Stockpile, use during outbreaks, re-stock and repeat

Clinical Question: How effective are oseltamivir and zanamivir at decreasing post-exposure transmission of influenza?

Bottom Line: For institutionalized seniors, six weeks of oseltamivir or 14 days of zanamivir or will prevent one additional influenza case in every 25-27 treated. For every 7-8 households given post-exposure prophylaxis (PEP), one household will avoid anyone developing influenza.

Evidence:
Mostly unpublished, industry-sponsored, Randomized Controlled Trials (RCTs)1 (from 1990s) and two systematic reviews.2,3 Results all lab confirmed, symptomatic influenza.

- Institutionalized seniors:
  - Zanamivir: PEP during influenza outbreak (ten cases or 10% with influenza):
    - Two RCTs of 14 days of zanamivir 10 mg/day versus rimantadine (was standard of care) or placebo in 385 (98% vaccinated) and 489 (9% vaccinated) residents, respectively.
    - Influenza at 15 days:
      - 2.9% versus 7.4% (rimantadine); statistically significant.
      - 6.3% versus 9.2% (placebo); not statistically different.
    - Pooled (by authors): 4.6% versus 8.3%, Number Needed to Treat (NNT)=27.
  - Oseltamivir: Six weeks of oseltamivir 75 mg/day or placebo in 548 (69% vaccinated) patients when influenza “noted in the community.”
    - Influenza at eight weeks: 0.3% versus 4.4% (placebo), NNT=25.

- Households:
  - Three clustered (by household) placebo-controlled RCTs when household member diagnosed with influenza-like illness. Contacts’ mean ages 24-33 years (children excluded), <15% vaccinated:
    - Zanamivir: Ten days of zanamivir or placebo; households with ≥1 new influenza case at 11 days (pooled): 1,4
• 4.6% versus 20.5% (placebo), NNT=7.
  ▪ Oseltamivir: Seven days of oseltamivir 75 mg/day or placebo; households with ≥1 new influenza case at 21 days: 1,5
  ▪ 2.1% versus 14.6% (placebo), NNT=8.
• Other outcomes:
  o Hospitalizations: No difference.2,3
  o Adverse effects: Multiple analyses performed.3
    ▪ Oseltamivir: Psychiatric events Number Needed to Harm (NNH)=95; headache NNH=32; nausea NNH=25.2,3
    ▪ Zanamivir: No difference in treatment trials.3
• Limitations: Inconsistent outcome definitions, selective reporting.2

Context:
• Canada stockpiles ~60 million doses of primarily oseltamivir, ~50% expire before use.6
• Guidelines recommend:
  o Closed facility outbreaks:
    ▪ Treating index case and vaccinating the unvaccinated.7
    ▪ PEP for 14 days or seven days after the onset of symptoms in the last infected person, whichever is longer.8
  o Household contact: PEP only if vaccination contra-indicated.7

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References:
   a. RCTs referenced: NAIA3003, NAIA3004, WV15825, NAI30031, NAI30010, WV15799.
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