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Information bias in estimating vaccine effectiveness due to informed consent for COVID-19 vaccine register

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Introduction: National vaccine registers are essential for high quality monitoring and evaluation of vaccination programs. Requirement of informed consent for registration of vaccinations causes non-consenting individuals to be classified as unvaccinated, leading to information bias. We quantified the bias of vaccine effectiveness (VE) and provide bias-corrected estimates.

Methods: We used national COVID-19 vaccination and hospitalization data from the period dominated by the Delta variant before the booster campaign (11 July to 15 November 2021). VE against COVID-19 hospitalization and ICU admission, calculated as (1-relative risk)*100%, was estimated for individuals 12-49, 50-69, and ≥70 years of age using negative binomial regression corrected for age and date. Informed consent rates by covariates birth year, sex, region, and date were based on anonymous data of individuals vaccinated by the Municipal Health Services (GGD) (86% of vaccinations) and extrapolated to vaccinations by other providers. To estimate corrected VEs, we iteratively assigned hospitalized patients without vaccination record a probability of being vaccinated, based on covariate dependent vaccination uptake, consent rate and VE estimated in the previous iteration, until convergence occurred. Absolute bias was calculated as change in VE; relative bias as uncorrected/corrected relative risk.

Results: In total 8,804 hospitalizations and 1,692 ICU admissions were observed. Both absolute and relative bias due to non-consent was largest in the 70+ age group. In this group, non-consent was 7.0%; VE of full vaccination with primary series against hospitalization was 75.5% (95%CI 73.5; 77.4) before and 85.9% (95%CI 84.7; 87.1) after correction (absolute bias -10.4 percentage point, relative bias 1.74); VE against ICU admission was 88.7% (95%CI 86.2; 90.8) before and 93.7% (95%CI 92.2; 94.9) after correction (absolute bias -5.0%, relative bias 1.79).

Conclusion: Modest non-consent in registration data results in substantial underestimation of VE estimates. Known non-consent rates can be used to estimate and correct for this bias.

Conflicts of interest to disclose: We declare no competing interests