

Influenza vaccine, evaluation of efficacy and immunogenicity

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Introduction: Influenza is a highly transmissible respiratory disease for which vaccination remains the primary preventive strategy [1–3]. This study provides a comprehensive evaluation of influenza vaccine effectiveness by comparing evidence from randomized controlled trials (RCTs) and test-negative design (TND) observational studies, while also quantifying the relationship between immunogenicity and clinical protection using hemagglutination inhibition (HAI) antibody titers, as originally characterized by Hobson in 1973 [4]. **Objective:** To evaluate the test-negative design (TND) as a potential alternative to randomized controlled trials (RCTs) for assessing influenza vaccine effectiveness, and to investigate the role of HAI titers as an immunological determinant of vaccine efficacy. **Methods:** A systematic electronic search identified studies assessing vaccine effectiveness, with methodological quality evaluated using standardized risk-of-bias instruments [5,6]. For immunogenicity analyses, studies indexed in PubMed and Scopus were screened to examine associations between HAI titers and vaccine efficacy. Meta-regression models were constructed to estimate functional relationships between antibody levels and protective efficacy, stratified by influenza strain and vaccine platform. **Results:** Seventy-three studies met inclusion criteria for effectiveness meta-analysis from 2,993 screened records. The pooled vaccine effectiveness in RCTs was 48% (95% CI: 42–54), whereas adjusted effectiveness in TND studies was 39.9% (95% CI: 31–48), demonstrating consistent protection estimates across methodological frameworks. In the immunogenicity review, 7 studies were included following screening of 550 records. Vaccine efficacy depending on HAI ranged from 26% to 96%, varying according to vaccine type, circulating strain, and population characteristics, with higher HAI titers strongly associated with increased clinical protection. **Discussion and Conclusion:** These findings support TND studies as a valid, efficient, and cost-effective approach for monitoring seasonal influenza vaccine effectiveness relative to RCTs. Furthermore, HAI titers are a key determinant of influenza vaccine efficacy, reinforcing their utility as an immunological correlate of protection. Collectively, the results highlight the predictive value of quantitative immunogenicity models for estimating vaccine performance and informing evidence-based public health strategies.

Palavras-chave: Influenza Vaccine; Effectiveness; Immunogenicity.

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