Effect of influenza antiviral post-exposure prophylaxis and treatment on transmission in community and high-risk settings: A rapid systematic review

Report

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What is Known and What is New?

What is Known

Influenza antivirals have long been used for treatment and post-exposure prophylaxis, particularly when vaccination is unavailable, mismatched, or insufficient to prevent outbreaks. Previous systematic reviews have consistently shown that influenza antivirals, particularly oseltamivir and zanamivir, are effective for post-exposure prophylaxis and reduce the risk of symptomatic secondary influenza in households and other exposed populations. Across earlier reviews of randomized trials, pooled effect estimates for household pre- and post-exposure prophylaxis generally favored antivirals over placebo or no antiviral, with relative risks or odds ratios in the range of about 0.1 to 0.5. Earlier reviews also suggested that benefit is greatest when treatment or prophylaxis is started promptly, usually within 48 hours of symptom onset or exposure. However, most prior reviews focused on prevention of symptomatic infection and risk-benefit trade-off for exposed individuals rather than onward transmission from treated index cases, and many mostly focused on oseltamivir and zanamivir.

What is New

This review adds to the literature in several important ways. First, it focuses specifically on transmission related outcomes for post-exposure prophylaxis with or without index case treatment, including secondary attack rate and household secondary transmission. Second, it brings together evidence across randomized trials, non-randomized studies and modelling studies, which allows a broader assessment of how antivirals may affect influenza spread in household, institutional, and community settings. Third, it includes more recent comparative evidence for post-exposure prophylaxis and or index case treatment involving antivirals that are approved in Canada including baloxavir marboxil, oseltamivir, peramivir, and zanamivir.

Executive Summary

Background

Influenza continues to cause substantial morbidity, mortality, and healthcare utilization in Canada. Although vaccination is the cornerstone of prevention, its effectiveness varies by season and population, and outbreaks continue to occur. Antiviral medications—oseltamivir, zanamivir, baloxavir marboxil, and peramivir—are frequently used for treatment and post-exposure prophylaxis, particularly in outbreak and high-risk settings. Existing reviews have largely focused on individual level prevention and treatment rather than influenza transmission. In this review we aimed to evaluate the effect of influenza antiviral post-exposure prophylaxis or treatment, compared with no antiviral use, on measures of influenza transmission among exposed asymptomatic or infected individuals in community and high-risk settings.

Methods

This rapid systematic review followed Cochrane methods, PRISMA 2020 reporting, and the GRADE approach. The MEDLINE, Cochrane Library, Epistemonikos, and TRIP databases were searched from 2000 to 2026. Randomized controlled trials (RCTs), non-randomized studies (NRS), and modelling studies evaluating antiviral post-exposure prophylaxis or treatment were included. Transmission was assessed using the secondary attack rate as the primary outcome, with secondary outcomes including the basic reproduction number, effective reproduction number, serial interval, bottleneck analysis, and duration of viral shedding.

Results

Fifty-one studies met inclusion criteria, with 28 contributing to quantitative analyses. Evidence from RCTs demonstrates that antiviral post-exposure prophylaxis probably reduces influenza transmission, with secondary attack rates reduced by approximately half compared with placebo or no antiviral use. This effect was consistent across households, community settings, and long-term care or healthcare facilities, with high certainty in household and community settings. Antiviral prophylaxis also reduced viral shedding in one trial.

Evidence for treatment of index cases was more limited but suggested a ~30% relative reduction in onward transmission compared with no treatment. Early treatment initiated within 24 hours of symptom onset was associated with lower transmission than delayed or no treatment. Head-to-head comparisons between antiviral agents were predominantly based on non-randomized studies and were of low to very low certainty. These analyses suggested that baloxavir marboxil, zanamivir, and peramivir may be associated with lower secondary attack rates than oseltamivir, but the certainty of this evidence is very low. Longer treatment duration may reduce transmission more than shorter duration (e.g., 5 vs. 10 days of oseltamivir prophylaxis) but also this evidence is of very low certainty. Modelling studies supported reduced transmission with antiviral use, particularly when initiated early and used broadly.

