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Inverse Probability of Attrition Weighting (IPAW)

A Beginner's Guide to overcome the attrition bias in clinical research

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Key Points: Navigating the Presentation

- 1 Attrition Bias**
- 2 The need for Inverse Probability of Attrition Weighting (IPAW)**
- 3 What is IPAW analysis?**
- 4 Understanding the terminologies**
- 5 A step-by-step approach of IPAW procedure**
- 6 IPAW in action: Case Study**
- 7 Comparison with traditional methods**
- 8 Key Takeaways**



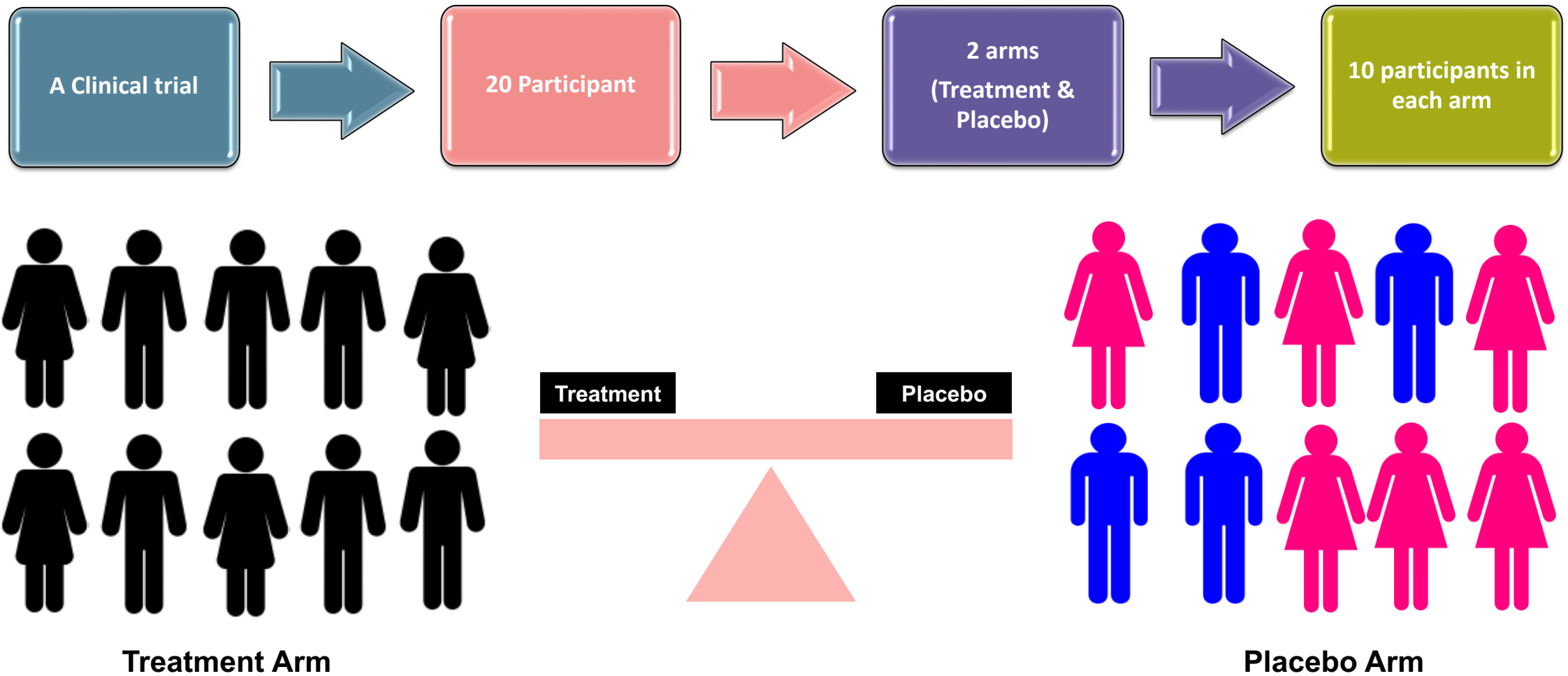
Attrition Bias

Definition

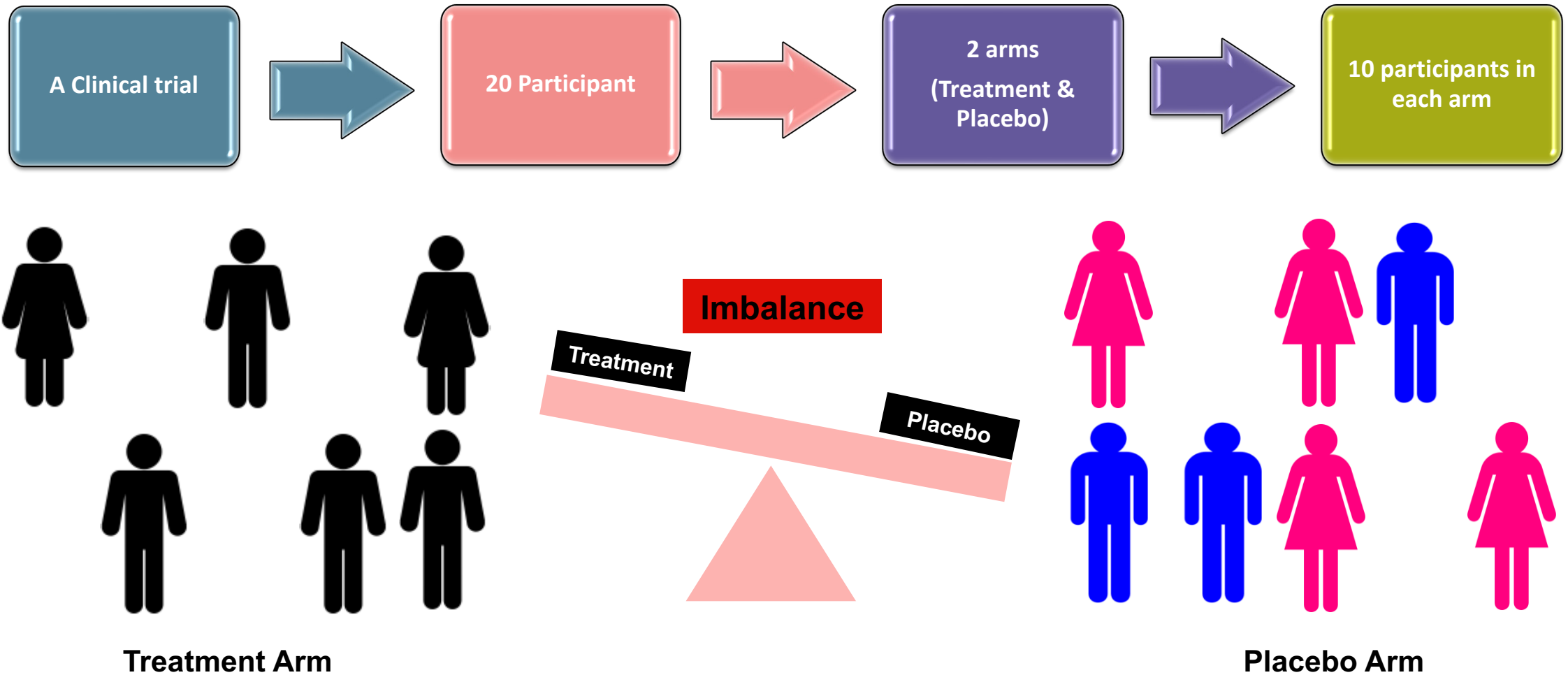
Reasons of attrition

Impact of attrition on a clinical trial

Attrition Bias – An Example



Attrition Bias – An Example



The Need of IPAW

1

Addressing attrition bias

2

**Loss of information and sample
representativeness**

3

Biased treatment effect estimates

4

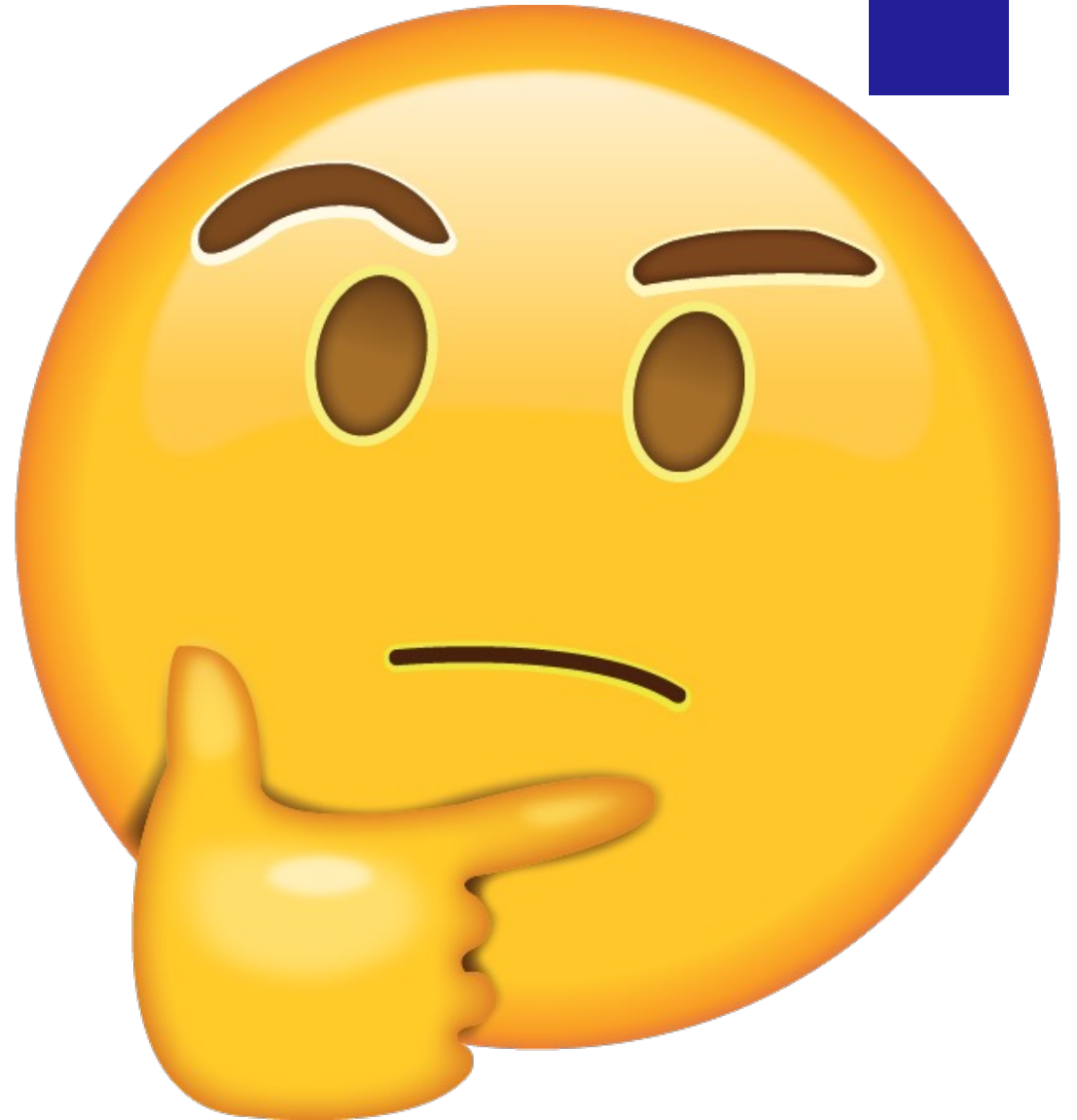
**Edge over traditional methods like complete
case analysis, propensity matching**

What is IPAW analysis?

- ❑ Inverse probability weighting is a statistical technique for calculating statistics, standardized to a pseudo-population which is different than originally collected data.
- ❑ Weighting – Correct implementation can potentially improve the efficiency.
- ❑ By incorporating these weights into the analysis, IPAW helps account for the missing data and potential biases introduced by attrition.
- ❑ It aims to balance the characteristics of retained and attrited individuals in the study sample.

