Performance of Transportability Methods Under Effect Measure Modifier Omission: A Plasmode Simulation Study in Lung Cancer Screening

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BACKGROUND

- Trial transport method allows us to extend inference from one population to an external population
- Key assumption is that the transport model needs to be correctly specified, such as including all important effect measure modifiers (EMMs)

OBJECTIVE

Compare the performance of two trial transport methods (e.g., inverse-odds weighting and parametric g-computation) when the models were misspecified by omitting an important EMMs using plasmode simulations

STUDY POPULATION

Trial Population

<u>All NLST participants</u>

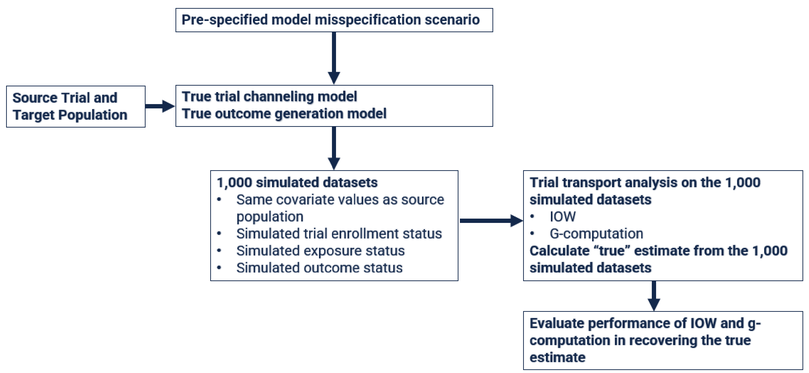
- Randomization to 3 annual rounds of screening of LDCT vs. chest radiography (CXR)
- Participants were: 1) 55-74 years old; 2) Current or former user of tobacco smoking who quit ≤ 15 years; 3) had ≥ 30 pack-years of smoking

Target Population

<u>2022 Behavioral Risk Factor Surveillance System (BRFSS) screening-eligible population</u>

- Nationwide telephone-based survey on adult health behaviors
- Applied NLST eligibility criteria
- Sample 70K from the unweighted BRFSS respondents (n=15,779) with replacement

SIMULATION SETUP



MODEL SPECIFICATIONS

Trial channeling model

- Multivariable logistic regression
- Outcome: trial enrollment status
- Covariates: potential EMMs

Outcome generation model

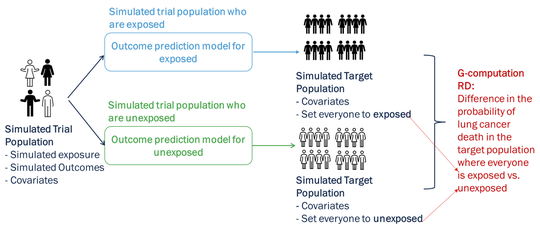
- Multivariable log-linear regression
- Outcome: lung cancer death (5-year risk difference)
- Covariates: exposure, potential EMMs

Transport model misspecification

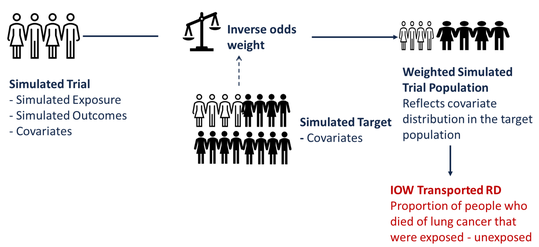
- Transport models incorrectly omitted any terms with the specified EMM
- Alter the strength of modification of the omitted EMM

TRIAL TRANSPORT METHODS

Inverse Odds Weighting (IOW)



Parametric G-Computation



Performance Evaluation

<u>Bias</u>: Transport RD – True RD

<u>Variance</u> of RDs

<u>Root mean square error</u> (RMSE): $\sqrt{(bias^2 + var)}$

95% <u>confidence interval coverage</u>

LIMITATIONS

- Findings may be specific to the lung cancer screening trial and target population
- Risk difference was the primary estimand and is insensitive to competing risks
- True outcome generation model was nonlinear, but effect measure of interest was on the linear scale

RESULTS

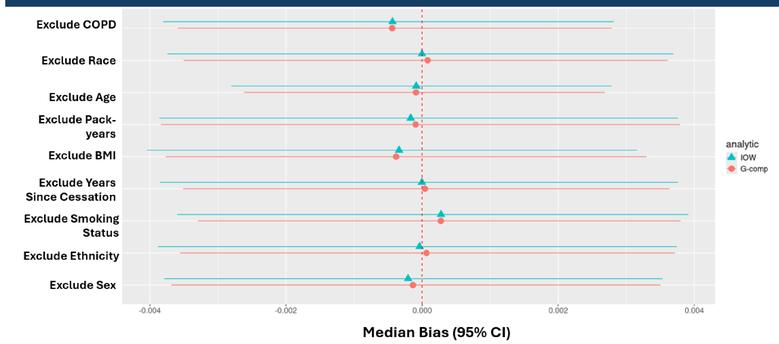


Fig 1. Median bias (95% CI) across exclusion of different EMMs: IOW vs. G-computation

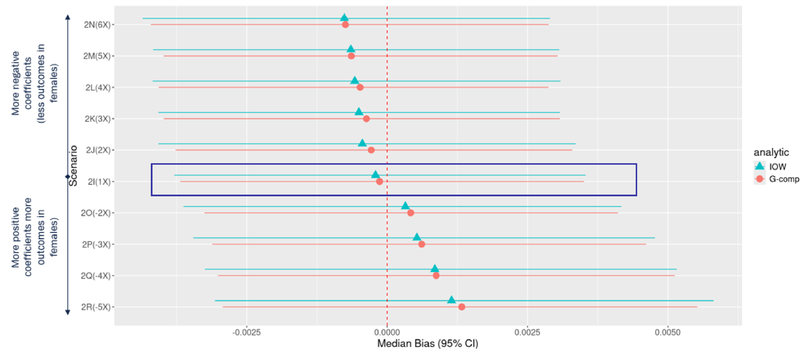


Fig 2. Median bias (95% CI) excluding sex as the EMM and varying its strength of modification: IOW vs. G-Computation

MAIN TAKEAWAYS

Expected	• G-computation estimates were more precise than those from IOW • Bias increased with greater magnitude of effect modification
Surprises	• Bias was not pronounced unless modification was strong
Implications	• Omitting EMMs may not greatly bias transported estimates in practice • Strong, influential EMMs should still be modeled carefully

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