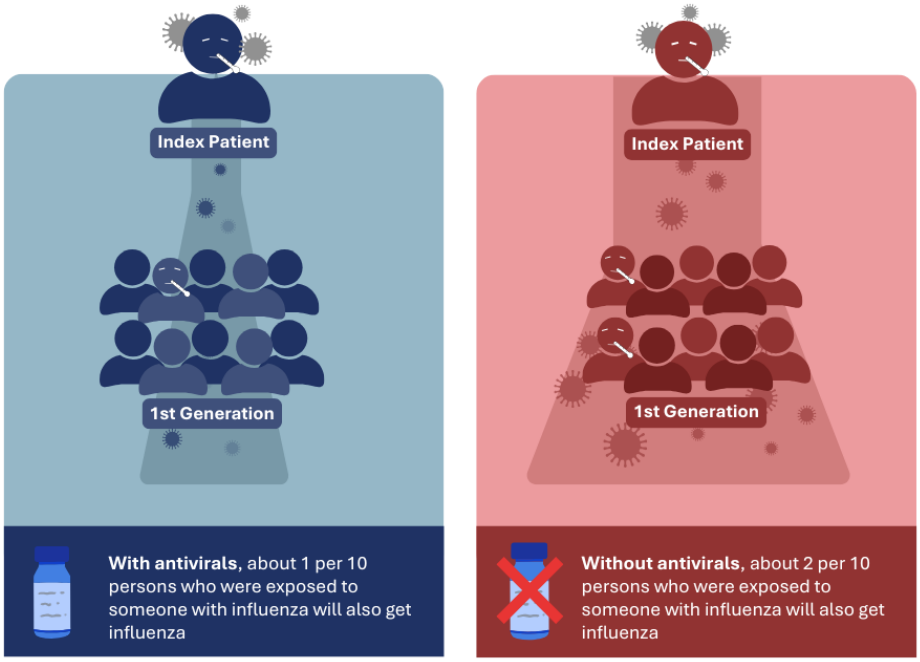
Conclusions

Influenza antivirals probably reduce transmission, especially when used for post-exposure prophylaxis and initiated early; however, this conclusion is driven primarily by evidence from secondary attack rate outcomes, with more limited data available for other transmission metrics. The strongest evidence supports prophylaxis strategies. Uncertainty remains regarding the optimal choice of antiviral agent and treatment duration, underscoring the need for additional high-quality research focused on transmission outcomes.

Visual Summary

Antivirals probably prevent onward transmissions of influenza in the community and high-risk settings

Antivirals probably make it **half as likely** to get and transmit influenza in healthy persons who have been in close contact with someone who has influenza.



The index patient with influenza often also receives an antiviral

Introduction

Background and Rationale

Acute respiratory infections remain a leading cause of morbidity and mortality [1], causing 4.25 million deaths each year or ~6% of all deaths globally [2]. Influenza is one of the most common respiratory pathogens and a leading cause of community-acquired pneumonia, health service use, and mortality [3]. In Canada, influenza causes over 12,200 hospitalizations each year, and each lab-confirmed case costs CA$14,612 on average [4].Mitigation of influenza transmission therefore has the potential to substantially improve health outcomes and reduce health care costs at the population level. While vaccination is the primary preventive strategy, if sufficiently available and obtained, vaccine effectiveness varies by season, strain, and population, and outbreaks continue to occur even in highly vaccinated communities [5]. When vaccine-derived protection is limited, antiviral treatment and prophylaxis, particularly post-exposure prophylaxis, may serve as an important strategy for prevention of influenza symptoms and onward transmission to others, especially among individuals at increased risk of severe outcomes [6]. As a result, additional strategies to mitigate influenza transmission remain an important public health priority.

