

A SAS Macro for Variable Ratio Treatment vs. Placebo in Propensity Score Matching



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Acknowledgement



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Agenda

- Matching Analysis
 - Similar Groups
- Propensity Score
 - Computation
 - Propensity Score Matching (PSM)
- Introduction to Methods
- Key Questions
 - One-to-Many Match (Variable Ratio)
- To demonstrate the implementation of SAS Macro

Motivation

- A story of.....*Million dollar question*
 - Clinical trial with no 'Placebo' arm
 - FDA questioned about effectiveness of Treatment vs Placebo
 - *Can we save the Clinical Trial from being conducted again?*
 - How to achieve it?

Comparison Is Questionable

Non-randomized experiment because of non-random allocation of patients to surgeons.



Haha...Only 5
of mine died. I
**must be a
better surgeon**

No...no...no.. My
patients were probably
**older and had a higher
risk** than your patients



Matching Analysis

- Technique to evaluate treatment effect by comparing the treated (Cases) and the non-treated units (Controls)
- Goal
 - **Identifying pairs** of subjects/units from two treatment groups who are similar in their profiles (observable characteristics)
- Enables a meaningful comparison of clinical outcome(s)

Propensity Score (PS)

- Propensity means natural tendency to behave in a particular way
- Probability of a unit (viz. person) being assigned to a particular treatment (Yes =1/No = 0) given a set of observed covariates
- Computation: Logistic Regression (PROC LOGISTIC)
- PSM: Matching using PS

Introduction to methods

- Exact Matching on the covariates
 - To obtain **exact** match
 - Matched set in this case is identical for comparison of treatments
 - Easy to understand but difficult to get exact matches
- Nearest available matching PS
 - To obtain the **nearest** 'case' to match with 'control' based on PS
 - No restriction on 'nearness'
- Nearest available Mahalanobis metric matching within calipers
 - Caliper: One quarter of a standard deviation of the logit of the propensity score
 - Optimal/Best technique

Key Questions

- How to maximize the number of propensity score matches?
- One - to - Many Matching
- Is it possible based on 'Optimal Method'?

Implementation of SAS Macro (EXAMPLE)

- Data
 - Hypothetical data was used for demonstration purpose
 - Covariates (Age, Sex, Country, Time since symptoms, Number of relapses etc.)
- Population
 - Number of patients who received Placebo (**'Controls'**): $N(P) = 600$ and Treatment (**'Cases'**): $N(T) = 2629$
- The analyst is allowed to specify the number of cases to match with each control (or vice versa.)
- Here, 1:K (Where $K = 3$) is explained

Macro Parameters and their Description:

```
%macro match(data, class, yvar, xvar, var, id, K);
```

```
/**--Defining Variable--**/
```

- 1) **data**- The dataset containing all the case and control subject information
- 2) **class**- The categorical independent variables for calculating Propensity Score in PROC LOGISTIC
- 3) **yvar**- Treatment variable i.e. Treatment=0 for Control and Treatment=1 for Case. Also, the dependent variable for calculating Propensity Score in PROC LOGISTIC
- 4) **xvar**- The set of independent variables for calculating Propensity Score in PROC LOGISTIC
- 5) **var**- The key variables (including propensity score as one key variable) for calculating the Mahalanobis distance
- 6) **id**- The Patient ID i.e. USUBJID
- 7) **K**- Variable Ratio/The number of iteration for propensity score matching

Matching Algorithm

- Compute PS for every patient
- Sort control group randomly and select the first control
- Identify the cases within the caliper (*here, 0.18*). These are initial matched patients
- Three situations can arise;
 - i) No candidate is located within the caliper
 - ii) Only one candidate is identified
 - iii) **Two or more candidates are identified**
- Mahalanobis Distance

Continued...

