



Complete Summary

GUIDELINE TITLE

Prevention of influenza in the general population: recommendation statement from the Canadian Task Force on Preventive Health Care.

BIBLIOGRAPHIC SOURCE(S)

Langley JM, Faughnan ME. Prevention of influenza in the general population: recommendation statement from the Canadian Task Force on Preventive Health Care. CMAJ 2004 Nov 9;171(10):1169-70. [11 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

A complete list of planned reviews, updates and revisions is available under the What's New section at the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released:

- [April 02, 2008, Relenza \(zanamivir\)](#): GlaxoSmithKline informed healthcare professionals of changes to the warnings and precautions sections of prescribing information for Relenza. There have been reports (mostly from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who are receiving neuraminidase inhibitors, including Relenza.
- [March 4, 2008, Tamiflu \(oseltamivir phosphate\)](#): Roche and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of neuropsychiatric events associated with the use of Tamiflu, in patients with influenza. Roche has updated the PRECAUTIONS section of the package insert to include the new information and guidance under the Neuropsychiatric Events heading.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis

RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

SCOPE

DISEASE/CONDITION(S)

Influenza

GUIDELINE CATEGORY

Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To systematically review the evidence for the prevention of influenza infection in the general population

TARGET POPULATION

Healthy adults, children and adolescents

INTERVENTIONS AND PRACTICES CONSIDERED

1. Immunization with injectable inactivated influenza vaccine or nasally administered live-attenuated vaccine in healthy adults or children before each winter respiratory virus season

2. Prophylactic administration of neuraminidase inhibitors (oseltamavir and zanamavir) to household or close contacts within 36 to 48 hours of symptom onset of influenza in the index case

MAJOR OUTCOMES CONSIDERED

- Incidence of influenza virus infection (laboratory-confirmed infection, influenza-like illness, febrile illness during peak influenza period, severe febrile illness, upper respiratory tract illness)
- Economic outcomes associated with respiratory illnesses not confirmed by laboratory methods to be influenza (lost work days due to illness, health care provider visits and use of prescription antibiotics and over-the-counter medications)
- Efficacy of neuraminidase inhibitors
- Adverse effects of interventions

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Extraction of Evidence

Relevant articles were sought using MEDLINE between the years 1966 to March 2003, using the following search strategy for influenza vaccination trials: (("influenza vaccine"[Medical Subject Heading (MeSH) Terms] AND Clinical Trial[ptyp]) AND (("human"[MeSH Terms] OR "hominidae"[MeSH Terms]) OR "Human"[MeSH Terms])) AND ("1966"[PDat] : "2003/03"[PDat])). The search strategy for the effectiveness of neuraminidase inhibitor prophylaxis was the following: (((("Neuraminidase/antagonists and inhibitors"[MESH] AND Clinical Trial[ptyp]) AND (("human"[MeSH Terms] OR "hominidae"[MeSH Terms]) OR "Human"[MeSH Terms])) AND ("1966"[PDat] : "2003/03"[PDat])) AND (clinical trials or randomized clinical trials) for the antiviral search. The Cochrane Collaboration Library was also searched using the MESH terms "influenza vaccine" and "neuraminidase" for these two searches respectively.

The inclusion criteria for this review were: 1) any randomized controlled trial of influenza vaccines or neuraminidase inhibitors in humans, and 2) an outcome measured of clinical efficacy against prevention of naturally occurring influenza in healthy persons. A trial was considered randomized if the authors described assignment of study drug/vaccine by random allocation or quasi-random allocation (alternation, case record number, etc.) and controlled if there was a concurrent comparison group. Clinical efficacy measurement had to be determined by either a clinical definition of influenza or laboratory diagnosis; studies that measured only immunogenicity of vaccine were excluded. Studies were excluded

if they were not in English or French or were targeted at high-risk groups, since recommendations already exist for these groups.

