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PROGRAM AND ABSTRACTS
MONTE CARLO SIMULATION OF THE DIRECT AND INDIRECT IMPACT OF RISK Factor INTERVENTIONS ON CORONARY HEART DISEASE. AN APPLICATION OF THE G-FORMULA

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Background: WHO has established a project on comparative risk assessment for coronary heart disease (CHD) which addresses the overall impact of several public health interventions on the risk of CHD. As there are multiple direct and indirect risk factors that are part of the causal web of CHD, such an evaluation has to consider not only the direct effect of the risk factors under intervention but has to include the effect mediated through other risk factors. As various risk factors simultaneously act as confounders and as intermediate steps, traditional regression analysis fails and alternative methods have to be used. Our goal was to evaluate the impact of several interventions on CHD risk factors using the g-formula.

Methods: We used data of the Framingham Offspring Study, in which risk factor and disease status of 5124 subjects was assessed in one baseline and 4 follow-up exams over 20 years. Based on a causal diagram which represented prior knowledge about the causal links among CHD risk factors, potential risk factors, confounders, and intermediate variables were defined. We used the g-formula to estimate the counterfactual CHD risk in the Framingham Offspring data under each intervention. The g-formula (Robins, 1986) is a general nonparametric method that allows to compute counterfactual proportions under the assumption of no unmeasured confounders. In a first step, we fit pooled logistic regression models to predict risk factor distributions and the risk of CHD based on the given risk factor history. In a second step, Monte Carlo technique was used to simulate a sample of 10000 counterfactual subjects and their experience regarding risk factors and CHD. Bootstrap methods were used to estimate 95% confidence intervals (CI) of the counterfactual CHD risks and relative risks (RR). All analyses were performed separately by gender. Evaluated strategies included interventions on smoking, alcohol consumption, body mass index (BMI), low density lipoprotein (LDL), and a combined strategy.

Results: After exclusions, our analyses included 2230 men (47.8%) and 2440 (52.2%) women with 189 and 68 CHD events, respectively. The observed 12-year risk of CHD in the study population was 8.47% (CI: 7.37%-9.73%) for males and 2.79% (CI: 2.19%-3.54%) for females. The simulated 12-year risk of CHD under no intervention was 8.48% for males (CI: 6.72%-10.24%) and 2.82% for females (CI: 2.10%-3.54%). Smoking cessation at baseline in all male and female smokers had a relative risk of 0.80 (CI: 0.70-0.91) and 0.83 (CI: 0.70-1.00), respectively. The relative risk after shifting the LDL distribution to the distribution of the Chinese population was 0.68 (CI: 0.52-0.89) for men and 0.48 (CI: 0.35-0.67) for women. Shifting alcohol consumption to moderate alcohol intake or constantly lowering BMI to 22kg·m² did not change CHD risk significantly. The combined intervention on smoking cessation, BMI, and LDL reduced the CHD risk by 53% (RR: 0.47; CI: 0.32-0.69) in men and by 61% (RR: 0.39; CI: 0.23-0.67) in women.

Conclusions: The g-formula could be applied in a situation where traditional regression analysis could not be used, because risk factor variables were confounders as well as intermediate steps. Highest risk reductions could be achieved by interventions on smoking cessation and LDL. Combined interventions may reduce CHD risk by more than 50%.