Subgroup analysis when using the propensity score

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Lack of randomization

- Lack of randomization in *observational studies*, *registry databases* and *indirect comparisons* could lead to allocation bias or confounding

- Exposure = D (drug A versus drug B)

Drug A	Drug B
Female = 30%	**Female = 70%**
Mean age = 20	**Mean age = 50**
Quality of Life = 0.45	**Quality of Life = 0.65**
…….	**…….**

The propensity score (PS) (1)

- Treatment groups cannot be compared on the effectiveness without adjustment on covariates
- The PS is "*…the conditional probability of assignment to a particular treatment given a vector of observed covariates.*" (Rosenbaum & Rubin, 1983: 41)
- Instead of using all covariates, it could be interpreted as using **1 supercovariate**

The propensity score (PS) (2)

- The PS is estimated in a logistic regression function
- Adjustment on the PS balances the covariates over exposure groups: it results in a less biased estimate of the treatment effect
- It only adjusts for measured covariates, unmeasured or unknown covariates could still give hidden bias

The PS and subgroups

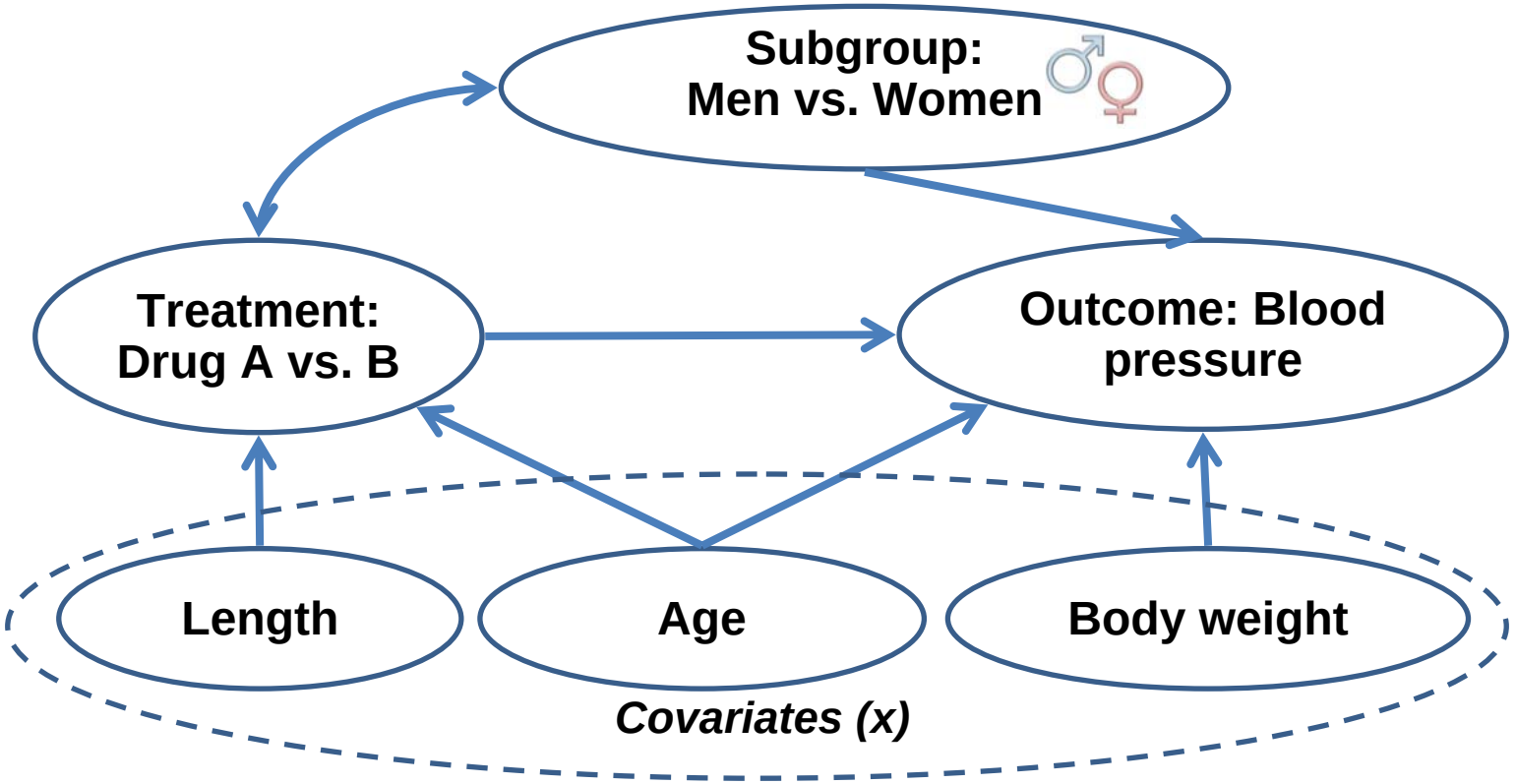
- What if Drug A is assumed to be more effective in men than in women compared to Drug B, and the PS should be used?
- A subgroup is based on a patient characteristic