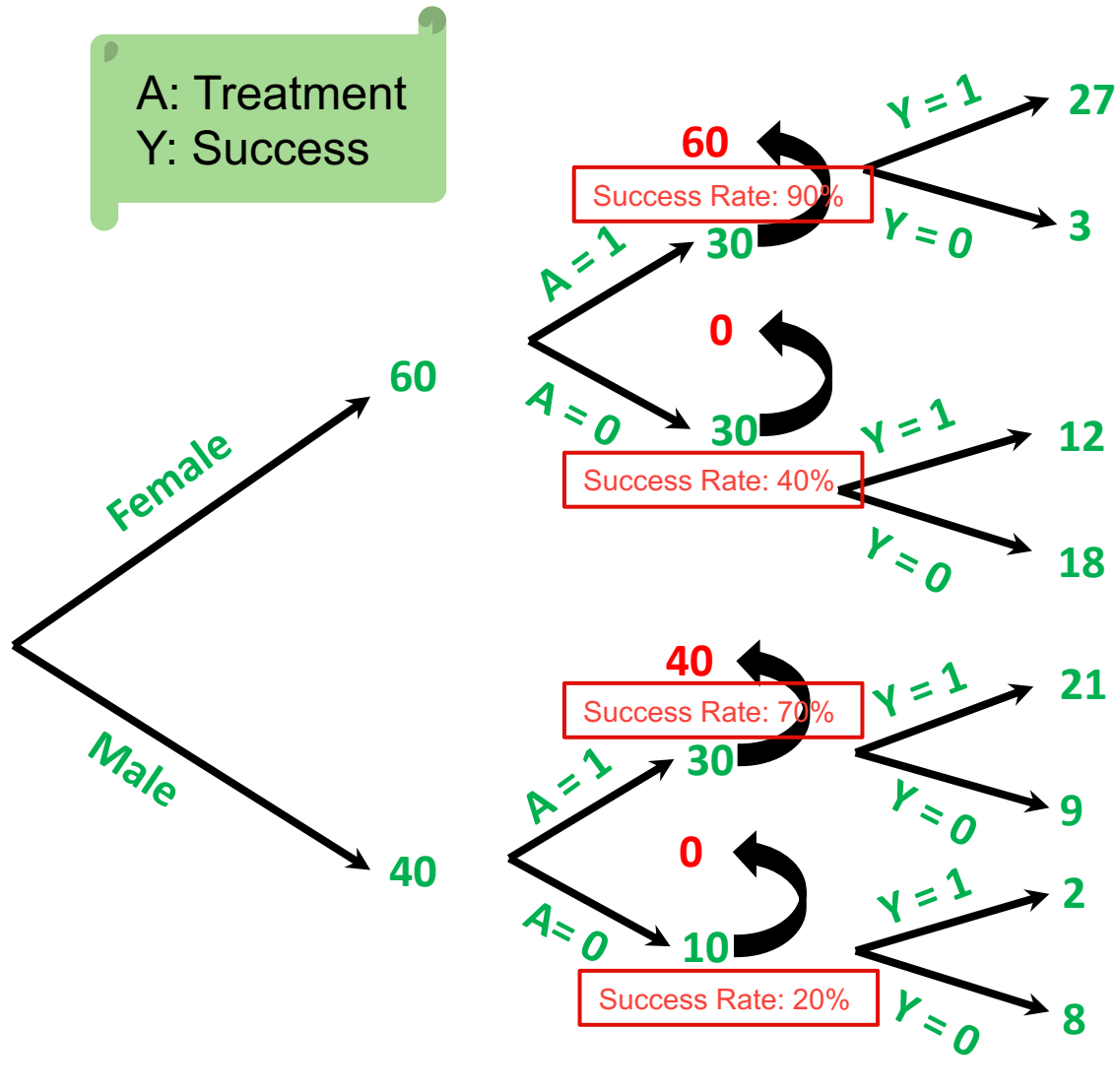
Terminologies

- ❑ What is Inverse probability weighting?
- ❑ What is pseudo-population?
- ❑ How weights deal with attrition?
- ❑ Relation between weights and probability?



An example to familiarize IPAW

A: Treatment
Y: Success



Calculations

All Treated

54

6

Each treatment counts 2 times

0

0

28

12

Each treatment counts 4/3 times

0

0

Weight =	2 =	$\frac{1}{P(A=1 \text{Female})}$
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$P(A=1 \text{Female}) = 1/2$

Weight =	$4/3 =$	$\frac{1}{P(A=1 \text{Male})}$
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$P(A=1 \text{Male}) = 3/4$

