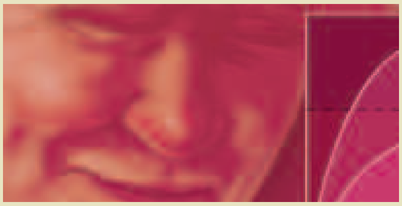
abstract



Recent evidence has shown that vaccination against influenza is effective in reducing the complications of influenza (pneumonia, hospitalization for influenza or pneumonia, and deaths due to influenza or pneumonia) for those 60 years and over living in long-term care facilities (LTCs) during periods of high viral circulation if the vaccine has a good match to the circulating strain. Vaccination was found to be similarly effective for those 60 and over living in the community.
There is further evidence that health care workers should be vaccinated for their own benefit, as vaccination is demonstrably effective for healthy adults under 60, and most health professionals are under 60. There is some evidence that vaccination of these workers may provide additional protection for residents of LTCs from the complications of influenza. Influenza can be detected by rapid office-based tests and should be used when the pretest probability of influenza is less than 30%. The evidence suggests that oseltamivir and zanamivir are effective in reducing the symptoms of cases and reducing infections in households and contacts of cases.

Key words: *influenza, older adults, vaccination, prevention of influenza, antivirals*

Preventing and Treating Influenza in Older Adults

Roger E. Thomas, MD, Ph.D., CCFP, MRCGP, *Professor, Department of Family Medicine, University of Calgary, and Cochrane Coordinator, University of Calgary, Calgary, AB.*

Prevention through Influenza Vaccination of Older Adults

The Center for Disease Control (CDC) states that the primary goal of vaccinating older adults against influenza is to reduce the risk of complications among those who are most vulnerable, particularly adults aged 65 years or older, and residents of long-term care facilities (LTCs).[1,2] This review assesses whether there is evidence to support these recommendations.

A recent systematic review examined the value of influenza vaccination for those 60 and older either living in the community or in LTCs. It included 49 cohort studies, 29 of them concerning individuals in residential communities with 6,702 observations during periods of high viral circulation and 27,282 during periods of low viral circulation, and 20 concerning individuals freely living in the community with over three million observations. There were also ten case-control studies with 20,582 observations and five RCTs with just over 5,000 observations.[3,4] Six outcomes were assessed: influenza-like influenza (a clinical definition), serologically proven influenza, pneumonia, prevention of hospitalization for influenza or pneumonia, prevention of deaths due to influenza or pneumonia, and prevention of deaths from all causes. Death from all causes is usually studied as an outcome of interest, but unless the cause (e.g., influenza) comprises a substantial component of total mortality, a study with large numbers would be needed to demonstrate an effect on total mortality; because many causes affect total mortality, attributing a change to any particular cause of mortality is questionable.

Prevention through Vaccination of LTC Residents Age 60 and Older

For residents of LTCs during periods when there were many influenza illnesses in the community and when there was a good match of the viruses included in the vaccine to the circulating strain(s), there were reductions in

– the number of cases of pneumonia (vaccine effectiveness [VE] = 46%; 95 % confidence interval [CI]= 30% to 58%)
– hospitalization for influenza or pneumonia (VE = 45%; 16–64%)
– the number of deaths due to influenza or pneumonia (VE = 42%; 17–59%)
– the number of influenza-like illnesses (VE = 23%; 6–36%)

There was no reduction in cases of serologically proven influenza (RR = 1.04 [0.43–2.51]) (Table 1).

During periods of frequent influenza illnesses when the viruses included in the vaccine did not provide a good match to the viruses circulating in the community, there were no significant effects.[3,4] Some of these confidence intervals are quite wide, reflecting the heterogeneity of the studies.

In about 50% of the LTC studies, the residents were older than 75 years, with multiple chronic pathologies and high dependency scores, but correction for confounders such as age, gender, smoking status, and chronic diseases is not possible as these were rarely reported by vaccine exposure.[3,4]

Table 1: Vaccine Effectiveness for Long-term Care Residents during Periods of High Viral Circulation*

Outcome measure	Good match of vaccine to the circulating strain(s)	Poor match of vaccine to the circulating strain(s)
Pneumonia	**VE = 46% (30–58%)**	(RR = 0.64 (0.35 –1.16)
Prevention of hospitalization for influenza or pneumonia	**VE = 45% (16–64%)**	No data
Prevention of deaths due to influenza or pneumonia	**VE = 42% (17–59%)**	RR = 0.34 (0.11–1.02)
Influenza-like illnesses	VE = 23% (6–36%)	RR = 0.77 (0.56–1.06)
Serologically proven Influenza	RR = 1.04 (0.43–2.51)	RR = 0.47 (22–1.04)

Source: Rivetti, 2006[3]; Jefferson, 2006.[4]
Legend: VE = vaccine effectiveness = VE = 1-relative risk (RR) or VE=1-odds ratio (OR). Relative risks (RR) with 95% confidence intervals (CI) are usually presented when results are not significant.
*In this and subsequent tables evidence of vaccine effectiveness is highlighted in bold.

