

Centenario de la Gripe Española de 1918. La peor pandemia en la historia contemporánea mundial: lecciones para el futuro

Centenary of the 1918 Spanish Influenza, the Worst Pandemic in the Recent History of the World: Lessons for the future

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ABSTRACT

Influenza vaccine effectiveness and impact: current knowns and unknowns

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Annual influenza epidemics result in 290,000-650,000 deaths influenza associated respiratory deaths per year. The most effective way to prevent the disease is through vaccination. In most countries vaccine recommendations focus on high-risk population groups such as the elderly and those with chronic health conditions. Since human influenza viruses are subject to permanent antigenic changes, WHO issues twice a year recommendations for seasonal vaccine composition aiming to antigenically match the vaccine with the circulating viruses. Given that influenza vaccine is reformulated each year, the influenza vaccine effectiveness (IVE) has to be annually evaluated.

Measuring the IVE is a challenge due to the complexities of the factors influencing it and their interaction. This is especially true for observational studies which are currently preferable to randomized controlled trials for estimating the IVE, due mostly to ethical reasons. Among the study designs available for estimating IVE, the test-negative design (TND) has been widely used, comparing the odds of vaccination between influenza positive and negative patients. The TND is the design used by international teams participating in the Global Influenza Vaccine Effectiveness (GIVE) Collaboration that provides IVE results to the WHO Strain Selection Committee.

At European level, since 2008, the I-MOVE (Influenza Monitoring of Vaccine Effectiveness) and I-MOVE+ networks measure IVE against specific laboratory-confirmed outcomes, at primary care and hospital level, by pooling data from various countries sharing a common protocol. Along with other research groups in this field, I-MOVE/IMOVE+ studies have contributed to understand many aspects of IVE acknowledging that IVE can vary by age, type/subtype of virus, genetic clade or vaccine type. It has been evidenced that waning of vaccine protection with time since vaccination occurs mainly for A(H3N2) influenza, and sometimes this IVE decrease was restricted to specific population groups rather than affecting the overall population.

A recent meta-analysis of TND results including studies around the world suggest that influenza vaccines provided substantial protection against H1N1pdm09, H1N1 (pre2009), and type B, and reduced protection against H3N2. Concordance between the circulating and vaccine strains is not anymore the most plausible explanation for the vaccine performance in the respective season. One of the current questions that international teams try to understand is how past influenza vaccinations may modify current season IVE on the ability of subsequent vaccinations to prevent infection. Recent observational studies suggest that previous season(s) vaccination may adversely affect vaccine effectiveness in some seasons, particularly for H3N2. Although the antigenic distance hypothesis, proposed by Smith in 1999 provides a framework for explaining this interference on current VE among those vaccinated in the prior year, many aspects on the immunologic mechanisms and clinical significance of previous season(s) vaccination effects are still unknown. Further research is needed to better understand the effect of previous season(s) exposure taking into account the IVE against virus harboring mutations in key antigenic sites, the natural immunity and its duration, or the first childhood imprinting to influenza virus.

Besides estimating the IVE, it is important to quantify the benefits of vaccinating, mainly in the vaccine recommended groups. Even with limited vaccine protection against confirmed infection, influenza vaccine can result in a considerable reduction of influenza related complications and mortality. The public health impact of an influenza program should be measured in terms of influenza-associated outcomes prevented each season by influenza vaccination. That would improve communication of results on IVE studies and would help increasing the acceptability of the vaccine among population including healthcare workers.

In this talk an overview of the current estimates on influenza vaccine effectiveness and the impact of vaccination program will be presented, with references to the main open questions regarding protection conferred by influenza vaccination.