The MEDLINE search for influenza vaccine trials yielded 533 studies and the Cochrane search identified four reviews. All of the studies identified through the Cochrane search (Cochrane) were also found through the MEDLINE search. Review of the 533 titles led to exclusion of 3 of the Cochrane reviews (ineligible patient population) and of individual studies for the following reasons: high risk populations (n=149 studies), language other than French or English (n= 56), and interventions other than influenza vaccine (e.g. educational, compliance, *Haemophilus influenzae*) (n=81). Review of the abstracts of the remaining 247 titles identified led to the exclusion of 182 studies. The most common reason was that the study outcome was vaccine immunogenicity or that it was a review article. Review of the methods of the 65 remaining studies identified 33 satisfying inclusion and exclusion criteria. The antiviral search identified two reviews in the Cochrane database and 43 studies in MEDLINE. Review of these articles identified five satisfying inclusion and exclusion criteria and one Cochrane review.

NUMBER OF SOURCE DOCUMENTS

537

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Research Design Rating

I: Evidence from randomized controlled trial(s)

II-1: Evidence from controlled trial(s) without randomization

II-2: Evidence from cohort or case-control analytic studies, preferably from more than one centre or research group

II-3: Evidence from comparisons between times or places with or without the intervention; dramatic results from uncontrolled studies could be included here

III: Opinions of respected authorities, based on clinical experience; descriptive studies or reports of expert committees

Quality Rating

Good: A study (including meta-analyses or systematic reviews) that meets all design- specific criteria* well

Fair: A study (including meta-analyses or systematic reviews) that does not meet (or it is not clear that it meets) at least one design-specific criterion* but has no known "fatal flaw"

Poor: A study (including meta-analyses or systematic reviews) that has at least one design-specific* "fatal flaw", or an accumulation of lesser flaws to the extent that the results of the study are not deemed able to inform recommendations

*General design-specific criteria are outlined in Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D. Current Methods of the U.S. Preventive Services Task Force: A Review of the Process. Am J Prev Med 2001; 20 (suppl 3):21-35.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Task Force reviewed 1) the initial analytic framework and key questions for the proposed review; 2) the subsequent drafts of the complete manuscript providing critical appraisal of the evidence prepared by the lead authors, including identification and double, independent critical appraisal of key studies or recent systematic reviews, and ratings of the quality of this evidence using the task force's established methodological hierarchy (See Appendix 1 of the original guideline document); and 3) a summary of the evidence and proposed recommendations.

Evidence for this topic was presented by the lead authors and deliberated upon during task force meetings in January 2000, February 2001, and June 2003. Expert panelists addressed critical issues, clarified ambiguous concepts and analyzed the synthesis of the evidence. At the end of this process, the specific clinical recommendations proposed by the lead authors were discussed, as were issues related to clarification of the recommendations for clinical application and any gaps in evidence. The results of this process are reflected in the description of the decision criteria presented with the specific recommendations. The group and lead authors arrived at final decisions on recommendations unanimously.

Procedures to achieve adequate documentation, consistency, comprehensiveness, objectivity and adherence to the Task Force methodology were maintained at all stages during review development, the consensus process, and beyond. These

were managed by the Task Force Office, under supervision of the Chair, and ensured uniformity and impartiality throughout the review process.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendations Grades for Specific Clinical Preventive Actions

A: The Canadian Task Force (CTF) concludes that there is **good** evidence to recommend the clinical preventive action.

B: The CTF concludes that there is **fair** evidence to recommend the clinical preventive action.

C: The CTF concludes that the existing evidence is **conflicting** and does not allow making a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

D: The CTF concludes that there is **fair** evidence to recommend against the clinical preventive action.

E: The CTF concludes that there is **good** evidence to recommend against the clinical preventive action.

I: The CTF concludes that there is **insufficient** evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision-making.