Prevention through Vaccination of Community-dwelling Adults Age 60 and Older

For those 60 and older living in the community during periods when there were many influenza illnesses in the community and with a good match of the viruses included in the vaccine to the circulating strain(s), vaccination was associated with

- reduced hospitalization for influenza or pneumonia (VE = 26%; 12–38%)
- fewer deaths from all causes (VE = 42%; 24–55%)

There was no effect for influenza-like illness, influenza, pneumonia, hospitalizations for cardiac disease, or death from respiratory disease (Table 2).

Results were more statistically significant when the effectiveness of inactivated influenza vaccines for older adults living in the community was adjusted for the confounders gender, age, smoking, and comorbidities. There were reductions in

- hospitalization for influenza or pneumonia (OR = 0.73; 0.67–0.79)
- hospitalization for respiratory diseases (OR = 0.78; 0.72–0.85)
- hospitalization for cardiac disease (OR = 0.76; 0.70–0.82)
- mortality from all causes (OR = 0.53; 0.46–0.61) (Table 3)[3,4]

Vaccine Safety

The Cochrane Systematic Review of vaccination for older adults identified four randomized controlled trials (2,606 observations) that assessed the side effects of parenteral inactivated vaccines.[3,4] There were more systemic events in the treatment groups (general malaise, fever, nausea, headache) as compared with the placebo groups but the difference was not statistically significant. There was a statistically significant larger number of local adverse events such as sore arm or tenderness in the treatment compared to the placebo groups.[3,4]

Three studies (based on the entire population of the U.S.) assessed the effects of influenza vaccination on the development of Guillain-Barré Syndrome (GBS), an acquired immune-mediated inflammatory disorder of the peripheral nervous system. There was a strong (RR = 5.2; 95% CI = 3.9 to 7.0) and significant association between A/New Jersey/76 swine vaccine and GBS during the 1976 to 1977 influenza season, but no relationship (95% confidence intervals for the odds ratios included one) was shown

Table 2: Vaccine Effectiveness for Community-dwelling Older Adults during Periods of High Viral Circulation

Outcome measure	Good match of vaccine to the circulating strain(s)
Hospitalizations for influenza or pneumonia	**VE = 26% (12–38%)**
Deaths from all causes	**VE = 42% (24–55%)**
Hospitalizations for cardiac disease	RR = 0.87 (0.67–1.12)
Influenza-like illness, influenza, or pneumonia; death from respiratory disease	No effect

Source: Rivetti, 2006[3]; Jefferson, 2006.[4]
RR with 95% CI usually presented when results are not significant.

Table 3: Effectiveness of Inactivated Influenza Vaccines for Community-dwelling Older Adults

Outcome measure	Good match of vaccine to the circulating strain(s)
Hospitalizations for influenza or pneumonia	OR = 0.73 (0.67–0.79)
Hospitalizations for respiratory diseases	OR = 0.78 (0.72–0.85)
Hospitalizations for cardiac disease	OR = 0.76 (0.70–0.82)
Deaths from all causes	OR = 0.53 (0.46–0.61)

Source: Rivetti, 2006[3]; Jefferson, 2006.[4]
Note: Results adjusted for the confounders gender, age, smoking, and comorbidities.

for later seasons for vaccines not containing A/New Jersey/76.[3,4]

Prevention through Influenza Vaccination of Health Care Workers

The CDC Advisory Committee on Immunization Practices recommends vaccination of all health care workers.[5] There is evidence to support these recommendations.

A recent systematic review of the vaccination of health care workers against influenza who work with older adults[6,7] identified two related cluster-randomized controlled trials (2,476 patients) with moderate risk of bias and one cohort study (12,784 patients) at high risk of bias. Staff vaccination had a significant effect on influenza-like illness (VE = 86%; 40–97%) only when patients were also vaccinated. If patients were not vaccinated, staff immunization had no effect. Vaccinating health care workers did not appear efficacious against serologically proven influenza (RR = 0.87; 0.46–1.63) and there was no significant effect of vaccination on lower respiratory tract infections (RR = 0.70; 0.41–1.20). However, deaths from pneumonia were significantly reduced (VE = 39%; 2–62%), as were deaths from all causes (VE = 40%; 27–50%).

