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A Case Application of Propensity Score Matching in the Outcomes Evaluation of Medication Therapy Management at Retail Pharmacy

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ABSTRACT

Propensity score matching (PSM) is commonly used in observational studies to reduce the potential selection bias. The process of PMS includes propensity score estimation, matching and evaluation. This paper presents a case application in outcome evaluation of medication therapy management at retail pharmacy. It illustrates how baseline outcome balance check could help detect potential omissions of covariates that could affect both the treatment and the outcomes. Further, it shows how in retail MTM setting, it is possible to find a common set of covariates that affect multiple studies outcomes and perform a single propensity score matching rather than a separate matching for each individual study outcome.

KEYWORDS: Observational study, selection bias, propensity score matching

INTRODUCTION:

Propensity Score Matching is widely used in observational studies. The basic idea of PSM is to match an untreated group to the treated group such that the matched group is comparable to the treated group in all aspects of characteristics except the treatment. The observed outcome for the matched group can then be used as the counterfactual, and the treatment effect is estimated simply as the difference between the average outcomes of the two groups.

The challenge of PSM is that the propensity score is unknown and must be estimated with a propensity score model. The quality of propensity score model is evaluated solely on the covariates balance between the treated and untreated groups. Conventional balance tests typically check for differences in average covariates between the treated and un-treated groups to see if there remain any significant differences between the two groups after propensity score matching.

It is obviously important that the propensity score model balances the covariates. But how do we ensure that all covariates relevant to the study are incorporated into the model? The current paper attempts to address this very issue by way of a case application, in which we examined multiple baseline study outcomes to verify that the PSM model is correctly specified with all relevant covariates. Conventionally, when a study involves multiple outcomes, PSM is performed for each individual outcome. In our current case application, a single PSM was done for multiple study outcomes. We then check for balance in all study outcomes at baseline, between the treated and un-treated groups, after propensity score matching. A correctly specified PSM model should balance all study outcomes at baseline.

CASE APPLICATION IN MEDICATION THERAPY MANAGEMENT AT RETAIL PHARMACY

A medication therapy management program at a national retail pharmacy chain provides its patients comprehensive medication review (CMR) to promote safe and effective use of medications. During a review session, a store pharmacist meets one-on-one with his patient to: 1.organize the patient's medications, 2.evaluate the patient's medications for cost-saving alternatives, 3.review medications for side effects or harmful drug-drug interactions, 4.provide patient with a list of active medications the patient is on, 5. educate the patient on the importance of medication adherence, answer any questions that patient may have about his prescriptions, and coordinate any medication changes with his primary physician.

A retrospective cohort study with a propensity matched control was conducted to evaluate the effects of CMR on brand to generic drug savings, medication adherence and immunization rates among the study subjects. The treatment group consisted of patients who had at least one completed CMR between Jan 2011 and Jun 2011. The control group consisted of patients who received no CMR and had at least one prescription filled at Walgreens between Jan 2011 and Jun 2011. A 3.5% random sample (1,482,330 patients) was drawn from Walgreens EDW to serve as the pool for control group.

BASELINE COVARIATES BEFORE PROPENSITY SCORE MATCHING

As numbers shown in Table 1, the baseline covariates were not balanced between the treatment and control groups before propensity matching.

Table 1. Baseline Covariates Before Propensity Score Matching

Covariates		Treatment (7,229)		Control (1,482,330)		p-value
		N	%	N	%	
Age	Under 18	4	0.1%	356,453	24.0%	
	[18, 36)	58	0.8%	356,264	24.0%	
	[36, 50)	297	4.1%	288,926	19.5%	
	[50, 65)	1,219	16.9%	284,825	19.2%	
	[66, 80)	4,308	59.6%	145,887	9.8%	
	[80+	1,343	18.6%	49,975	3.4%	< 0.0001
	Mean Age (S.D.)	70.7	11.0	37.7	23.0	
Gender	Female	4,437	61.4%	848,814	57.3%	
	Male	2,792	38.6%	633,516	42.7%	< 0.0001
Insurance Plan	Cash	12	0.2%	157,901	10.7%	
	Commercial	1,960	27.1%	662,915	44.7%	
	Medicaid	7	0.1%	186,674	12.6%	
	Medicare	5,243	72.5%	406,496	27.4%	
	Other	0	0.0%	5,142	0.3%	
	PSC	4	0.1%	32,665	2.2%	
	Tricare	3	0.0%	30,537	2.1%	< 0.0001
# of Therapeutics	<= 3	680	9.4%	1,075,348	72.5%	
	<= 6	1,407	19.5%	264,230	17.8%	
	<= 9	1,921	26.6%	90,943	6.1%	
	>= 10	3,221	44.6%	51,809	3.5%	< 0.0001
Copay	Mean (S.D.)	$384	$489	$84	$221	< 0.0001
Total Drug Costs	Mean (S.D.)	$2,181	$2,151	$398	$1,062	< 0.0001
# Competing Business	Mean (S.D.)	4.54	3.46	4.59	3.27	0.29
Community Income	Under Class	10	0.1%	1,121	0.1%	
	Working poor	171	2.4%	19,333	1.3%	
	Working class	4,081	56.5%	699,476	47.2%	
	Lower middle class	2,919	40.4%	733,112	49.5%	
	Upper middle class	48	0.7%	29,288	2.0%	< 0.0001
Community Race Mix	% White	0.79	0.2	0.79	0.2	0.14
	% Asian	0.03	0.06	0.04	0.07	< 0.0001
	% Black	0.15	0.19	0.14	0.2	< 0.0001
	% Hispanic	0.17	0.22	0.18	0.22	< 0.0001