COST ANALYSIS

Published cost analyses were reviewed. Six trials of immunization in adults used outcome measures that capture the economic burden associated with respiratory illnesses not confirmed by laboratory methods to be influenza: lost work days due to illness, health care provider visits and use of prescription antibiotics and over-the-counter medications. These showed no reduction to modest reductions in lost time from respiratory illness. A cost benefit analysis of one of these influenza vaccination trials in healthy working adults using days of work missed, days working but at reduced effectiveness, and days with a health provider visit for an influenza-like symptom showed that vaccination (live attenuated intranasal vaccine) reduced costs associated with all these outcomes. The mean break-even cost for the vaccine and its administration was US\$43.07 using Monte Carlo analysis.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Peer Review

After final revision, the manuscript was sent by the Task Force to two experts in the field (identified by Task Force members at the meeting). Feedback from these experts was incorporated into a subsequent draft of the manuscript which was incorporated into the technical report.

Recommendations of Others

Recommendations on prevention of influenza in the general population from the following groups were discussed: the United States Preventive Services Task Force (USPSTF), the US Centers for Disease Control and Prevention, and the National Advisory Committee on Immunization (Canada).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation grades [**A-E, I**] and levels of evidence [**I, II-1, II-2, II-3, III, good, fair, poor**] are indicated after each recommendation. Definitions for these grades and levels are provided at the end of the "Major Recommendations" field.

The Canadian Task Force on Preventive Health Care (CTFPHC) recommends influenza vaccination in healthy adults (**A recommendation**) and children (**A recommendation**) (Powers et al., 1995, [**I, good**]; Edwards et al., 1994 [**I, good**]; Keitel, Cate, & Couch 1988 [**I, good**]; Monto, Miller, & Massab, 1982 [**I, good**]; Mair, Sansome, & Tillett, 1974 [**I, good**]; Bridges et al., 2000 [**I, good**]; Nichol et al., 1999 [**I, good**]; Nichol et al., 1995 [**I, good**]; Williams et al., 1973 [**I, good**]; Waldman & Coggins, 1972 [**I, good**]; Hobson et al., 1970 [**I, good**]; Hammond et al., 1978 [**I, fair**]; Rytel et al., 1977 [**I, fair**]; Leibovitz et al., 1971 [**I, fair**]; Tannock et al., 1984 [**I, fair**]; Mixeu et al., 2002 [**I, fair**]; Edmonson, Graham, & Warburton, 1970 [**I, fair**]; Eddy & Davies, 1970 [**I, fair**]; Neuzil et al., 2001 [**I, good**]; Belshe et al., 2000 [**I, good**]; Belshe et al., 1998 [**I, good**]; Gruber et al., 1996 [**I, good**]; Clover et al., 1991 [**I, good**]; Gruber et al., 1990 [**I, good**]; Hoskins et al., 1973 [**I, good**]; Rudenko et al., 1993 [**I, good**]; Alexandrova et al., 1986 [**I, good**]; Feldman et al., 1985 [**I, fair**]; Hurwitz et al., 2000 [**I, fair**]; Colombo et al., 2001 [**I, fair**]; Maynard et al., 1968 [**I, fair**]; Khan et al., 1996 [**I, fair**]; Wesselius de Casparius, Masurel, & Kerrebijn, 1972 [**I, fair**])

There is good evidence to support neuraminidase inhibitor prophylaxis in the household setting if it can be initiated within 36 to 48 hours of symptom onset in the index case. (**A recommendation**) (Hayden et al., "Use of the oral neuraminidase inhibitor," 1999 [**I, good**]; Hayden et al., "Use of the selective oral neuraminidase inhibitor," 1999 [**I, good**]; Welliver et al., 2001 [**I, good**]; Kaiser et al., 2000 [**I, good**]; Hayden et al., 2000 [**I, good**]; Monto et al., 2002 [**I, good**])

Definitions:

Levels of Evidence

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D: The CTF concludes that there is **fair** evidence to recommend against the clinical preventive action.

