

Review Group Membership**MaHTAS Reviewer:**

Atikah Shaharudin
Dr Junainah Sabirin
Dr. Izzuna Mudla Mohamed
Ghazali

External Reviewer:

Dr. Yau Weng Keong
Dr. Nor Azlina Abu Bakar
Dr A'aisah binti Senin

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For further information please contact:

Malaysian Health Technology
Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
Level 4, Block E1, Precinct 1
Government Office Complex
62590 Putrajaya.

Tel: 603 8883 1229

Fax: 603 8883 1230

Available at the following website:
<http://www.moh.gov.my>

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Introduction

Influenza infection is associated with considerable yearly morbidity and elderly population are among those at highest risk of serious outcomes. Annual influenza vaccination that is considered most-effective strategy to prevent influenza by the World Health Organization (WHO) is recommended for the elderly. Worldwide, these annual epidemics are estimated to result in about three to five million cases of severe illness, and about 290 000 to 650 000 deaths. In industrialised countries most deaths associated with influenza occurred among people age 65 or older. While a goal of reaching 75% vaccination coverage among older person by 2010 was set during 2003 World Health Assembly, only a few regions have reached this target, hence the target was extended to year 2015.

In tropical regions like Malaysia, influenza may occur throughout the year, with no clear seasonal trends, causing outbreaks more irregularly. Influenza A is usually detected more frequently than influenza B, although year-to-year variation may be considerable. The incidence of seasonal influenza remains unknown. However, there are issues with vaccinating the elderly for influenza, such as immunity conferred from vaccination is not lifelong and the presence of life threatening allergic reaction or severe allergy towards components of vaccine.

According to Drug Formulary, Ministry of Health (MOH), Influenza Vaccine (Inactivated) Injection is for prophylaxis of influenza for front liners (MOH staff and essential services personnel) and prophylaxis of influenza in high risk groups, particularly individuals who have chronic cardiovascular, pulmonary, metabolic or renal disease, or who are immunocompromised and elderly patients. Hence, this review was requested by the Head of Geriatric Unit in Hospital Queen Elizabeth to review the available evidence on influenza vaccination among the elderly and feasibility of implementing it in MOH.

Objective/Aim

To assess the efficacy or effectiveness, safety, organizational and societal issues as well as financial implication of influenza vaccination in the elderly population.

Results and Conclusions

A total of 301 records were identified through several databases and other sources. Five systematic review (SR) and meta-analysis (MA), five SR, one cohort, two cross-sectional studies, one case-control study and one cost-effectiveness study were included in this review. The studies were conducted in China, Australia, USA, Europe countries, Asia, Latin and Middle-east.

Effectiveness

Influenza rate: There was good level of retrievable evidence to suggest that influenza vaccination was effective in reducing influenza rate in the elderly. The evidence showed vaccinated elderly experienced less influenza compared to placebo. The IVE ranged from 31% to 58% depending on the types of influenza viruses.

Influenza Like-Illness: There was good level of retrievable evidence to suggest that vaccinated elderly experienced less ILI compared with unvaccinated elderly with IVE ranged from 19% to 45% among older patients aged ≥ 65 years old. The influenza vaccination also prevented ILI in type 1 and type 2 diabetic patients with IVE of 13%.

Mortality: All-cause mortality: There was fair to good level of retrievable evidence to suggest that influenza vaccination reduced all-cause mortality with IVE of 38%-56% among diabetic patients. **Influenza-related mortality:** There was fair to good level of retrievable evidence to suggest vaccination reduce mortality following

hospitalisation for pneumonia and influenza by 47% with IVE 25-62%. Study in US on seasonal-influenza, stated about 88.9% influenza-associated deaths averted among vaccinated group in the elderly while among French elderly population, showed that vaccination would avoid an influenza-attributable death with IVE of 35% compared to unvaccinated group.

Immune Response (Immunogenicity): There was fair to good level of retrievable evidence to suggest better immune response (immunogenicity) for all types of vaccine which include non-adjuvanted vaccine, aluminium hydroxide-adjuvanted vaccine, and AS03A-adjuvanted vaccine.

Organizational

The WHO recommended that northern hemisphere (including Malaysia) influenza season should use both trivalent or quadrivalent vaccines that contain both influenza type A and influenza type B virus (B/Colorado/06/2017-like virus of the B/Victoria/2/87-lineage) with a 75% vaccination coverage. In Malaysia, healthcare workers were included in annual immunization programme. According to Influenza Surveillance Programme in Malaysia, both National Public Health Laboratory (NPHL) Sungai Buloh and the Institute of Medical Research (IMR) found that influenza A virus was the most dominantly isolated virus with 291 (59.03%) positive isolates followed by influenza B with 202 (40.97%) isolates. However, data were not stratified according to age groups.

Safety

There was limited good level of retrievable evidence to suggest that the use of influenza vaccine was associated with non-significant adverse effects such as fever and nausea. The recent report regarding influenza-related death in South Korea was associated with the certain product brand for QIV.

Cost-effectiveness

SR on cost-effectiveness studies showing varying results ranging from being cost-effectiveness to not cost-effective in different population groups and countries. A cost-effectiveness study using societal perspective conducted in Singapore found the elderly plus some other age groups population to be the most cost-effective strategy.

Financial implication: Local economic evaluation cannot be conducted due to limitation of local data (epidemiological and costs data). Hence, the cost-effectiveness of Influenza vaccination among elderly population in Malaysia cannot be determined. Based on the financial implication analysis, the use of TIV (lowest cost) as an annual influenza vaccination is estimated to have an economic implication of approximately RM 5.447 million for a starting coverage rate of 10% (strategy 1). While in strategy 2, the lowest cost estimated for a coverage rate of 25% was RM 13.619 million per year. For strategy 3, the estimated lowest cost of TIV for elderly with diabetes mellitus with a prevalence of 41.5% a year was RM 22.61 million per year.

Methods

The following electronic databases were searched through the Ovid interface: Ovid MEDLINE® In-process and other Non-indexed citations and Ovid MEDLINE® 1946 to present, EBM Reviews - Cochrane Central Register of Controlled Trials - August 2019, EBM Reviews - Cochrane Database of Systematic Reviews - 2005 to August 2019, EBM Reviews - Health Technology Assessment – 4th Quarter 2018 and EBM Reviews – NHS Economic Evaluation Database 1st Quarter 2018. Searches were also run in EMBASE. PubMed and Google Scholar were used to search for additional web-based materials and information.

The references of retrieved articles were scrutinised for additional articles. No limits were applied. The last search was conducted on 23 January 20