# Worked example of visualization tools when estimating effects in target populations

Karolinska Institutet Tuesday, November 8, 2022



#### General breakdown

- Variable importance to transport figure
  - Breakout group session #1-7 minutes
- Diagnosing potential problems with weighted analyses
  - Breakout group session #2-10 minutes
- Performing and interpreting results
- General discussion



## Variable selection figures

**Task:** Conduct a high-level screening for potential effect measure modifiers within trial and target data sets **Approach:** Variable Importance for Treatment Transport (VITT) plot **(Figure 1)** 

**Task:** Implement a more flexible trial sampling moder including identified effect measure modifiers **Approach:** Allow model to incorporate interactions and other non-linearities

Task: Evaluate external positivity assumption

Approach: Evaluate distribution of trial sampling probabilities and overlap between trial and target (Figure 2)

**Task:** Assess balance of effect measure modifiers after applying inverse odds of sampling weights **Approach:** Assess balance of effect measure modifiers in the trial and target before and after weighting (Figure 3)

**Task:** Identify potentially influential observations with extreme weights **Approach:** Evaluate distribution of inverse odds of sampling weights in the weighted trial population (**Figure 4**)

**Task:** De-brief on steps 1-6 above.

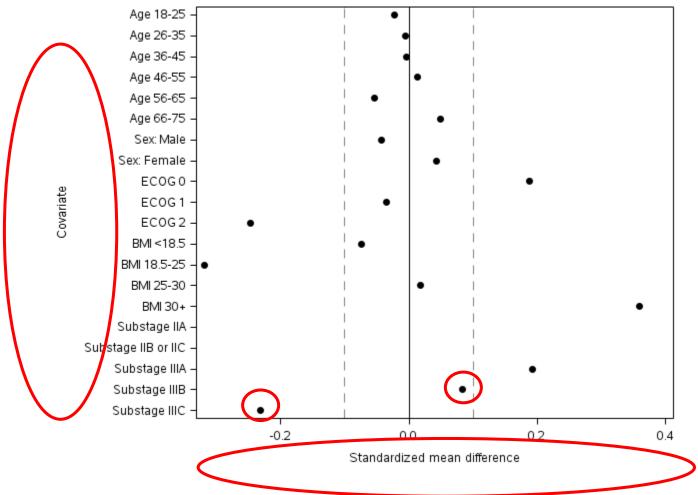


#### Variable selection/importance and external validity

- Remember that whichever method we use, we need to select variables for an adjustment set
- There is ongoing work on using directed acyclic graphs and selection diagrams for this purpose
- Due to their non-parametric nature, these tools say very little about the relative importance of each variable
- A new plot (VITT plot) of multivariable relationships can give some insight here (building on an existing plot, the LOVE plot)
  - These plots are method-agnostic

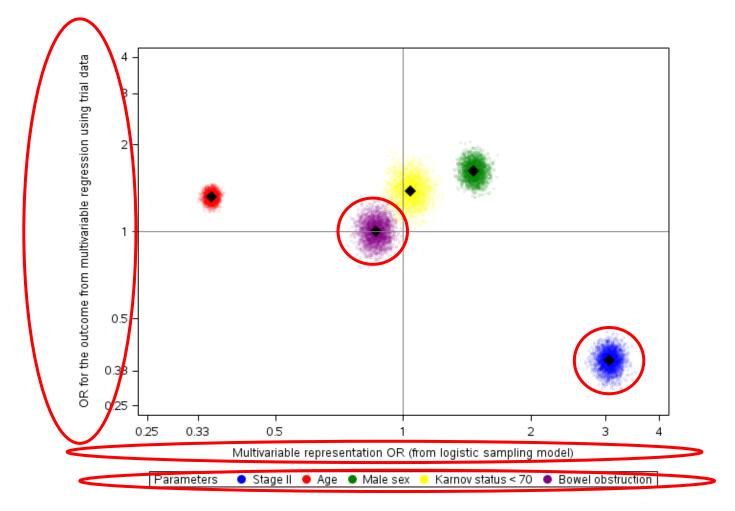


#### Love plots of standardized mean differences



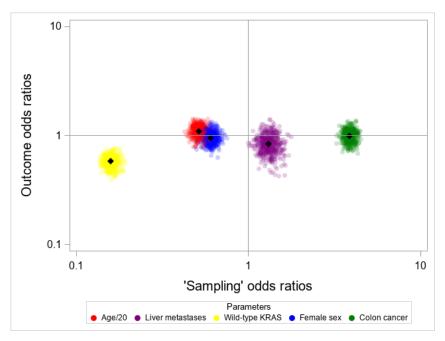


#### VITT plots of "sampling" and outcome ORs





#### **Discussion time: VITT plot**



Code to create this plot: VITT\_plot\_code

#### Questions:

- 1) What variables seem most important for inclusion in the adjustment set?
- 2) What variables seem the least important?
- 3) Are there any variables you would consider dropping completely?