E: The CTF concludes that there is **good** evidence to recommend against the clinical preventive action.

I: The CTF concludes that there is **insufficient** evidence (in quantity and/or quality) to make a recommendation; however, other factors may influence decision-making.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Maneuver: Influenza vaccination in the healthy adult

- *Level of Evidence:* I, good to fair (systematic review of 18 randomized controlled trials [RCTs])

Maneuver: Influenza vaccination in children

- *Level of Evidence:* I, good to fair (systematic review of 15 RCTs)

Maneuver: Prevention of Influenza with neuraminidase inhibitors

- *Level of Evidence:* I, good (systematic review of 6 RCTs)

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Prevention of influenza in the person receiving the vaccine or antiviral agent
- Decreased economic disruption from lost work days and health care provider visits

POTENTIAL HARMS

- Discomfort at the injection site for 24 to 48 hours after vaccination
- Rhinorrhea and sore throat may occur in recipients of nasally administered live-attenuated vaccine
- Nausea and vomiting may occur in recipients of oseltamivir

QUALIFYING STATEMENTS

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The Canadian Task Force on Preventive Health Care (CTFPHC) recognizes that in many cases, patient-specific factors need to be considered and discussed, such as the value the patient places on the clinical preventive action; its possible positive and negative outcomes; and the context and/or personal circumstances of the

patient (medical and other). In certain circumstances where the evidence is complex, conflicting, or insufficient, a more detailed discussion may be required.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Quick Reference Guides/Physician Guides

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Langley JM, Faughnan ME. Prevention of influenza in the general population: recommendation statement from the Canadian Task Force on Preventive Health Care. CMAJ 2004 Nov 9;171(10):1169-70. [11 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Nov

GUIDELINE DEVELOPER(S)

Canadian Task Force on Preventive Health Care - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

The Canadian Task Force on Preventive Health Care (CTFPHC) is funded through a partnership between the Provincial and Territorial Ministries of Health and Health Canada.

GUIDELINE COMMITTEE

Canadian Task Force on Preventive Health Care (CTFPHC)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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Resource Staff: Ruth Walton, Research Associate; Jana Fear, Research Assistant, Canadian Task Force on Preventive Health Care, Department of Family Medicine, The University of Western Ontario, London, Ont

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Competing interests: None declared.

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A complete list of planned reviews, updates and revisions is available under the What's New section at the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).

GUIDELINE AVAILABILITY

Electronic copies: Available from the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).

Print copies: Available from the Canadian Task Force on Preventive Health Care, Clinical Skills Building, 2nd Floor, Department of Family Medicine, University of Western Ontario, London, ON, N6A 5C1.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Stachenko S. Preventive guidelines: their role in clinical prevention and health promotion. Ottawa: Health Canada, 1994. Available from the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).
- CTFPHC history/methodology. Ottawa: Health Canada, 1997. Available from the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).
- Quick tables of current recommendations. Ottawa: Health Canada, 1997. Available from the [Canadian Task Force on Preventive Health Care \(CTFPHC\) Web site](#).
- Langley, J.M., Faughnan, M.E., and the Canadian Task Force on Preventive Health Care. Preventive Health Care, 2003 Update: prevention of influenza in the general population: systematic review and recommendations. CTFPHC Technical Report. March 2005. London, ON: Canadian Task Force. Available from the [CTFPHC Web site](#).
- Langley, J.M., Faughnan, M.E., and the Canadian Task Force on Preventive Health Care. Preventive Health Care, 2004 Update: prevention of influenza in the general population. Recommendation table. Available from the [CTFPHC Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 11, 2005. The information was verified by the guideline developer on August 25, 2005. This summary was updated by ECRI on November 21, 2006 following the FDA advisory on Tamiflu. This summary was updated by ECRI Institute on March 10, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Tamiflu (oseltamivir phosphate). This summary was updated by ECRI Institute on April 9, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Relenza (zanamivir).

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