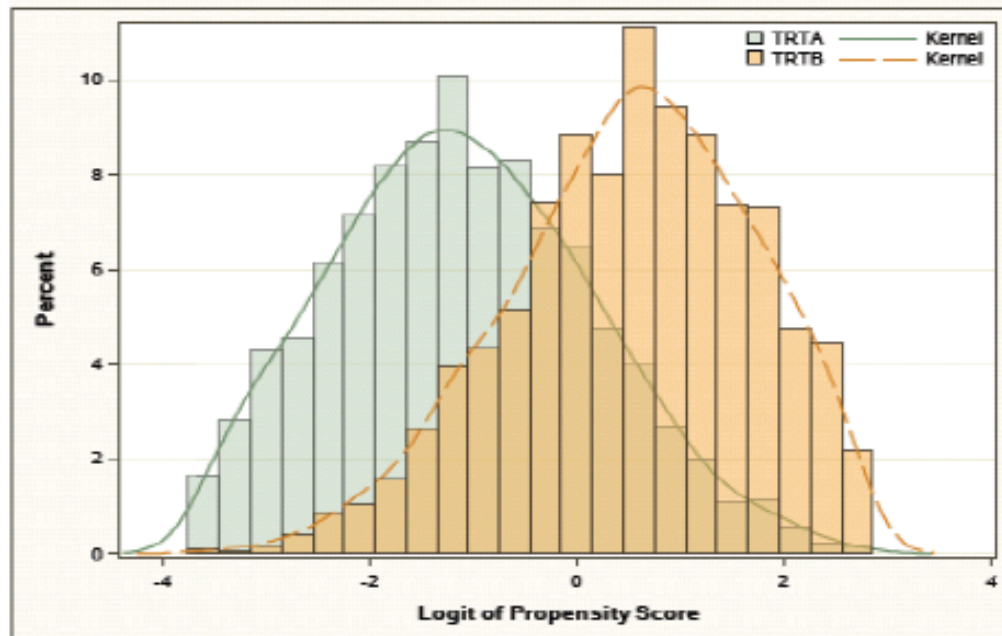


Table 1- Statistically Significant Baseline Covariates before and after Matching

Variable - Category	Statistic	TRT A (N=2752) Unmatched	TRT B (N=2137) Unmatched	P-value Unmatched	TRT A (N=951) Matched	TRT B (N=951) Matched	P-value Matched
Age at index date (Years)	N	2,752	2,137		951	951	
	Mean(Std)	54.2(19.8)	45.9(19.9)	<.0001	47.7(19.9)	48.0(20.0)	0.7969
Age Band				<.0001			1.0000
16-20	N(%)	116(4.2%)	239(11.2%)		75(7.9%)	75(7.9%)	
21-30	N(%)	261(9.5%)	349(16.3%)		144(15.1%)	144(15.1%)	
31-40	N(%)	404(14.7%)	344(16.1%)		167(17.6%)	167(17.6%)	
41-50	N(%)	434(15.8%)	380(17.8%)		160(16.8%)	160(16.8%)	
51-60	N(%)	406(14.8%)	285(13.3%)		133(14.0%)	133(14.0%)	
61-70	N(%)	425(15.4%)	236(11.0%)		119(12.5%)	119(12.5%)	
71-80	N(%)	434(15.8%)	191(8.9%)		94(9.9%)	94(9.9%)	
81-90	N(%)	237(8.6%)	96(4.5%)		47(4.9%)	47(4.9%)	
91+	N(%)	35(1.3%)	17(0.8%)		12(1.3%)	12(1.3%)	
Patient's Gender				<.0001			0.7130
Female	N(%)	1,243(45.2%)	1,339(62.7%)		506(53.2%)	514(54.0%)	
Male	N(%)	1,509(54.8%)	798(37.3%)		445(46.8%)	437(46.0%)	

Table 2- Statistically Significant Baseline Co-Medication before and after Matching

Variable - Category	Statistic	TRT A (N=2752) Unmatched	TRT B (N=2137) Unmatched	P-value Unmatched	TRT A (N=951) Matched	TRT B (N=951) Matched	P-value Matched
Hormonal contraceptives				<.0001			0.2702
No	N(%)	2,657 (96.5%)	1,883 (88.1%)		882 (92.7%)	869 (91.4%)	
Yes	N(%)	95 (3.5%)	254 (11.9%)		69 (7.3%)	82 (8.6%)	
Sex hormones				0.0224			0.7747
No	N(%)	2,608 (94.8%)	1,992 (93.2%)		891 (93.7%)	894 (94.0%)	
Yes	N(%)	144 (5.2%)	145 (6.8%)		60 (6.3%)	57 (6.0%)	
Antidepressant / Antipsychotic drugs				<.0001			0.5712
No	N(%)	1,999 (72.6%)	1,416 (66.3%)		697 (73.3%)	686 (72.1%)	
Yes	N(%)	753 (27.4%)	721 (33.7%)		254 (26.7%)	265 (27.9%)	
Immunosuppressants, ex glucocorticoids				0.0003			1.0000
No	N(%)	2,737 (99.5%)	2,103 (98.4%)		944 (99.3%)	944 (99.3%)	
Yes	N(%)	15 (0.5%)	34 (1.6%)		7 (0.7%)	7 (0.7%)	

CONCLUSION

- ◉ Main challenges (Programmer's perspective):
 - Decision on best matching method to use
 - Guidance on which covariates should be selected for the propensity score model
 - May have to advise team on variable selection via exploratory analysis and prior experience
 - Team decision on variable selection is final!
- ◉ Matching successfully implemented: 1902 matched subjects out of 4,889
- ◉ The two groups were balanced on all variables
- ◉ Confident that the cost results were based on subjects with the same baseline characteristics and confounding reduced.

ACKNOWLEDGEMENTS

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