

# Twice boosted, double shielded? Dissecting the real-world marginal effectiveness of the second booster against COVID-19 admission and death using a multi-database linkage approach

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## ABSTRACT

**Introduction:** This study leveraged a multi-database approach to estimate the marginal vaccine effectiveness (VE) of the second COVID-19 booster dose. **Methods:** The Malaysian COVID-19 vaccination registry (MyVas) for COVID-19 vaccinations, Medical Treatment Report System, MyHealthDataWarehouse (MyHDW) for hospital admissions and the Ministry of Health COVID-19 line lists for cases and deaths were deterministically linked. Marginal VE against admission and deaths was modelled using an adjusted Cox regression with a time-varying coefficient to account for the waning of vaccines. Analysis was further stratified by age and healthcare-worker status. **Results:** Marginal VE against hospital admissions was 32% (95% CI: 0.26, 0.37) for the second booster compared to the first booster dose. Stratified findings indicate a higher appreciable of the marginal VE of 42% (95% CI: 0.36, 0.47) against admission in individuals over 60. VE against deaths for the second booster dose compared to the first booster dose was 30% (95% CI: -0.07, 0.54) and 35% (95% CI: -0.02, 0.59) in the general population and individuals above 60, respectively, with both confidence intervals crossing unity. **Conclusion:** This study's findings suggest the benefit of a second booster dose against hospital admission among older age groups. Its corresponding effectiveness against death is less appreciable due mainly to the low numbers of deaths observed across the study period. Leveraging modern observational approaches using multi-database linkage and big-data approaches allows for continuous monitoring of vaccine effectiveness within the population. Such comprehensive and dynamic approaches should be considered crucial in shaping future pandemic control frameworks.