Assessing the vaccine effectiveness of seasonal influenza vaccines: a systematic review and meta-analysis of randomized controlled trials and observational studies

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Introduction: Influenza is a respiratory disease caused by the highly transmissible influenza virus in humans [1]. Vaccination is a crucial strategy for preventing influenza and its associated complications [2,3]. This paper aims to provide a comprehensive assessment of the vaccine effectiveness (VE) of seasonal influenza vaccines (SIVs) in individuals aged 15 to 64 years through a systematic review and meta-analysis of randomized controlled trials (RCTs) and observational studies (TNDs). **Methods:** A systematic review with meta-analysis was performed to identify all relevant studies that examined the effectiveness of SIVs. The primary outcome measure of interest was the VE against laboratory-confirmed influenza, regardless of the viral strain. To evaluate the quality of the included studies, the researchers utilized the Cochrane risk-of-bias tool for RCTs and the ROBINS-I tool for TNDs, which assessed the methodological quality and potential biases in study design, conduct, and analysis. **Results:** The search process yielded a total of 2993 records, and after a thorough evaluation, 125 studies from 73 papers met the inclusion criteria and were included in the meta-analysis. Among the included studies, 9 were RCTs, which provide a higher level of evidence, and 116 were TNDs, which offer valuable real-world data. The pooled VE estimate for RCTs was determined to be 48% with a 95% confidence interval (CI) ranging from 42% to 54%. This finding indicates that, on average, SIVs reduced the risk of laboratory-confirmed influenza by 48% among individuals aged 15 to 64 years in the RCTs. For the TNDs, the adjusted VE estimate was found to be 39.9% with a 95% CI of 31% to 48%. Adjusted VE accounts for potential confounding factors that may influence the vaccine's effectiveness, such as age, comorbidities, and other variables. Additionally, the non-adjusted VE estimate for TNDs was 41% with a 95% CI of 37% to 45%. **Conclusion:** The key factor influencing VE is the match between the influenza strains included in the vaccine and the strains currently circulating in the population. A high level of strain match enhances the effectiveness of SIVs in preventing laboratory-confirmed influenza cases. These findings highlight the importance of ongoing surveillance and timely updates of the vaccine composition to ensure optimal protection against the circulating influenza strains.

Keywords: Influenza; observational studies; randomized controlled trials; seasonal influenza vaccines; vaccine effectiveness;

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