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Biological Standardization

Internal

2nd IABS Workshop on Real World Evidence: Alternative Approaches to Phase 3 Clinical Trials for Vaccine Efficacy and Licensure: the role of Real World Evidence

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Abstract (max: 250 words)

Title: Lessons from the pragmatic randomized trials of high-dose vs. standard-dose influenza vaccine against severe clinical outcomes (FLUNITY-HD)

Background

The burden of hospitalized influenza, including influenza-attributable cardiovascular disease burden, has been recognized through epidemiological excess morbidity and mortality studies for nearly a century. The benefits of routine vaccination for reducing those events has been documented mostly through observational studies. Individually randomized studies to confirm causal benefits of vaccination against severe, rare events require large sample sizes.

Methods

Large-scale, pragmatic, individually-randomized trials against hospitalisation outcomes have been conducted in Denmark and Spain to measure the relative vaccine effectiveness (rVE) of high-dose (HD-IIV) vs standard dose (SD-IIV) influenza vaccines against severe clinical outcomes in older adults aged 65 years or older during the 2022–23, 2023–24, and 2024–25 influenza seasons. Participants were randomly assigned (1:1) to receive either HD-IIV or SD-IIV and followed up until May 31 the following year. The primary endpoint was hospitalisation for influenza or pneumonia. Secondary endpoints were cardiorespiratory disease, laboratory-confirmed influenza, all-cause hospitalisation, all-cause mortality, hospitalisation for influenza (ICD-10), and hospitalisation for pneumonia (ClinicalTrials.gov, NCT06506812).

Results

The analysis included 466 320 participants. The primary endpoint occurred in 1312 (0.56%) of 233 311 participants in the HD-IIV group compared with 1437 (0.62%) of 233 009 participants in the SD-IIV group (rVE 8.8%, 95% CI: 1.7 to 15.5; $p=0.0082$). HD-IIV also reduced the incidence of cardiorespiratory hospitalisation (rVE 6.3%, 2.5 to 10.0), laboratory-confirmed influenza hospitalisation (31.9%, 19.7 to 42.2), and all-cause hospitalisation (2.2%, 0.3 to 4.1).

Conclusion

Large, randomized, pragmatic trials can be used for causal vaccine inference. In this prespecified analysis, HD-IIV demonstrated superior protection compared with SD-IIV against hospitalisation for: influenza or pneumonia; cardiorespiratory disease; laboratory-confirmed influenza and all-causes.

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