Both studies took place in Glasgow, Scotland. The initial study by Potter[8] was potentially affected by performance bias because 67% of staff in active arm 1 and only 43% in active arm 2 were vaccinated. Attrition bias (differential loss of subjects from the experimental and control groups) was unknown because a flow sheet of admissions and discharges during the five months of the study was not presented. Detection bias (incomplete ascertainment of outcomes of interest) was present because paired samples were obtained from only 225 (43%) of the 521 unvaccinated patients, and the numbers of influenza or influenza-like infections that occurred in health care workers were not reported.[6,7] The later study by Carman[9] also had performance bias (incomplete vaccination of the population of health care workers in the experiental arms of the study in the LTC institutions) because only 51% of health care workers received vaccine in the LTC hospitals where vaccine was offered, and 4.8% where it was not; and 48% of patients received vaccine in the arm where health care workers were offered vaccination, and 33% in the arm where they were not. Attrition bias was unknown because no flow sheet of admissions and discharges during the study was presented. There was also detection bias because virological samples were obtained for only 17 of 103 deaths in the hospitals where health care workers received vaccine and for 30 of 154 in hospitals where they did not. The analysis was not corrected for clustering, unlike the Potter study.[6,7]

Demicheli[10] found in healthy adults younger than 60 years that when both the vaccine matched the circulating strain and cases were serologically confirmed, the vaccine was effective (VE = 75%; 62–84%). This group includes most health care workers. There is thus independent evidence that vaccinating older adults in institutions and vaccinating the healthy under 60 is effective, but there is limited evidence of a synergistic benefit to older adults from vaccinating the health care workers who care for them.

Prevention of Influenza in Health Care Facilities by Organizational Interventions

There are patient, administrative, health care worker, and societal factors that affect influenza vaccination rates in older adults, and they will be systematically reviewed in a Cochrane Collaboration systematic review.[11] Patients are more likely to request the vaccine if they perceive themselves as susceptible to influenza, believe the vaccine is effective, and have few or no concerns about side effects. Some studies have explored the means and cost-effectiveness of encouraging patients to be vaccinated, such as reminder letters followed up by a phone call. Others have provided patient education. One study used financial incentives, and one used seniors themselves to advocate vaccination. Some investigators have queried whether there is a ceiling effect wherein all those who will respond to such cues have responded.[11]

Administrative measures to increase vaccination rates include increasing administrative access to vaccination services through telephone campaigns, providing more clinics, better clinic hours, including vaccination during existing home visits, arranging home visits specifically to provide vaccination, and decreasing administrative barriers such as paperwork. Decreasing economic barriers includes making vaccines available at free or low cost. Decreasing administrative barriers for staff can entail annual standing vaccine orders and transferring responsibility to other staff (for example, from physicians to nurses). System-wide administrative initiatives have featured continuous quality-improvement activities.[11]

Health care worker factors include personal beliefs and attitudes about whether individuals are susceptible to influenza and whether vaccination is effective and safe for themselves and their patients. Relevant professional behaviours include the frequency of taking a vaccination history, documenting vaccination, identifying high-risk patients, organizing reminders, providing reminders during annual physical examinations, and organizing and participating in educational campaigns or meetings for health care workers. Some studies have identified that recommendations by these professionals are important in vaccine acceptance by older adults. Other studies have investigated campaigns by professionals such as pharmacists.[11]

Societal interventions include administrative frameworks and campaigns that differ between societies and affect vaccination rates, feedback, or remuneration to health care workers for increasing vaccination rates, and being paid for achieving specific vaccination targets as in the UK.[11]

In LTCs, methods of increasing vaccination rates have involved providing automatic influenza vaccination annually without sign-in or physician order, allocating achieving vaccine completeness to a nurse, free vaccinations, vaccination campaigns, making vaccination available on all wards and all shifts, and instituting methods of reducing cases, morbidity, and mortality by rapidly diagnosing sentinel cases by direct immunofluorescence. Other efforts included quarantining affected wards, using antivirals promptly, and swiftly and effectively handling cases with respiratory or cardiac complications.[11]