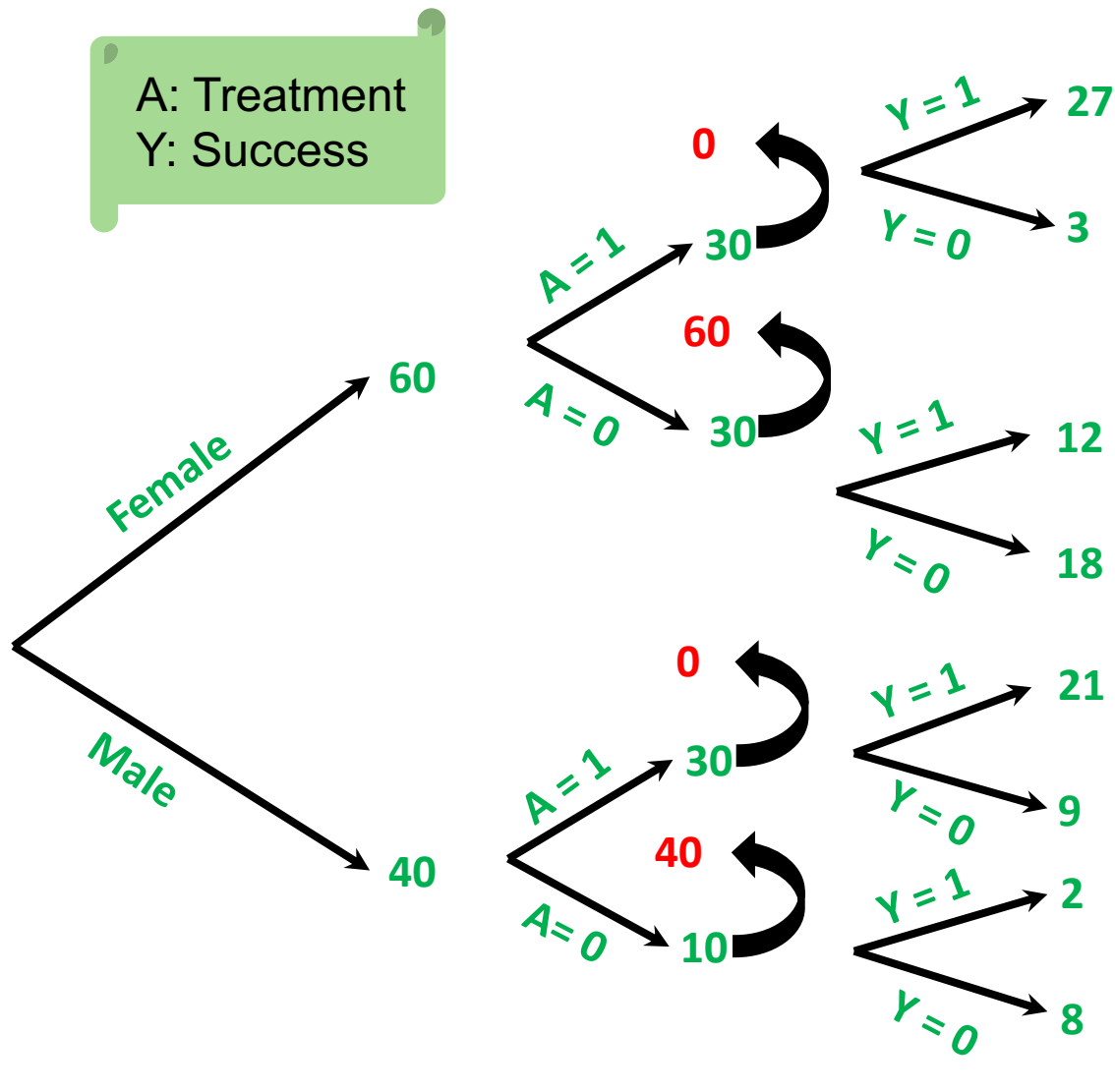
$$\hat{E}[Y^{a=1}] = \frac{54*(1) + 6*(0) + 28*(1) + 12*(0)}{54 + 6 + 28 + 12} = 82\%$$

$$\frac{\sum w_i y_i}{\sum w_i} = \frac{27*(2)*(1) + 3*(2)*(0) + 21*(4/3)*(1) + 9*(4/3)*(0)}{27*(2) + 3*(2) + 21*(4/3) + 9*(4/3)} = 82\%$$

Interpretation: 82% probability of success if everyone received treatment.

An example to familiarize IPAW

A: Treatment
Y: Success



All Untreated

0

0

24

36

0

0

8

32

Calculations

$E[Y^{a=0}] =$	$24(1) + 36(0) + 8(1) + 32(0)$	$= 32\%$
	$24 + 36 + 8 + 32$	

Interpretation: 32% probability of success if no one received treatment.