## Diagnosing potential problems

#### Solving the external validity problem with weights

- Once you have identified the key variables, it is necessary to choose an analytic method
- Here we'll be focusing on weights and potential issues that can arise (especially the lack of transport positivity)
- When using these weights, some preliminary visualizations can help diagnose potential problems
  - Histograms and density plots of estimated probabilities
  - Pre- and post-weighting Love plots
  - "Skyscraper" plots of the weights to be used



Task: Identify a set of variables that may be conditionally associated with the outcome based on existing knowledge **Approach:** Review of literature, clinical input, or use of directed acyclic graphs/selection diagrams

Task: Conduct a high-level screening for potential effect measure modifiers within trial and target data sets Approach: Variable Importance for Treatment Transport (VITT) plot (Figure 1)

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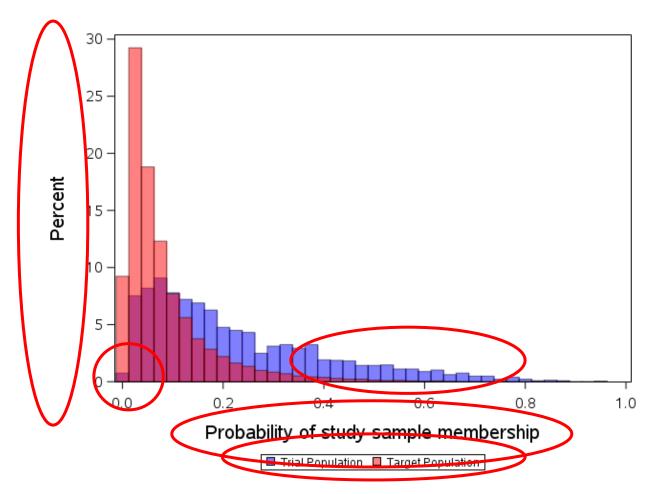
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Approach: Evaluate distribution of inverse odds of sampling weights in the weighted trial population (Figure 4)

Task: De-brief on steps 1-6 above.



### Histograms of "sampling" probabilities





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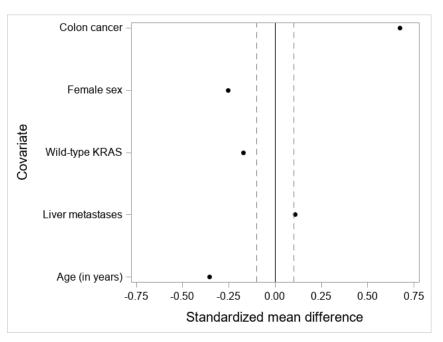
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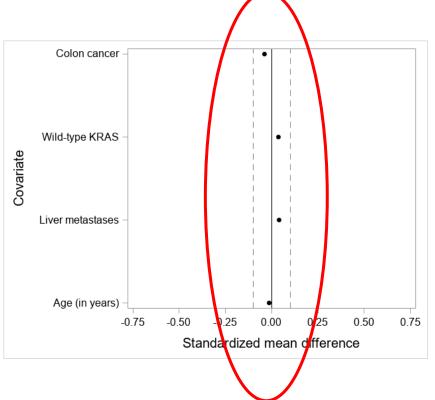


#### Love plots to examine balance

#### Before inverse odds weights

#### After inverse odds weights







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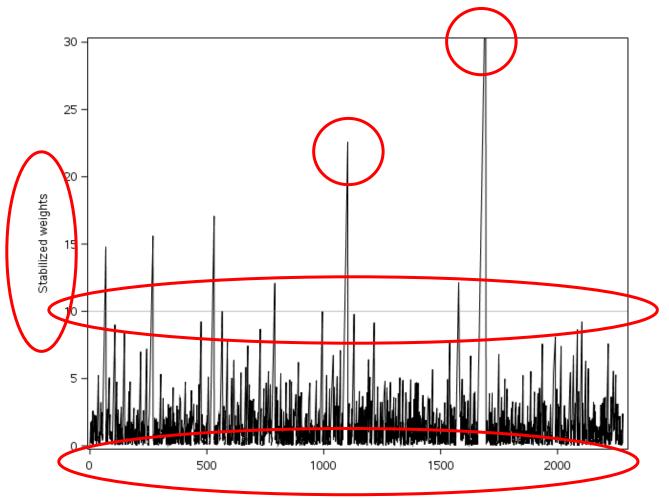
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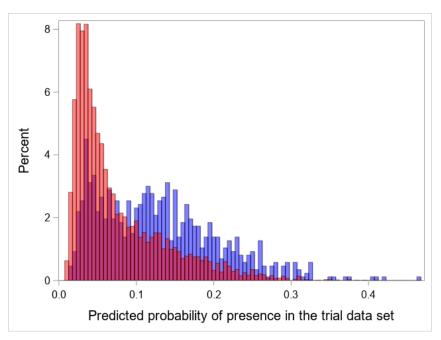


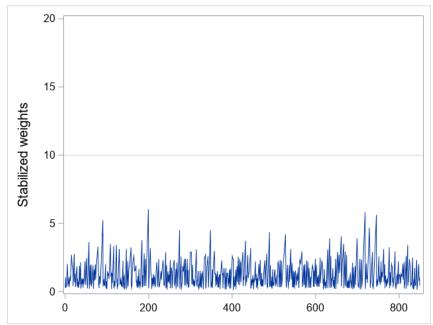
## "Skyscraper" plots to identify high weights





#### Discussion time: probability and skyscraper plots





Code to create this plot: Density\_plot\_code

Code to create this plot: Skyscraper\_plot\_code

#### Questions:

- 1) Do you see any potential problems with using this model based on the density plot?
- 2) What about the skyscraper plot? Do you see any potentially problematic weights?
- 3) Purely based on these plots, would you be comfortable proceeding with the analysis?



# **Analyzing data**

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#### Weighted analytics

- Having completed our diagnostics, how do we actually estimate a treatment effect?
- PROC PHREG conveniently allows use of a "WEIGHT" statement, as does many R packages for estimating hazard ratios
- Notably, traditional tools for estimating variance can ignore variability from sampling your target population
- Instead, we have bootstrapped, re-drawing from both the trial and target each iteration
  - And balancing each treatment arm separately



#### **Final results**

Target population	Progression- free survival hazard ratio	95% confidence limits	Confidence limit ratio
PRIME trial	0.97	0.84, 1.11	1.33



## Questions? mawc@live.unc.edu