Diagnosis and Treatment of Influenza

The symptoms of influenza-like illness of fever, cough, rigors, and sweats have poor individual predictive value for influenza. It is recommended that rapid office-based testing should be used but only if the pretest probability of influenza is less than 30%[12] (computed by ascertaining how many of the cases of influenza-like illness in a community are serologically proven cases of influenza). Outside the influenza season, if the pretest probability is 2%, a negative rapid test gives a probability of influenza of less than 1% and a positive test a probability of 27%. When the pretest probability is 5–10% (e.g., in the "shoulder seasons," early or late in influenza outbreaks), a negative rapid test gives a probability of 1–3% and a positive test a probability of 49–67%. Testing is not advocated in the middle of an influenza season if the pretest probability of a patient with symptoms having influenza is 30–50% because a negative test still yields a probability of 11–22%, and a positive test adds nothing by giving a probability of 89–95 %.[13] Medications that are effective against both Influenza A and B are oseltamivir (usually 75 mg orally twice daily) and zanamivir (usually 10 mg inhaled twice daily), each for five days, and both have discontinuation rates of less than 3% due to side effects. Treatment within 30 hours of the onset of symptoms decreases symptoms by two days, and within 48 hours by one day.[13]

A systematic review by Jefferson[13] (with four RCTs of prophylaxis with a mean of 492 patients in the zanamivir arms and 598 in the oseltamivir arms), and eight RCTs of treatment with a mean of 297 patients in the zanamivir arms and 384 in the oseltamivir arms) found that oseltamivir at 150 mg daily is effective for cases of symptomatic influenza (VE = 73%; 33–89%), for prevention of respiratory infections in influenza cases (OR = 0.32; 0.18–0.57), for postexposure prophylaxis for households (VE = 58.5%; 15.6–79.6), and for postexposure prophylaxis for contacts of index cases (VE = 58%; 34.9–84.2%, and up to VE = 89%; 67–97%) (Table 4). However, oseltamivir compared to placebo has a higher incidence of nausea (OR = 1.79; 1.10–2.93), with more nausea at higher dosages (OR = 2.39; 1.34–3.92). The reviewers recommended only using these neuraminidase inhibitors in influenza epidemics or pandemics.[14]

Table 4: Effectiveness of the Neuraminidase Inhibitors Oseltamivir and Zanamivir against Cases of Symptomatic Influenza and for Contacts of Influenza Cases

Outcome measure	Oseltamivir	Zanamivir
For cases of symptomatic influenza	**75 mg od: VE = 61%; 15–82%)** **150 mg od: (VE = 73%; 33–89%)**	**10 mg od: VE = 62%; 15–83%)**
Prevention of respiratory infections in influenza cases	**150 mg od: (OR = 0.32; 0.18–0.57)**	
Postexposure prophylaxis for households	**VE = 58.5%; 15.6–79.6%**	
Postexposure prophylaxis for contacts of index cases	**(VE = 58%; 34.9–84.2%) and up to (VE = 89%; 67–97%)**	

Source: Jefferson et al., 2006.[13]

Key Points

Systematic reviews have shown that vaccination against influenza effectively reduces the complications of influenza for those 60 years and over living in long-term care facilities (LTCs) during periods of high viral circulation, given a good match to the circulating strain.

Vaccination has been proven effective against complications of influenza for those 60 and over living in the community.

There is evidence that health care workers should be vaccinated for their own benefit, as vaccination is demonstrably effective for healthy adults under 60.

Influenza can be detected by rapid office-based tests; these tests should be used when the pretest probability of influenza is less than 30%.

There are many patient, administrative, health care worker, and societal factors that affect influenza vaccination rates in older adults, and many setting-appropriate measures are being investigated to increase vaccination rates, but there may be a ceiling effect to the rate of response.

The symptoms of influenza-like illness of fever, cough, rigors, and sweats have poor individual predictive value for influenza, and it is recommended that rapid office-based testing should only be used if the pretest likelihood of influenza is less than 30%.

Medications that are effective against both Influenza A and B are oseltamivir and zanamivir, each for five days, both of which are well-tolerated.

A systematic review recommended against using amantidine or rimantidine because of their rate of side effects.[14]

Conclusions

Influenza can be detected by rapid office-based tests, and their greatest usefulness is when the pretest probability of influenza is less than 30%. Oseltamivir and zanamivir are effective in reducing the symptoms of cases and preventing infections in households and contacts of cases.

Vaccination against influenza is effective against the complications of influenza for those 60 years and over living in LTCs or in the community. Vaccination is also effective for the healthy under 60 years of age (which includes most health care workers), suggesting that health care workers should be vaccinated for their own benefit. There is some evidence that vaccination of health care workers may protect residents of LTCs from the complications of influenza, but more evidence is required to prove a synergistic benefit for older adults.

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