  for example gender, SES, psychopathology

Research questions:

1. How to define the PS: Univariate or Multivariate?
2. Include or exclude the subgroup in the PS?
3. What is the influence of simulated features on the estimated effects?

Monte Carlo simulation



- Method of analysis: **Covariance adjustment**

1. Univariate or multivariate PS? (1)

1. Univariate PS:

$$PS(x) = pr\langle Drug = A \,|\, X = x \rangle$$

Defined on treatment assignment

Used in: $Y = \beta_0 + \beta_1 PS(x) + \beta_2 Drug + \beta_3 Gender + \beta_4 Drug * Gender$

2. Multiple PS, extended on subgroup:

$$PS(drug, gender, x) = pr\langle Drug = drug, Gender = gender \,|\, X = x \rangle$$

Defined on both treatment assignment and subgroup variable

Used in: $Y = \beta_0 + \beta_1 PS(drug, gender, x) + \beta_2 DG_2 + \beta_3 DG_3 + \beta_4 DG_4$

1. Univariate or multivariate PS? (2)

- *Multivariate* PS gives overall least biased results
- *Univariate* PS gives least biased results for effect of treatment (regression weight of D), but the estimation of the interaction term is more biased
- Difference in methods is, in part of simulated situations, small

2. Include or exclude the subgroup in the PS?

Multivariate PS

- Within multivariate PS, subgroup is not included in PS, but in definition of the PS

Univariate PS

- PS **without subgroup** variable gives overall less biased results

- Both defined PSs: Only variables **related to outcome** included in PS

3. Influence of simulated features on estimated effects? (1)

	Absolute bias
Correlation independent variables ↑	↑
Correlation with subgroup ↑	↑
Sample size ↑	↓

3. Influence of simulated features on estimated effects? (2)

- Bias higher if outcome (Y) is defined non-linear
  - *Linear PS model is not sufficient then*
  - *Effect of correlation is smaller or even contradictory*

- Bias **not** influenced by:
  - *Categorized variables*
  - *Skewness in independent variables*
  - *Kurtosis in independent variables*

Conclusion

- Multivariate PS is overall most appropriate, while the difference within a part of the simulations is small compared to the univariate PS
- Univariate PS: the interaction effect within the regression model is found least accurate
- Univariate PS: the variable for subgroups should not be included in the PS
- Variables related to outcome should be included in the PSs
- First quidance to do subgroup analysis when applying the PS

Issues for discussion

- Subgroup is defined categorical only – what if it is continuous or more subgroups should be analysed?
- PS is only defined in a logistic regression, linearly – should optimize model that defines PS?
- Covariance adjustment only one method – how would matching, stratification or inverse probability of treatment weighing behave in subgroup analysis?

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