BASELINE COVARIATES AFTER PROPENSITY SCORE MATCHING

The initial PSM model includes the following baseline covariates

- Age
- Gender
- Co-pay
- Total Drug Cost
- Average Cost per Rx
- Number of therapeutic classes
- Insurance Plan
- Average community Income
- Community Race composition

Different methods can be used to estimate propensity score: probit / logistics models, classification trees, neural networks etc. We opted for SAS PROC LOGISTIC and below are the SAS codes for the initial PSM model with the above listed covariates and the treatment assignment variable EVENT. The estimated propensity scores are stored in the variable PROB and saved in the SAS dataset PSMScore

```
%let predictors = Agecat gndr_cd copay total_drug_cost RevenuePerRx nTherapClass Insurance
                  incomegroup __White __Asian __Black __Hispanic;

proc logistic data = &PSMdata descending;
     class   Agecat gndr_cd nTherapClass Insurance incomegroup
             nTherapClass;
     model   Event=&predictors;
     output  out = PSMScore(drop=_LEVEL_ index=(event=(event))) prob=prob;
run;
```

We used caliper matching algorithm to match the control group to the treatment group on a 1-to-1 ratio without replacement. The algorithm adjusts the caliper width from 4 to 1 decimal places so that it finds the "best" match first and the "next-best" match next. In the event of multiple matches, the algorithm randomly selects a control for the treatment.

The actual SAS codes are included in the appendix with the following parameters:

- InData: input SAS data set for propensity score matching
- OutData: output SAS data set after propensity score matching
- DependentVar: dependent variable for group assignment (0,1 coded, 1=treatment 0=control)
- EstimatedProb : variable holding propensity score value
- N: propensity matching ratio (1:N matching)
- MaxDigit : starting decimal places used to match propensity score
- PickupMethod : either select the first (FIXED) or a random control for the treatment In the event of multiple controls
- Method: matching with or without replacement (REPLACEMENT or NOREPLACEMENT)

Covariates balance check after propensity score matching indicated that the baseline covariates were comparable between the two groups (Table 2).

Table 2. Baseline Covariates After Propensity Score Matching

Covariates		Treatment (7,166)		Control (7,166)		p-value
		N	%	N	%	
Age	Under 18	4	0.1%	7	0.1%	
	[18, 36)	58	0.8%	60	0.8%	
	[36, 50)	297	4.1%	287	4.0%	
	[50, 65)	1,218	17.0%	1,258	17.6%	
	[66, 80)	4,253	59.3%	4,265	59.5%	
	[80+	1,336	18.6%	1,289	18.0%	0.77
	Mean Age (S.D.)	70.7	11.1	70.2	11.6	
Gender	Female	4,395	61.3%	4,379	61.1%	
	Male	2,771	38.7%	2,787	38.9%	0.78
Insurance Plan	Cash	12	0.2%	5	0.1%	
	Commercial	1,956	27.3%	2,000	27.9%	
	Medicaid	7	0.1%	3	0.0%	
	Medicare	5,184	72.3%	5,148	71.8%	
	Other	0	0.0%	4	0.1%	
	PSC	4	0.1%	3	0.0%	
	Tricare	3	0.0%	3	0.0%	0.16
# of Therapeutics	<= 3	680	9.5%	631	8.8%	
	<= 6	1,406	19.6%	1,393	19.4%	
	<= 9	1,910	26.7%	1,903	26.6%	
	>= 10	3,170	44.2%	3,239	45.2%	0.45
Copay	Mean (S.D.)	$383	$487	$396	$811	0.23
Total Drug Cost	Mean (S.D.)	$2,165	$2,093	$2,243	$3,670	0.12
# Competitors	Mean (S.D.)	4.54	3.47	4.53	3.35	0.90
Community Income	Under Class	10	0.1%	12	0.2%	
	Working poor	171	2.4%	172	2.4%	
	Working class	4,040	56.4%	4,066	56.7%	
	Lower middle class	2,897	40.4%	2,855	39.8%	
	Upper middle class	48	0.7%	61	0.9%	0.71
Community Race Mix	% White Mean (S.D.)	0.79	0.20	0.79	0.20	0.70
	% Asian Mean (S.D.)	0.03	0.06	0.03	0.06	0.29
	% Black Mean (S.D.)	0.15	0.19	0.15	0.19	0.37
	% Hispanic Mean (S.D.)	0.17	0.23	0.17	0.24	0.20