Each treatment counts 2 times

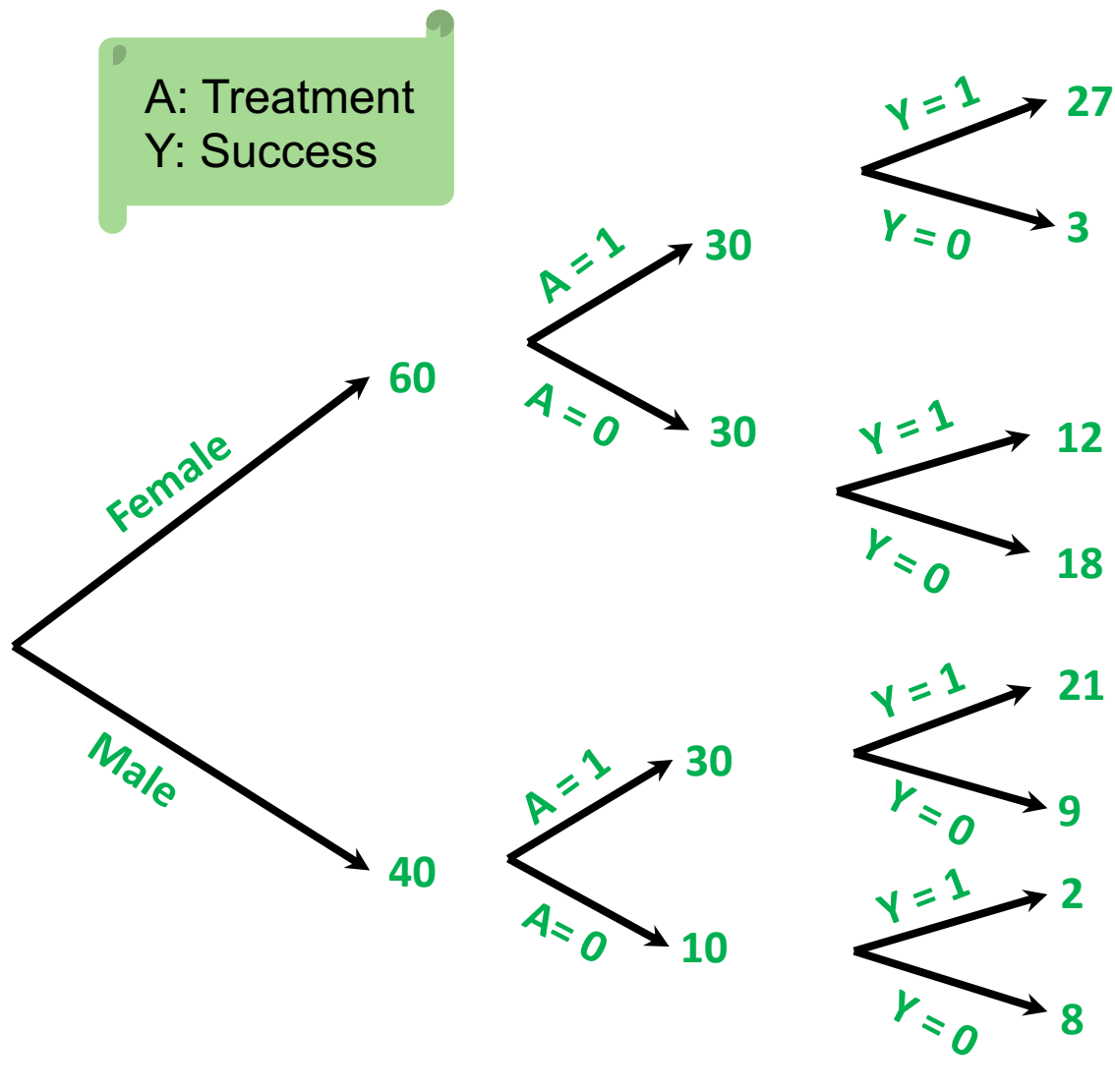
Weight =	2 =	1
		P (A = 0 Female)

Each treatment counts 4 times

Weight =	4 =	1
		P (A = 0 Male)

Pseudo-population

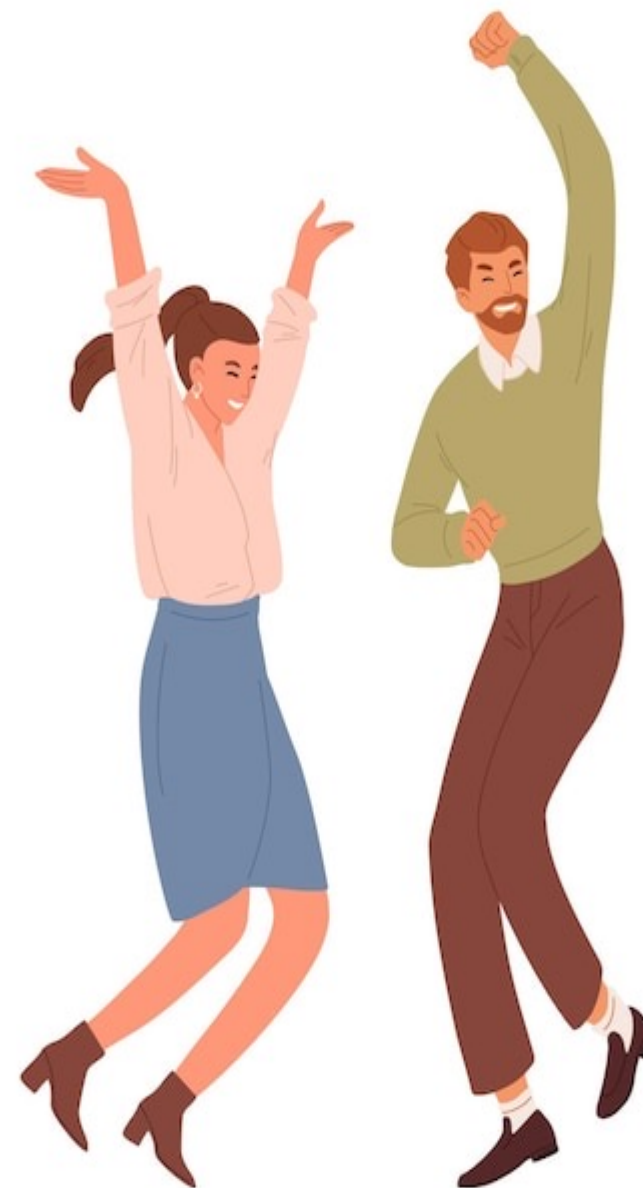
A: Treatment
Y: Success



Y (a=1)

Y (a=0)

54	0
6	0
0	24
0	36
28	0
12	0
0	8
0	32



A step-by-step approach of IPAW procedure

- ❑ Identifying variables associated with dropout.
- ❑ Estimating the probability of attrition, example: *Logistic regression*.
- ❑ Calculating inverse of probability weights
- ❑ Applying weights to the analysis.