Previous systematic reviews have demonstrated that antiviral post-exposure prophylaxis with neuraminidase inhibitors can reduce the incidence of influenza [7] and the risk of symptomatic infection among individuals and households [8]. These reviews have primarily evaluated individual-level preventive efficacy and safety outcomes and have often focused on a subset of antiviral classes. Although newer agents such as baloxavir marboxil have been assessed for prophylactic efficacy in randomized controlled trials [9], the comparative role of different antiviral classes in reducing transmission of influenza in community settings remains unclear, particularly beyond trial settings. To date, no comprehensive evidence synthesis has focused on transmission-specific outcomes, such as secondary attack rates or other epidemiologic measures of spread, across antiviral agents and study designs. A targeted synthesis of transmission-related evidence from treatment and post-exposure prophylaxis is therefore needed to inform outbreak management and public health decision-making.

Research Question

Among exposed (asymptomatic) or infected individuals in community and high-risk settings, what is the effect of influenza antiviral post-exposure prophylaxis or treatment, compared with no antiviral use, on measures of transmission?

Methods

Methods for this rapid systematic review were based on the Cochrane Handbook for Systematic Reviews [10] and the GRADE approach [11]. Reporting aligns with the PRISMA 2020 statement [12].

Eligibility Criteria

Table 1 outlines the study inclusion and exclusion criteria applied for this rapid systematic review.

Table 1: Eligibility Criteria

	Include	Exclude
Population	• Individuals exposed to (asymptomatic) or infected with influenza in community settings or high-risk settings • Subgroups: influenza strains and subtypes; underserved populations (e.g., equity-seeking groups based on income, housing instability, access to care, remoteness including northern locations; only if reported. Based on demographics: age, sex, gender, Indigenous status, racialized groups; only if reported)	
Intervention	• Antivirals for post-exposure prophylaxis or treatment of pandemic or seasonal influenza: oseltamivir, zanamivir, baloxavir marboxil & peramivir	• Pre-exposure prophylaxis • Antivirals for post-exposure prophylaxis to prevent animal to human transmission of zoonotic influenza (include if the study reports human to human transmission outcomes).
Comparator	• No antivirals (placebo) • Head-to-head comparisons among oseltamivir, zanamivir, baloxavir marboxil, and peramivir	• Head-to-head comparisons with any other antivirals
Outcome	• Influenza transmission rate • Primary outcome: secondary infection rate (household, institutional or close contact); • Secondary outcomes: basic reproduction number, effective reproduction number, serial interval, bottleneck analysis, duration of viral shedding	• Clinical efficacy of antivirals • Clinical safety of antivirals • Studies that report prevention of individual infection risk without data on transmission to others
Setting	• OECD countries • Community settings = general population • High-risk settings = frontline health care settings, long-term care homes, correctional facilities and detention centres, shelters and transitional housing, group homes, multi-generational or crowded	

	households including those common in some Indigenous communities in rural and remote locations where shared living arrangements are more likely to exist.	
Study Design	• Systematic reviews • Randomized controlled trials (RCTs) • Non-randomized studies, including cohort studies, case control studies, quasi-experimental designs • Modelling studies (Primarily models that examine how antiviral treatment or post exposure prophylaxis influence influenza transmission and draw on empirical data from households or other congregate living environments where available. Key parameters such as secondary attack rates, reproduction numbers, timing and coverage of antiviral use, characteristics of the setting would help support interpretation of antiviral effects on transmission)	• Animal studies • Basic science/lab studies • Case reports or small case series without a comparator group or without assessment of transmission • Cross-sectional studies that do not evaluate temporal or onward transmission • Narrative reviews • Trial registry protocols • Conference abstracts for which no full-text publication can be found
Other		• Non-English studies

Information Sources and Search Strategy

We conducted a comprehensive literature search in February and March 2026, including databases that capture grey literature, to identify relevant studies. The following electronic databases were searched:

- Ovid MEDLINE – 1946 to February 19, 2026
- Cochrane Library – from inception to March 11, 2026
- Epistemonikos – from inception to March 11, 2026
- TRIP Database (formerly known as Turning Research Into Practice) – from inception to March 12, 2026

Results from all electronic database searches were limited to the years 2000-2026 because oseltamivir and zanamivir were approved in late 1999.

Reference lists of eligible systematic reviews were also screened to identify relevant studies.