*Chi-squared test and paired t test were used

BASELINE OUTCOMES CHECK:

However, baseline study outcomes check revealed that even though the propensity score model balanced the baseline covariates, it did not balance the baseline outcomes generic dispense rates (GDR). As was shown in table 3, the baseline GDR for the treatment group was nearly twice that of the control group after propensity score matching.

Table3: Baseline Generic Dispense Rate after Propensity Score Matching

Group	# Patients	Baseline Generic Dispense Rate	P-value
Treatment	1367	11.7%	
Control	1383	6.7%	<.0001

We could incorporate baseline GDR into the propensity score model to force a baseline GDR balance. However, to do so would most likely require us to do a separate propensity matching for each study outcomes. In addition, baseline GDR was balanced does not necessarily mean the model is correctly specified with all relevant covariates. It's important to try to uncover any additional confounders that was not considered in the model and could potentially affect the study outcomes.

BASELINE COVARIATES RECHECK AFTER PROPENSITY SCORE MODEL ADJUSTMENT

A closer examination of the data revealed that the index dates, which defined GDR baselines for the two groups, were not balanced. We then added the index month in the propensity model, re-matched the two groups and checked the baseline GDR again. As was shown in table 4, the baseline GDR now appeared to be balanced.

Table 3. Baseline Covariates After Propensity Score adjustment

Covariates		Treatment (7,142)		Control (7,142)		p-value
		N	%	N	%	
Age	Under 18	4	0.1%	10	0.1%	
	[18, 36)	58	0.8%	54	0.8%	
	[36, 50)	297	4.2%	290	4.1%	
	[50, 65)	1,219	17.1%	1,226	17.2%	
	[66, 80)	4,230	59.2%	4,238	59.3%	
	[80+	1,334	18.7%	1,324	18.5%	0.72
	Mean Age (S.D.)	70.6	11.1	70.3	11.7	0.08
Gender	Female	4,381	61.3%	4,394	61.5%	
	Male	2,761	38.7%	2,748	38.5%	0.82
Insurance Plan	Cash	12	0.2%	13	0.2%	
	Commercial	1,956	27.4%	1,973	27.6%	
	Medicaid	7	0.1%	7	0.1%	
	Medicare	5,160	72.2%	5,140	72.0%	
	Other	0	0.0%	6	0.1%	
	PSC	4	0.1%	2	0.0%	
	Tricare	3	0.0%	1	0.0%	0.25
# of Therapeutics	<= 3	680	9.5%	635	8.9%	
	<= 6	1,407	19.7%	1,438	20.1%	

	<= 9	1,907	26.7%	1,941	27.2%	
	>= 10	3,148	44.1%	3,128	43.8%	0.52
MTM Complete Month	01/2011	428	6.0%	412	5.8%	
	02/2011	727	10.2%	670	9.4%	
	03/2011	1,165	16.3%	1,209	16.9%	
	04/2011	1,531	21.4%	1,552	21.7%	
	05/2011	1,575	22.1%	1,600	22.4%	
	06/2011	1,716	24.0%	1,699	23.8%	0.57
Copay	Mean (S.D.)	$384	$488	$386	$704	0.85
Total Drug Cost	Mean (S.D.)	$2,170	$2,134	$2,103	$3,445	0.16
Revenue Per Rx	Mean (S.D.)	$70	$219	$68	$151	0.56
Neighborhood Income	Under Class	10	0.1%	9	0.1%	
	Working poor	170	2.4%	171	2.4%	
	Working class	4,029	56.4%	4,081	57.1%	
	Lower middle class	2,885	40.4%	2,832	39.7%	
	Upper middle class	48	0.7%	49	0.7%	0.93
Neighborhood Race	% White Mean (S.D.)	0.79	0.20	0.79	0.20	0.60
	% Asian Mean (S.D.)	0.03	0.06	0.03	0.05	0.99
	% Black Mean (S.D.)	0.15	0.19	0.15	0.20	0.66
	% Hispanic Mean (S.D.)	0.17	0.23	0.17	0.23	0.70