- All controls, initially matched with 'best' cases
- Remove the control completely if it fails to get matched case during iteration
- At each iteration, pool the un-matched cases
- Combine all matched pairs
- Final dataset gives the matched group, such that each control matched with K (specified) cases

Table 1: Original Population (Un-matched Data)

	Placebo	Treatment	p-value
Total Patients , n	600	2629	
Age, mean (SD), years	34.7 (9.17)	36.2 (9.04)	0.0002
Sex - Female, n (%)	392 (65.33)	1806 (68.70)	0.111
Country - USA, n (%)	177 (29.50)	472 (17.95)	<.0001
Ethnicity - Not Hispanic, n (%)	357 (59.50)	723 (27.55)	<.0001
Race - White, n (%)	363 (60.50)	1432 (54.51)	<.0001
Height, mean (SD), cm	169.6 (9.05)	169.1 (9.19)	0.1899
Weight, mean (SD), kg	75.5 (19.15)	72.3 (16.91)	0.0002
Baseline EDSS score, mean (SD)	2.2 (1.08)	2.5 (1.27)	<.0001
Time since first MS symptom, mean (SD), years	3.8 (4.26)	6.5 (6.22)	<.0001
Number of relapses past 1 year, mean (SD)	1.6 (0.83)	1.5 (0.76)	0.0065
Number of relapses past 2 years, mean (SD)	2.4 (0.96)	2.3 (1.12)	0.1893
Number of prior DMTs taken, mean (SD)	0.5 (0.71)	0.4 (0.71)	0.3036
Propensity Score	1.3 (0.53)	1.7 (0.76)	<.0001

