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Review

Strategies to maximize influenza vaccine impact in older adults

Jennifer A. Whitaker [a], Mitchell S. von Itzstein [b], Gregory A. Poland [c,*]

[a] Division of Infectious Diseases, Mayo Clinic, Rochester, MN USA
[b] Department of Medicine, Griffith University, Gold Coast, Australia
[c] Mayo Vaccine Research Group, Department of Medicine, Mayo Clinic, Rochester, MN, USA

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ABSTRACT

Older adults are disproportionately affected by influenza morbidity and mortality. In most high income countries, influenza vaccine policies target persons age ≥65 years for influenza vaccination. Many low-resource settings do not utilize seasonal influenza vaccination. Barriers to influenza prevention among older adults around the globe are multiple and some vary between high- and low-resource settings. To maximize influenza prevention in the older adult population, gaps in influenza vaccination coverage and improvements in vaccine efficacy are needed. The focus of this article is on the data for currently available vaccine strategies to maximize influenza vaccine impact, with a focus on high-resource settings. We also discuss novel influenza vaccine strategies needed for older adults worldwide.

Contents

* Corresponding author at: Mayo Vaccine Research Group, Mayo Clinic, Guggenheim 611C, 200 First Street SW, Rochester, MN 55905, USA.
E-mail address: poland.gregory@mayo.edu (G.A. Poland).

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1. Introduction

Influenza immunization is the most effective means of influenza prevention. Influenza causes significant morbidity and mortality worldwide among adults ≥65 years. Some countries, such as the United States [1,2], Canada [3], and Australia [4], recommend annual influenza immunization for all persons older than 6 months of age. Others recommend influenza immunization only for those at the highest risk of infection and complications. Despite global differences in national influenza immunization policies, the World Health Organization (WHO) has recommended influenza immunization be prioritized for the following high-risk groups: pregnant women, children between the ages of 6 months and 5 years old, people ≥65 years of age (older adults), those with chronic medical conditions, and healthcare workers. However, critical gaps remain in influenza immunization coverage, vaccine immunogenicity, and effectiveness/efficacy in these high-risk groups. Herein, we review challenges facing influenza vaccine efficacy among older adults and review potential solutions to these challenges. Globally maximizing the preventive effects of influenza vaccines in older adults requires strategies to expand vaccine coverage in this population (may not be appropriate with the currently available vaccines in all locations), the development of more efficacious vaccines, and overcoming barriers to introduction of influenza vaccines in resource-limited settings. Worldwide, most influenza vaccines are distributed to high-income countries [5]. Low- and middle-income countries (LMICs) face unique challenges in influenza prevention. The main focus of this article will be on influenza vaccine strategies for high-income countries. Influenza vaccine technologies to meet global needs, including those of LMICs, will be discussed under "Critical Data Gaps."

2. Statement of the problem

2.1. Expansion of the elderly population

The need for more effective influenza vaccine strategies among the elderly population is critical given that this population is exploding in size across the world. In the United States, this phenomenon has been termed the "silver tsunami" by one of the authors (GAP). Although higher-income countries have the oldest populations, developing countries are not immune. In 2010, 525 million people (8% of the world's population) were ≥65 years old. This number is expected to increase to 1.5 billion by 2050, and this population will represent 16% of the global population [6]. By the end of 2050, it is projected that there will be nearly three persons age 60 years or older for every child less than 15 years of age in Europe [7].

2.2. Influenza morbidity and mortality among the elderly

WHO has estimated that seasonal influenza causes 3–5 million cases of severe influenza annually and leads to 250,000–500,000 deaths worldwide [8]. A recent global modeling study using data from 33 countries during the years 1999–2015 predicted even higher rates of influenza-associated mortality than previously reported, with worldwide annual rates of influenza-associated respiratory excess mortality of 291,243–645,832 cases [9]. The overall number of deaths due to influenza is likely even higher, as these rates did not take into account influenza-associated non-respiratory causes of death. This study clearly demonstrated that the elderly are the group with highest influenza-associated respiratory excess mortality rates worldwide across all regions of the world. For people <65 years, mean annual influenza-associated respiratory excess mortality ranged from 0.1 to 6.4 per 100,000 individuals; for those age 65–74 years, the rate was 2.9 to 44.0 per 100,000; for those ≥75 years, the rate was 17.9 to 223.5 per 100,000. The U.S. Centers for Disease Control and Prevention (CDC) estimates influenza deaths for adults ≥65 years in two ways: (1) via reports of pneumonia and influenza deaths and (2) via reports of respiratory and circulatory deaths attributable to influenza [10]. In an analysis of influenza mortality from 1996 to 2007, the CDC determined that 89% of influenza-related respiratory and circulatory deaths attributable to influenza occurred among adults ≥65 years old [11], even though they only comprised roughly 15% of the U.S. population at that time. Furthermore, from 1979 to 2001, adults ≥65 years old represented roughly 60% of influenza-related hospitalizations [12]. Influenza-related deaths increase progressively with increasing age [13]. Influenza mortality varies by season and is subtype specific. Thus, it is difficult to make generalizations when reviewing only one influenza season. Nonetheless, recent U.S. estimates from the 2015–2016 influenza season demonstrate similar findings to the data noted above and estimate that roughly 50% of influenza-related hospitalizations occurred among ≥65-year-old adults [10], and 64% of pneumonia and influenza-related deaths occurred in this age group [10]. These complications occurred despite a 63% influenza vaccine coverage for the 2015–2016 influenza season among U.S. adults ≥65 years old [10]. Reports from Central and South America [14], Europe [15], Africa [16], and Southeast Asia are concordant and report higher influenza morbidity and mortality in older adults [17–19].

2.3. Underutilization of influenza vaccines in older adults

Successful influenza infection prevention by immunization faces many challenges: the requirement for annual administration, match of the vaccine and circulating viral strains, barriers to immunogenicity among the immunocompromised and immunosenescent, waning immunity among the elderly, vaccine hesitancy, adequate supply of vaccine, geographic, and economic barriers. Many of these barriers contribute to suboptimal vaccine uptake among the elderly. Some of these barriers differ between LMICs and high income countries and also among countries within these classifications. In LMICs, thermostability, insufficient infrastructure of public health systems, lack of access to adequate vaccine supply, current public health policy, and the cost of vaccines may all be significant challenges to influenza vaccination programs. A working group of international authorities convened by WHO concluded that "existing influenza vaccines are not well-suited for LMICs" [20]. The rationale for this statement was most LMICs do not have adequate public health systems to deliver the current influenza vaccines. It is difficult for many LMICs to incorporate the current influenza vaccines into their routine immunization programs given "arbitrary expiration dates timed for temperate country markets" [20] and need for year-round vaccination in many countries with tropical climates. Furthermore, this working group noted current influenza vaccines have been developed and marketed for prevention of any influenza illness rather than demonstration of prevention of severe illness, which is the major priority for introduction of new vaccines in LMICs [20].

Vaccine hesitancy or perception of low risk of influenza infection is a global problem [21]; however, in LMICs other barriers may overshadow vaccine hesitancy as a barrier to influenza vaccination. In high-income countries, barriers related to vaccine hesitancy may seem to be more significant than those posed by cost or vaccine delivery systems. For example, a recent systematic review of barriers to influenza vaccination intention and behavior, mostly based on studies from North America and Europe, found that a lack of confidence in the seasonal influenza vaccine and perception of low vaccine effectiveness led to influenza vaccine hesitancy in the elderly [22].

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