*Chi-squared test and paired t test were used

Table 4: Baseline Generic Dispense Rate after Final Propensity Score Matching

Group	# Patients	Baseline Generic Dispense Rate	P-value
Treatment	1501	11.7%	
Control	1481	10.9%	0.36

OTHER BASELINE OUTCOMES:

We then checked the baseline pneumovax and zoster immunization rates (table 5 and 6) and again they appeared to be balanced between the two groups.

Table 5 Baseline Pneumovax immunization Rate after Final Propensity Score Matching

Group	# Patients	Baseline Pneumovax immunization Rate	P-value
Treatment	7,142	0.3%	
Control	7,142	0.3%	0.75

Table 6 Baseline Zoster immunization Rate after Final Propensity Score Matching

Group	# Patients	Baseline Zoster immunization Rate	P-value
Treatment	7,142	0.4%	
Control	7,142	0.4%	1.00

Lastly, we checked the baseline medication adherence as measured in proportion of days covered or PDC for 5 select drug categories (table 7) and once more they appeared to be balanced between the two groups.

Table 7 Baseline Proportion of Days Covered (PDC) after Final Propensity Score Matching

Drug Category	Treatment Group		Control Group		p-value
	N	PDC	N	PDC	
ANTIDIABETICS	3,320	0.87	2,008	0.87	0.87
ANTIHYPERLIPIDEMICS	3,792	0.89	2,745	0.90	0.24
ANTIHYPERTENSIVES	3,693	0.91	2,814	0.91	0.82
BETA BLOCKERS	2,205	0.91	1,782	0.90	0.19
CALCIUM CHANNEL BLOCKERS	1,500	0.92	1,137	0.92	1.00
OVERALL	14,510	0.90	10,486	0.90	0.30

CONCLUSION

The propensity score model balanced all the study outcomes on top of the covariates, which, to a degree, validated the model and we were able to conduct the study as if it were a pseudo randomized study with just a single matching to evaluate multiple outcomes.