1: 1 Matching

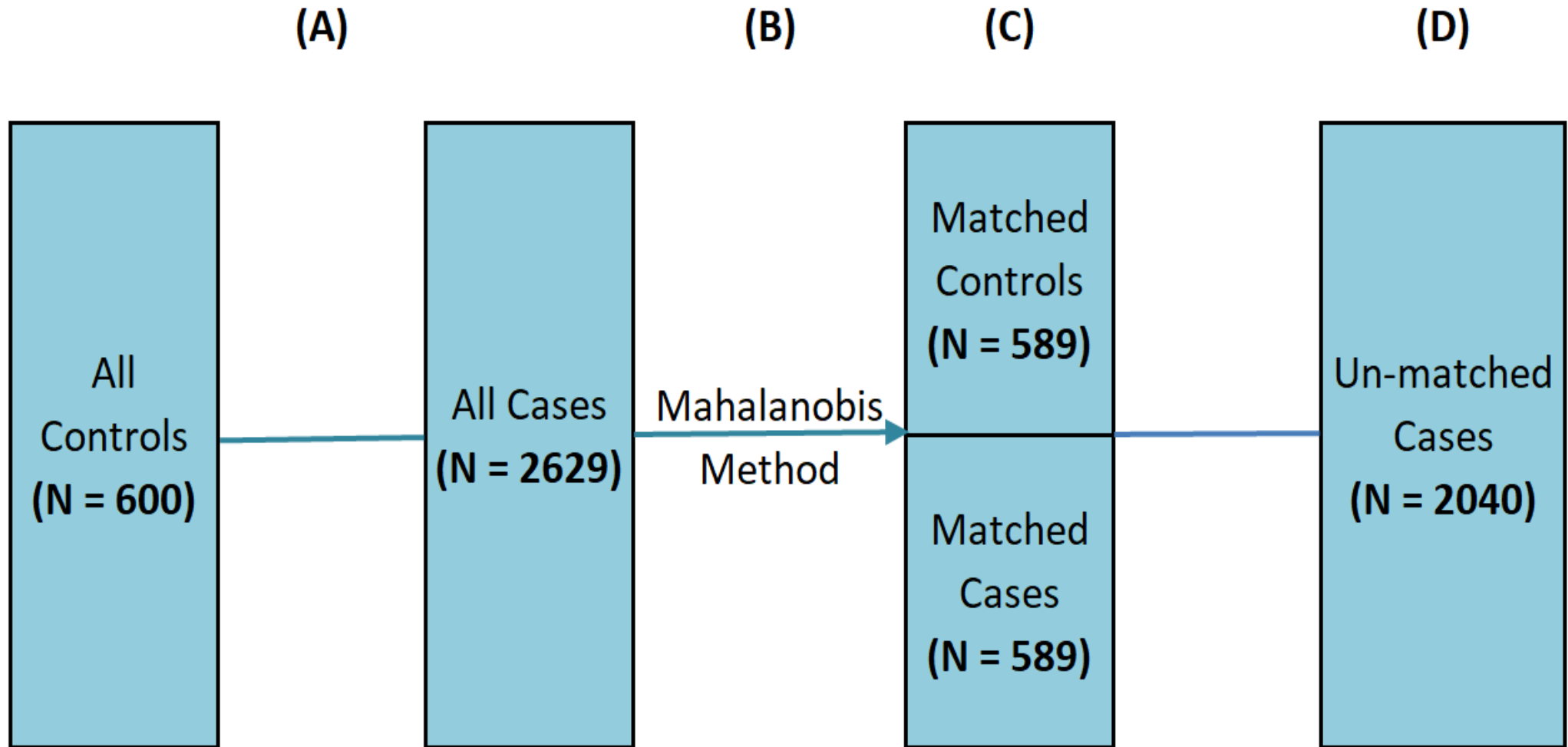


Table 2: 1: 1 Matched Population

	Placebo	Treatment	p-value
Total Patients , n	589	589	
Age, mean (SD), years	34.6 (9.17)	34.6 (8.70)	0.9974
Sex - Female, n (%)	385 (65.37)	391 (66.38)	0.7123
Country - USA, n (%)	177 (30.05)	131(22.24)	<.0001
Ethnicity - Not Hispanic, n (%)	352 (59.76)	210 (35.71)	<.0001
Race - White, n (%)	358 (60.78)	337 (57.31)	<.0001
Height, mean (SD), cm	169.6 (9.05)	169.6 (8.43)	0.9735
Weight, mean (SD), kg	75.5 (19.19)	75.0 (17.15)	0.6535
Baseline EDSS score, mean (SD)	2.2 (1.07)	2.2 (1.03)	0.9448
Time since first MS symptom, mean (SD), years	3.7 (4.23)	3.6 (4.05)	0.6085
Number of relapses past 1 year, mean (SD)	1.6 (0.83)	1.6 (0.74)	0.6572
Number of relapses past 2 years, mean (SD)	2.4 (0.96)	2.3 (1.05)	0.7724
Number of prior DMTs taken, mean (SD)	0.5 (0.71)	0.4 (0.71)	0.2882
Propensity Score	1.3 (0.53)	1.3 (0.52) 16	0.9872