IPAW in Action: Case Study

From 1,088 randomized patients with multiple sclerosis, we identified 772 individuals with MRI assessment at baseline & at Year 2.

All participants with MRI assessment were individually reviewed.

Subjects were excluded if technical limitations were identified.

Following the quality review, a total of 318 subjects meeting quality criteria were included in the analysis.

Analysis population and model

- ❑ **Analysis Population:** Subjects who had non-missing MRI assessment at baseline and non-missing brain volume change at Year 2 (Week 108).
- ❑ **Model:** Logistic regression with appropriate covariates (listed further) was used to calculate the probability of attrition.
- ❑ **Efficacy direction:** Brain volume loss was expected to slow down over time in the treatment arm, therefore, reduction indicates efficacious results.

Covariates included in the model analysis

- ❑ AGE
- ❑ GENDER
- ❑ TIME SINCE FIRST DIAGNOSIS OF MS
- ❑ BASELINE EDSS SCORE
- ❑ PROPORTIONAL GD LESION AT BASELINE
- ❑ PRIOR DMT USING IN PAST 2 YEARS
- ❑ TOTAL LESION VOLUME
- ❑ T2 LESION VOLUME
- ❑ NORMALIZED BRAIN VOLUME
- ❑ T25FTW Z SCORE
- ❑ FATIGUE IMPACT SCORE