REFERENCES

1. Lori S. Parsons, “Performing a 1: N Case-Control Match on Propensity Score”, May 2004, SUGI29

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Appendix

```
%macro _MPSMSingleMatch(Out =, InCase= , InControl=, EstimatedProb = prob, No=No, Recordno= recordno, Digit = 5) ;
      * Step 0: data  preparation;
      data _null_; set &InCase;
            if _n_=&recordno then do;
                call  symput('_LocalPSScore'  ,roundP);  call  symput('M_CaseSeqn'        ,  seqn);  call  symput('M_CaseUniqueID',  UniqueID);
            end;
       run;
      * Step 1: in the event of multiple match s, first match is selected;
      %let M_Status=fail; %local iOrder; %let iOrder = 1; %let total  = 0;
      %if %upcase(&PickupMethod) ne FIXED %then %do;
       %let total = 0;
      proc sql noprint;
           select count(*) into :total from &InControl where roundP = &_LocalPSScore;
      quit;
      data _null_; if &total >= 1 then do; call symput('iOrder', floor(1 + &total*ranuni(9646429)));  end;  run;
  %end;
  %put total = &total iOrder = &iOrder;
  data tmp(keep=CaseUniqueID MatchID CaseSeqn ControlSeqn);
       set &InControl(where=( roundP=&_LocalPSScore )) nobs=total;
       if total>=1 then call symput('M_Status',"succeed");
       if  _n_  =&iOrder then do;
            CaseUniqueID=&M_CaseUniqueID;
            MatchID     = &Digit;
            CaseSeqn    = &M_CaseSeqn;
            ControlSeqn = seqn;
            call symput('M_ControlSeqn',seqn);
```

```
                output;
            end;
        run;
    * Step 3: Remove selected observations from the control pool;
    %if &M_Status eq succeed %then %do;
        %if %upcase(&method) eq NOREPLACEMENT %then %do;
                data &InControl;
                    set &InControl;
                    if seqn = &M_ControlSeqn then delete;
                run;
        %end;
        proc append base=&Out data=tmp force;run;
        proc sql;
                update &InCase
                set status = 'YES'
                where seqn =  &M_CaseSeqn;
        quit;
%end;
%mend _MPSMSingleMatch;

%macro _mPSMatch(Indata=, OutData=, DependentVar=, EstimatedProb=prob, N=1, MaxDigit= 6, PickupMethod=Fixed
            , method=NOREPLACEMENT);
          OPTION SPOOL nosymbolgen nomprint nomlogic;
          * Step 0: Generate case and Control data set with a unique ID;
         data _case(drop=EventCount NonEventCount)  _control(drop=EventCount NonEventCount);
                set   &Indata;
                where &EstimatedProb ne . ;
                retain EventCount    1; retain NonEventCount 1;
                if    &DependentVar =1 then do; UniqueID = EventCount; output _case; EventCount = EventCount + 1; end;
                else  do; UniqueID = NonEventCount; output _control; NonEventCount = NonEventCount + 1; end;
         run;
         %global _nTotalCases _nMatchedCases;
                proc sql noprint;select count(*) into :_nTotalCases from _Case; quit;
                %local k;
                %do k=1 %to &N;
                    proc sort data=_case       ;  by &EstimatedProb; run;
                    proc sort data=_control   ;  by &EstimatedProb; run;
                    data _case    _CaseOrig   ;  set _case   ; seqn = _n_;Status = 'NO ';run;
                    data _control _ControlOrig;  set _control; seqn = _n_;Status = 'NO ';run;
                    * Step 1: make sure the output file is new;
                    %if %sysfunc(exist(_TMPMatchedOut)) %then %do;
                        proc sql; drop table _TMPMatchedOut; quit;
                     %end;
```

```
* Step 2: Matching with varied Caliper width / decimal places;
%local i j;
%do i=1 %to &MaxDigit;
        %let Number =0;
        proc sql noprint;select count(*) into :Number from _case;quit;
        data _case; set _case; roundP = round(&EstimatedProb,10**(- %eval(&MaxDigit - &i + 1) )); run;
        data _control; set _control; roundP = round(&EstimatedProb,10**(- %eval(&MaxDigit - &i + 1) )); run;
        %do j=1 %to &Number;
              %_MPSMSingleMatch(Out =_TMPMatchedOut, InCase=_case, InControl=_control
                                    , EstimatedProb = prob, Recordno= &j, Digit = %eval(&MaxDigit - &i + 1) );
        %end;
        data _case; set _case; where status ^= 'YES'; run;
 %end;
 * Merge Original Data together;
 data Link; set _TMPMatchedOut; PairID = _n_; run;
 proc sql;
        create table _case&k(drop=seqn status) as
                select _caseOrig.*   ,Link.MatchID,Link.CaseUniqueID,Link.PairID  from _caseOrig   ,Link
                where  _caseOrig.seqn    = Link.CaseSeqn;
        create table _control&k(drop=seqn status) as
                 select _ControlOrig.*,Link.MatchID,Link.CaseUniqueID,Link.PairID
                 from _ControlOrig,Link where  _ControlOrig.seqn = Link.ControlSeqn;
       create table _case  as  select * from _caseOrig;
        create table _control as
                 select _ControlOrig.* from _ControlOrig where  _ControlOrig.seqn not in (select ControlSeqn from Link);
 quit;
 * Prepare output;
  %if &k eq 1 %then %do;
       data _CaseOut;  set _case&k;  run;
       data _ControlOut; set _control&k; run;
  %end;
  %else %do;
        proc sql;
              create table _CaseOut as
              select _caseout.* from _CaseOut as A   , _case&k as B  where A.CaseUniqueID=B.CaseUniqueID;
              create table _ControlOut as
               select A.* from _ControlOut as A, _control&k as B where A.CaseUniqueID=B.CaseUniqueID
               union
               select B.* from _ControlOut as A, _control&k as B where A.CaseUniqueID=B.CaseUniqueID;
        quit;
     %end;
%end;
 data &outData(drop=UniqueID PairID rename=(MatchID=MatchPrecision CaseUniqueID=GroupID)
```

```
                    index=(GroupID=(GroupID) &DependentVar=(&DependentVar)));
            set _CaseOut _ControlOut;
        run;
        proc sql noprint;select count(*) into :_nMatchedCases from _CaseOut; quit;
        *  Remove temp files from the matching process;
        proc sql noprint;
            drop table _case,_control,Link,Tmp,_Caseorig,_Controlorig,_tmpmatchedout;
        quit;
%mend  _mPSMatch;

%_mPSMatch(InData=PSMScore, OutData= data.CMRMatch, DependentVar=event, EstimatedProb = prob, N = 1, MaxDigit = 4,
        PickupMethod = RANDOM, method = NOREPLACEMENT);
```