1: 2 Matching

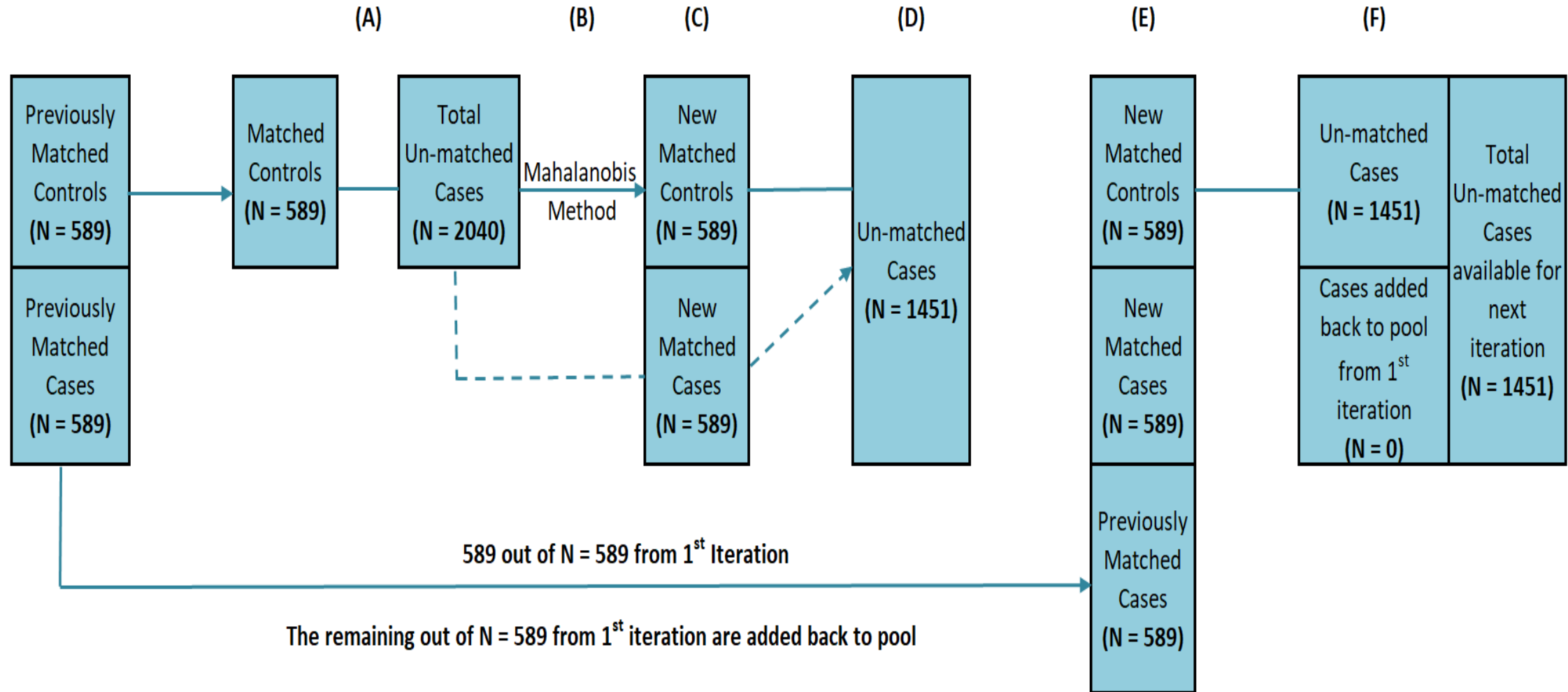


Table 3: 1: 2 Matched Population

	Placebo	Treatment	p-value
Total Patients , n	589	1178	
Age, mean (SD), years	34.6 (9.17)	34.5 (8.53)	0.8263
Sex - Female, n (%)	385(65.37)	781 (66.30)	0.6961
Country - USA, n (%)	177 (30.05)	267 (22.67)	<.0001
Ethnicity - Not Hispanic, n (%)	352 (59.76)	431 (36.65)	<.0001
Race - White, n (%)	358 (60.78)	669 (56.84)	<.0001
Height, mean (SD), cm	169.6(9.05)	169.7 (8.67)	0.8625
Weight, mean (SD), kg	75.5 (19.19)	74.8 (16.94)	0.4413
Baseline EDSS score, mean (SD)	2.2 (1.07)	2.2 (1.04)	0.6891
Time since first MS symptom, mean (SD), years	3.7 (4.23)	3.7 (4.07)	0.7175
Number of relapses past 1 year, mean (SD)	1.6 (0.83)	1.6 (0.78)	0.5829
Number of relapses past 2 years, mean (SD)	2.4 (0.96)	2.3 (1.05)	0.8387
Number of prior DMTs taken, mean (SD)	0.5 (0.71)	0.4 (0.74)	0.419
Propensity Score	1.3 (0.53)	1.3 (0.52) 18	0.89

