

Stockpile, use during outbreaks, restock, repeat

Michael R. Kolber MD CCFP MSc Christina Korownyk MD CCFP

Clinical question

How effective are oseltamivir and zanamivir for decreasing postexposure transmission of influenza?

Bottom line

For institutionalized seniors, 6 weeks of oseltamivir or 14 days of zanamivir will prevent 1 additional influenza case in every 25 to 27 patients treated. For every 7 to 8 households given postexposure prophylaxis (PEP), 1 household will avoid anyone developing influenza.

Evidence

Best evidence is from mostly unpublished, industry sponsored RCTs¹ (1990s) and 2 systematic reviews.^{2,3} Results are based on laboratory-confirmed, symptomatic influenza.

- Institutionalized seniors.
 - Two RCTs examined zanamivir PEP during an influenza outbreak (10 cases or 10% with influenza) using 14 days of zanamivir (10 mg/d) versus rimantadine (N=385, 98% vaccinated) or placebo (N=489, 9% vaccinated).
 - At 15 days 2.9% of those taking zanamivir had influenza versus 7.4% of those taking rimantadine (statistically significant); 6.3% of those taking zanamivir had influenza versus 9.2% for placebo (not significant).
 - Pooled (by authors): 4.6% versus 8.3%; NNT=27.
 - A study of 6 weeks of oseltamivir (75 mg/d) or placebo in 548 (69% vaccinated) patients when influenza was “noted in the community” found influenza at 8 weeks in 0.3% of patients versus 4.4% for placebo; NNT=25.
- For households, 3 clustered (by household) RCTs examined PEP when a household member was diagnosed with influenza-like illness (mean age of contacts 24 to 33 years; <15% vaccinated; children excluded).
 - Zanamivir or placebo for 10 days: 4.6% of households had 1 or more new influenza cases at 11 days (pooled)^{1,4} versus 20.5% for placebo; NNT=7.
 - Oseltamivir (75 mg/d) or placebo for 7 days: 2.1% of households had 1 or more new influenza cases at 21 days^{1,5} versus 14.6% for placebo; NNT=8.
- There was no difference in hospitalizations.^{2,3} Multiple analyses were performed for adverse effects.³ For oseltamivir: psychiatric events (NNH=95), headache (NNH=32), and nausea (NNH=25).^{2,3} For zanamivir: no difference in treatment trials.³ Limitations include inconsistent outcome definitions and selective reporting.²

Context

- Canada stockpiles about 60 million doses (primarily oseltamivir); about 50% expire before use.⁶

- In closed facility outbreaks, guidelines recommend treating the index case, vaccinating the unvaccinated,⁷ and PEP for the longer of 14 days or 7 days after the onset of symptoms in the last infected person.⁸ For households, PEP is recommended only if vaccination is contraindicated.⁷

Implementation

Antiviral PEP is not a substitute for influenza vaccination.⁸ Vaccine efficacy is determined by seasonal prevalence and vaccine matching. For every 13 long-term care residents vaccinated, 1 fewer will develop influenza.⁹ Evidence suggests vaccination of health care workers decreases long-term care residents' mortality.^{10,11} While 72% of FPs reported being vaccinated, overall health care worker vaccination rates are about 50%.¹² Institution outbreaks should be considered when 2 or more residents have influenza-like symptoms within 72 hours of one another.⁸

Dr. Kolber and Korownyk are Associate Professors in the Department of Family Medicine at the University of Alberta in Edmonton.

Acknowledgment

We thank **Dr T. Jefferson** for advising us of the location of the unpublished reports.

Competing interests

None declared

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

References

1. Jefferson T, Jones MA, Doshi P, Del Mar CB, Hama R, Thompson MJ. *Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children*. Durham, NC: Dryad; 2014. Available from: <http://dx.doi.org/10.5061/dryad.77471>. Accessed 2016 Oct 14.
2. Jefferson T, Jones MA, Doshi P, Del Mar CB, Hama R, Thompson MJ, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. *Cochrane Database Syst Rev* 2014;(4):CD008965.
3. Heneghan CJ, Onakpoya I, Jones MA, Doshi P, Del Mar CB, Hama R, et al. Neuraminidase inhibitors for influenza: a systematic review and meta-analysis of regulatory and mortality data. *Health Technol Assess* 2016;20(42):1-242.
4. Hayden FG, Gubareva LV, Monto AS, Klein TC, Elliot MJ, Hammond JM, et al. Inhaled zanamivir for the prevention of influenza in families. *N Engl J Med* 2000;343:1282-9.
5. Welliver R, Monto AS, Carewicz O, Schattman E, Hassman M, Hedrick J, et al. Effectiveness of oseltamivir in preventing influenza in household contacts. *JAMA* 2001;285:748-54.
6. *Canadian pandemic influenza plan for the health sector: The use of antiviral drugs during a pandemic*. Ottawa, ON: Public Health Agency of Canada; 2009. Available from: www.phac-aspc.gc.ca/cpip-pcicpi/assets/pdf/annex_e-eng.pdf. Accessed 2016 Oct 20.
7. Aoki FY, Allen UD, Stiver HG, Evans GA. The use of antiviral drugs for influenza: a foundation document for practitioners. *Can J Infect Dis Med Microbiol* 2013;24(Suppl C):1C-15C.
8. Harper SA, Bradley JS, Englund JA, File TM, Gravenstein S, Hayden FG, et al. Seasonal influenza in adults and children—diagnosis, treatment, chemoprophylaxis and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. *Clin Infect Dis* 2009;48:1003-32.
9. Rudenko LG, Arden NH, Grigorieva E, Naychin A, Reksin A, Klimov AI, et al. Immunogenicity and efficacy of Russian live attenuated and US inactivated influenza vaccines used alone and in combination in nursing home residents. *Vaccine* 2000;19:308-18.
10. Ahmed F, Lindley MC, Allred N, Weinbaum CM, Grohskopf L. Effect of influenza vaccination of healthcare personnel on morbidity and mortality among patients: systematic review and grading of evidence. *Clin Infect Dis* 2014;58(1):50-7.
11. Thomas RE, Jefferson T, Lasserson TJ. Influenza vaccination for healthcare workers who care for people aged 60 or older living in long-term care institutions. *Cochrane Database Syst Rev* 2016;(6):CD005187.
12. Buchan SA, Kwong JC. Influenza immunization among Canadian health care personnel: a cross-sectional study. *CMAJ Open* 2016;4(3):E479-88.



Tools for Practice articles in *Canadian Family Physician (CFP)* are adapted from articles published on the Alberta College of Family Physicians (ACFP) website, summarizing medical evidence with a focus on topical issues and practice-modifying information. The ACFP summaries and the series in *CFP* are coordinated by Dr G. Michael Allan, and the summaries are co-authored by at least 1 practising family physician and are peer reviewed. Feedback is welcome and can be sent to toolsforpractice@cfpc.ca. Archived articles are available on the ACFP website: www.acfp.ca.