The search strategy was developed using a combination of controlled vocabulary (i.e., MeSH) and free-text terms. It was designed by members of the research team and peer-reviewed by an information specialist (Tamara Navarro-Ruan) using the PRESS Checklist [13].

The MEDLINE search strategy was adapted for the other databases by translating controlled vocabulary (e.g., MeSH terms into free-text terms) and modifying syntax and operators where appropriate while maintaining an equivalent conceptual structure to the MEDLINE search.

Full search strategies for all databases are provided in *Appendix 1*.

Search results were exported to EndNote [14] and uploaded to Covidence [15]. For the TRIP database search, full metadata for each record was not available in the exported RIS file leading to numerous missing abstracts. As a solution, we used the 'Find Reference Updates' feature in EndNote to populate each record with more information before uploading the results to Covidence.

Duplicates were removed automatically by Covidence using their deduplication algorithm. Any duplicates missed by the algorithm were manually removed by the review team during screening.

Study Selection

Title and abstract screening was conducted independently by two reviewers using Covidence. Full-text articles were retrieved for records deemed potentially eligible. Full-text screening was conducted independently by two reviewers using the pre-defined eligibility criteria in *Table 1*. Discrepancies at both stages were resolved by a third reviewer (Stephanie Duda, Benita Hosseini, Robby Nieuwlaat). Reasons for exclusion at the full-text stage were recorded.

Data Extraction

Data were extracted from included studies using a standardized, piloted Excel form developed by the review team. Data extraction was conducted independently by one reviewer and verified by a second reviewer. Discrepancies were resolved through discussion or consultation with a third reviewer (Robby Nieuwlaat).

The following study level characteristics were extracted:

- Study identification (first author, year)
- Study design (e.g., RCT, modelling study, cohort study, etc.)
- Setting (country, study period)
- Population (description, total sample size, sex, age, ethnicity, influenza vaccination status)
- Intervention (antiviral agent, antiviral purpose [treatment, prophylaxis], antiviral dose, antiviral duration, sample size per intervention arm)
- Comparator (description, sample size per comparator arm, duration of follow-up)
- Outcomes
- Study limitations

For each outcome of interest, the following data were extracted:

- Numerical results (e.g., event counts, attack rate, secondary infection rate, 95% confidence intervals)
- Effect measures (e.g., relative risk, odds ratios)

For modelling studies, we additionally extracted model characteristics, including model type and data sources, transmission parameters and assumptions, antiviral coverage and timing assumptions, setting characteristics, scenario definitions, and modelled transmission outcomes.

Risk of Bias Assessment

The risk of bias of included studies was assessed using the Cochrane RoB 2.0 for RCTs [16], the Newcastle-Ottawa Scale for non-randomized studies of interventions [17], and CHEERS for modelling studies [18]. Although CHEERS is a reporting checklist for economic evaluations of health interventions, we used it as a proxy to assess risk of bias in modelling studies, as no tool specifically for this purpose is currently available. Risk of bias was not assessed for included systematic reviews as all reviews were published before the last 5 years and none of the reviews contained new information that wasn't already captured by the primary studies identified by our search. Given the rapid review methodology, modifications to standard risk of bias procedures were implemented to enhance efficiency. Specific modifications to streamline the process included: risk of bias assessments were conducted at the study level; andstudies were assessed by one reviewer (studies with uncertainty in the assessment were independently verified by a second reviewer). Discrepancies were resolved through discussion or consultation with a third reviewer (Robby Nieuwlaat).

An overall risk of bias judgment was assigned for each study based on tool-specific guidance.

Risk of bias assessments were incorporated into the evidence synthesis by informing GRADE certainty of evidence assessments. Also, sensitivity analyses were conducted whereby studies with high risk of bias were excluded from the meta-analysis when 3 or more studies were included.

Data Synthesis

Studies were eligible for pooling in meta-analysis if the population, intervention, comparator, and outcome measurements were sufficiently homogeneous, and sufficient details for primary data were available.