1: 3 Matching

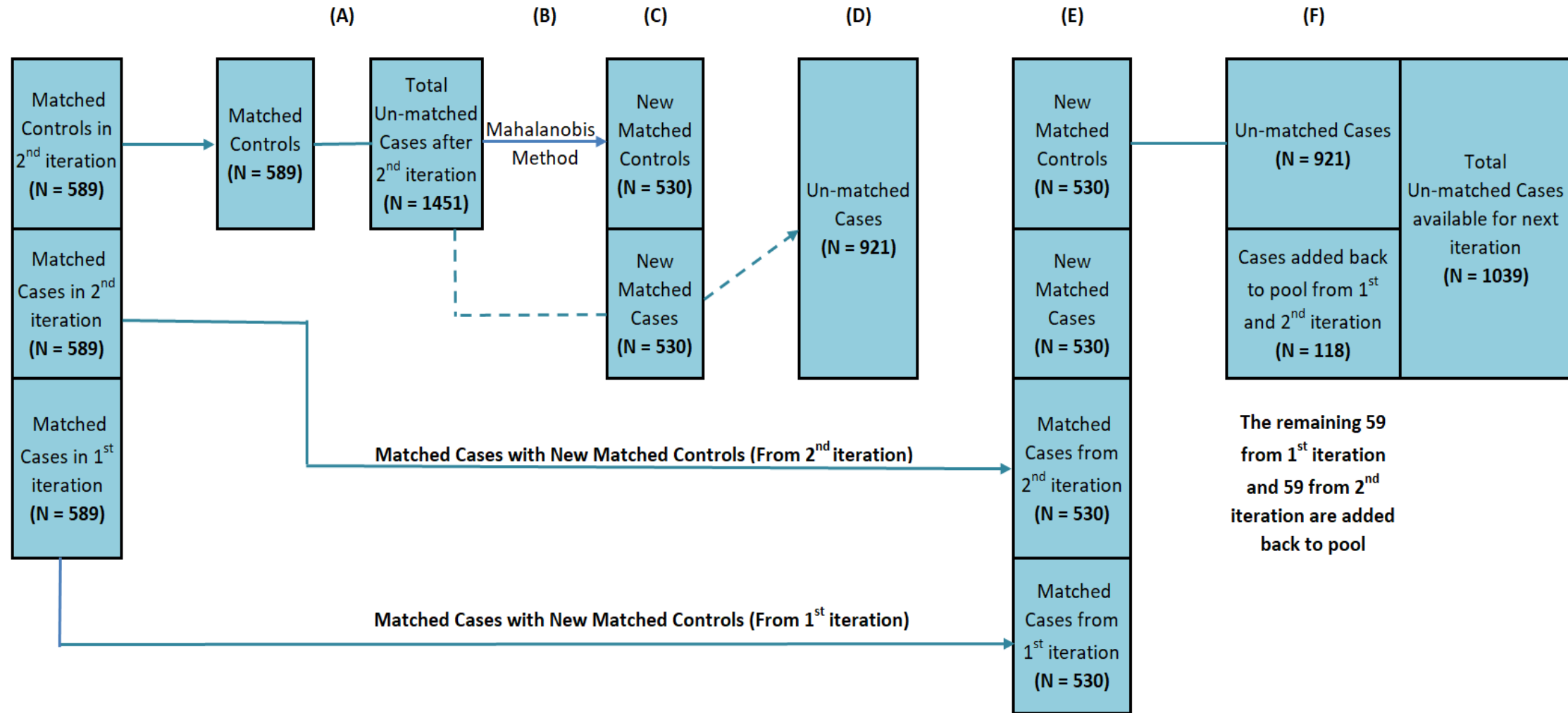


Table 4: 1: 3 Matched Population			
	Placebo	Treatment	p-value
Total Patients , n	530	1590	
Age, mean (SD), years	34.7 (9.24)	34.5 (8.83)	0.6016
Sex - Female, n (%)	356 (67.17)	1069 (67.23)	0.9787
Country - USA, n (%)	142 (26.79)	316 (19.87)	<.0001
Ethnicity - Not Hispanic, n (%)	315 (59.43)	565 (35.58)	<.0001
Race - White, n (%)	324 (61.13)	911 (57.33)	<.0001
Height, mean (SD), cm	169.4 (8.97)	169.2 (8.97)	0.7332
Weight, mean (SD), kg	73.5 (17.31)	72.8 (16.78)	0.4172
Baseline EDSS score, mean (SD)	2.3 (1.06)	2.3 (1.09)	0.9173
Time since first MS symptom, mean (SD), years	3.9 (4.14)	3.9 (4.00)	0.9869
Number of relapses past 1 year, mean (SD)	1.6 (0.84)	1.6 (0.78)	0.7161
Number of relapses past 2 years, mean (SD)	2.4 (0.98)	2.4 (1.09)	0.9406
Number of prior DMTs taken, mean (SD)	0.4 (0.68)	0.4 (0.70)	0.6916
Propensity Score	1.4 (0.50)	1.4 (0.49) 20	0.7213

Conclusions

- One-to-many matching helps to reduce bias and increase the number of matched pairs
- Very helpful to make groups comparable
- PSM can be useful to answer the complex questions in experiments

References

- Feng, Yu and Rong “A Method/Macro Based on Propensity Score and Mahalanobis Distance to Reduce Bias in Treatment Comparison in Observational Study”, 2006.
- Lori S. Parsons, “Performing a 1:N Case-Control Match on Propensity Score”
- Rosenbaum, P. R. and Rubin, D., B. (1983). "The Central Role of the Propensity Score in Observational Studies for Causal Effects". Biometrika Vol. 70

Any Questions?



Thank You...!