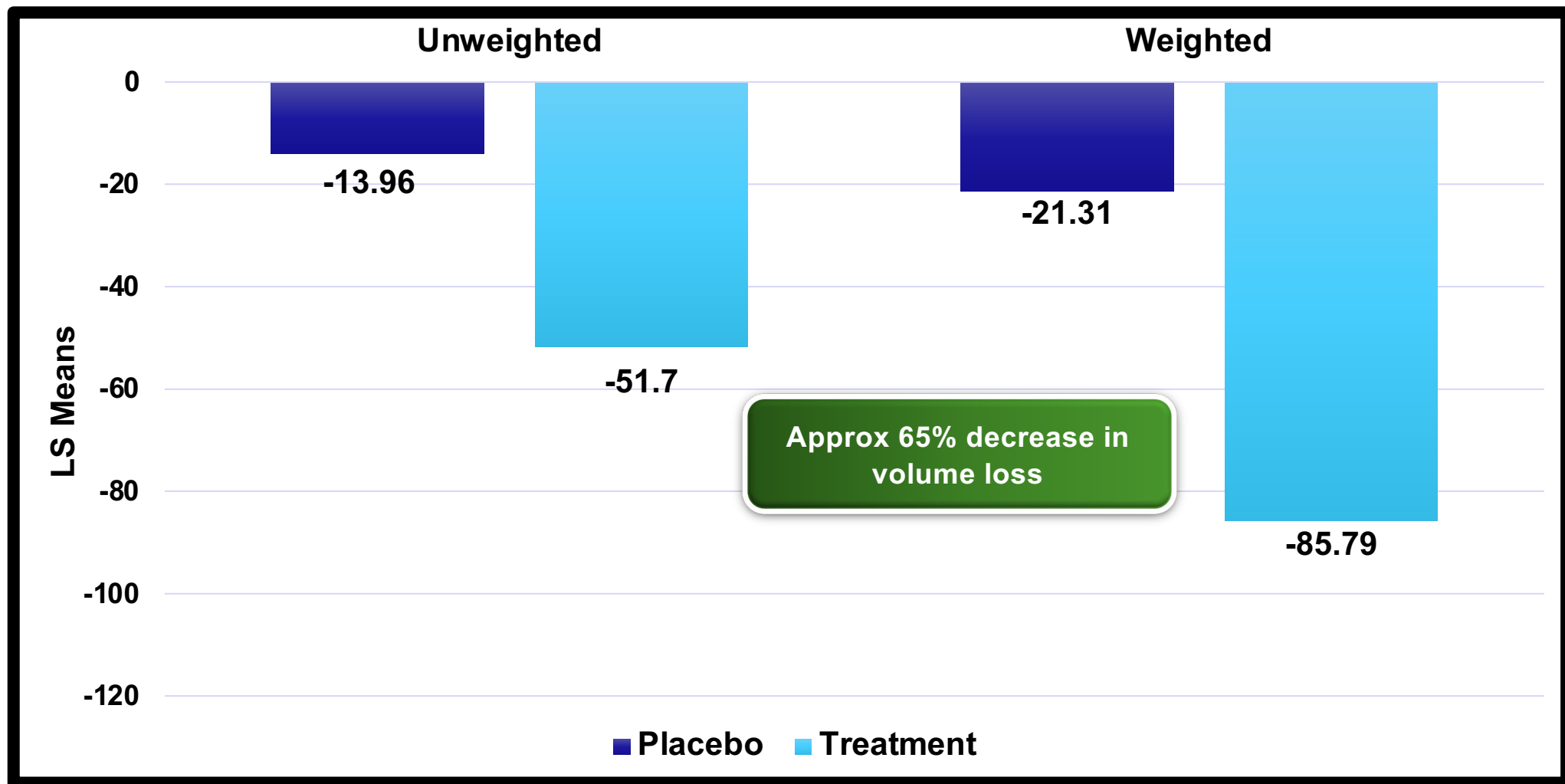
Calculation of weights from datasets

- ❑ **Calculating proportion of favorable event:** Proportion of patients who have MRI assessment.
- ❑ **Calculation of Unstabilized weights:** Reciprocal of predicted probability obtained by logistic regression model.
- ❑ **Stabilized weights:** Proportion (from step 1) / Predicted probability.

Baseline characteristics

CHARACTERISTICS	PLACEBO		TREATMENT	
	Unweighted Analysis	Weighted Analysis	Unweighted Analysis	Weighted Analysis
AGE, mean (SD)	36.80 (8.87)	36.68 (8.10)	38.69 (7.19)	38.57 (7.50)
GENDER, FEMALE n (%)	81 (85.3%)	78 (78.1%)	96 (79.3%)	94 (73.4%)
TIME SINCE FIRST DIAGNOSIS OF MS (YEARS) , mean (SD)	4.17 (4.71)	4.25 (4.51)	6.82 (6.06)	6.42 (5.42)
BASELINE EDSS SCORE, mean (SD)	2.43 (1.22)	2.71 (1.26)	2.50 (1.15)	2.67 (1.17)
PROPORTIONAL GD LESION AT BASELINE, (=0) n (%)	52 (55.91)	50 (54.95)	84 (69.42)	83 (70.94)
PRIOR DMT USING IN PAST 2 YEARS	19 (20.0%)	73 (78.0%)	39 (32.2%)	69 (67.4%)
TOTAL LESION VOLUME, mean (SD)	18.23 (18.56)	20.05 (18.86)	15.76 (15.35)	17.13 (15.58)
T2 LESION VOLUME, mean (SD)	15.35 (15.72)	16.83 (15.92)	13.14 (12.98)	14.20 (13.02)
NORMALIZED BRAIN VOLUME, mean (SD)	1496.71 (80.10)	1497.41 (78.88)	1494.45 (72.93)	1497.13 (72.78)
T25FTW Z SCORE, mean (SD)	0.00 (0.88)	-0.21 (1.00)	-0.11 (1.28)	-0.69 (2.51)
FATIGUE IMPACT SCORE, mean (SD)	36.56 (30.70)	41.60 (30.60)	50.35 (38.85)	57.90 (39.22)

Comparative analysis



Comparison with traditional methods

	IPAW	Complete Case Analysis	Propensity Score Matching
Approach	Assigns weights based on estimated attrition probabilities to balance sample characteristics	Includes only participants with complete data, excludes individuals with missing data	Matches dropped out participants with similar retained participants based on observed characteristics
Utilization of all available data	Yes	No	Partial (Depends on matched participants)
Handling differential attrition	Yes	No	Partial (Depends on matching variables)
Addressing biases introduced by attrition	Yes	No	Partial (Depends on matching quality)
Preserving internal validity	Yes	Risk of selection bias	Partial (Depends on matching quality)
Treatment effect estimation	Overall, more accurate estimates	Potential bias due to exclusion of individuals with missing data	Potential bias if unobserved confounders are not accounted for

Key Takeaways

- ❑ Attrition bias in clinical trial can compromise validity.
- ❑ IPAW deals effectively with attrition bias.
- ❑ Careful consideration of study design, data and assumptions are necessary.
- ❑ IPAW is a valuable tool, however, limitations like missingness and confounding factors should be acknowledged.
- ❑ More reliable and unbiased outcomes can be obtained using rigorous strategies like IPAW.

References

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Open for Discussion

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