For studies that reported the same outcome in different ways (e.g., after 5, 10, or 21 days of treatment, or for symptomatic only vs laboratory confirmed influenza cases) the authors selected the most appropriate outcome for evidence synthesis to prevent double-counting.

Where meta-analysis was not appropriate, we reported a narrative synthesis.

Systematic reviews were excluded from the data synthesis because all eligible systematic reviews were older (i.e., none published in the previous 5 years), and all primary studies included in the reviews were already captured and included by our search and screening process. Therefore, the identified systematic reviews only served as a source for eligible primary studies.

Data were prepared for synthesis by extracting outcome data, including events and total number of participants in each study arm, or by extracting reported adjusted, or otherwise unadjusted effect estimates with confidence intervals (CI).

Meta-analyses were conducted using Review Manager (RevMan)[19]. For dichotomous outcomes, effect estimates were pooled using risk ratios (RR) with 95% confidence intervals (CI) using the inverse variance method. A random-effects model was applied to account for between study variance estimated using the restricted maximum likelihood (REML) approach. Statistical heterogeneity was assessed using the I^2 statistic and Chi-square test (Q test).

When dichotomous data were unavailable, effect estimates were converted to natural logarithms (log odds ratio [log OR]) with standard error (SE), and pooled using generic inverse variance.

Subgroup analyses were conducted where data was available for the type of setting (e.g., households or community; long-term care homes or healthcare facility) and demographics (e.g., facility staff or resident).

Certainty of Evidence

The certainty of the evidence for the effect on each outcome was assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach [11] using GRADEPro GDT software [20]. GRADE certainty assessments for each outcome were conducted in singlet and verified by a senior methodologist (Robby Nieuwlaat). For judgments regarding imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel [9].

Results

Study Selection

The electronic database searches identified 2,231 records. No additional records were identified from reference lists of eligible systematic reviews. After removal of 232 duplicates, 1,999 unique records were screened by title and abstract. Of these, 1,796 records were excluded during title and abstract screening. The remaining 203 full-text citations were assessed for eligibility. One full-text technical report could not be found. A total of 51 studies met the inclusion criteria and were included in the review. Twenty-eight studies were included in our quantitative analysis. A PRISMA flow diagram of the study selection process is presented in *Figure 1*. A list of studies excluded at the full-text screening stage, along with reasons for exclusion, is provided in *Appendix 2*.

Study Characteristics

A total of 51 studies were included in this review, comprising 10 RCTs, 18 non-randomized studies, 17 systematic reviews, and 6 modelling studies.

Detailed characteristics of included studies are presented in *Appendix 3*.

Risk of Bias in Included Studies

Thirty-four primary and modeling studies were assessed for risk of bias. Amongst the ten RCTs, three studies had low risk of bias, five studies had some concerns, and two studies had high risk of bias. The most common sources of bias amongst RCTs were bias arising from the randomization process (4 RCTs with some concerns), bias due to deviations from the intended intervention (2 RCTs with some concerns, 1 RCT with high risk of bias), bias due to missing outcome data (2 RCTs with high risk of bias), and bias in the selection of the reported result (3 RCTs with some concerns). Amongst the eighteen NRS, five studies were good quality, one study was fair quality, and twelve studies were poor quality. The most common source of bias amongst NRS was failure to match groups or adjust for key confounders in the study's design or analysis (10 NRS had zero stars for the comparability domain). Detailed risk of bias assessments are presented in *Figure 2* for RCTs, and *Figure 3* for NRS. Amongst the six modelling studies, CHEERS reporting checklist was used to assess the reporting quality as a proxy for risk of bias. One study was a full economic evaluation [21], one was a partial economic evaluation [22], and four were non-

economic models [23-26] focused on viral transmission modelling. Overall, the two economic evaluation studies consistently addressed the key CHEERS domains, whereas the non-economic models had multiple domains that were not applicable. Across all modelling studies, the overall reporting quality was generally good for domains that were applicable. Limitations were primarily related to domains that were not applicable to non-economic models, rather than poor reporting.

Figure 1: PRISMA Flow Diagram

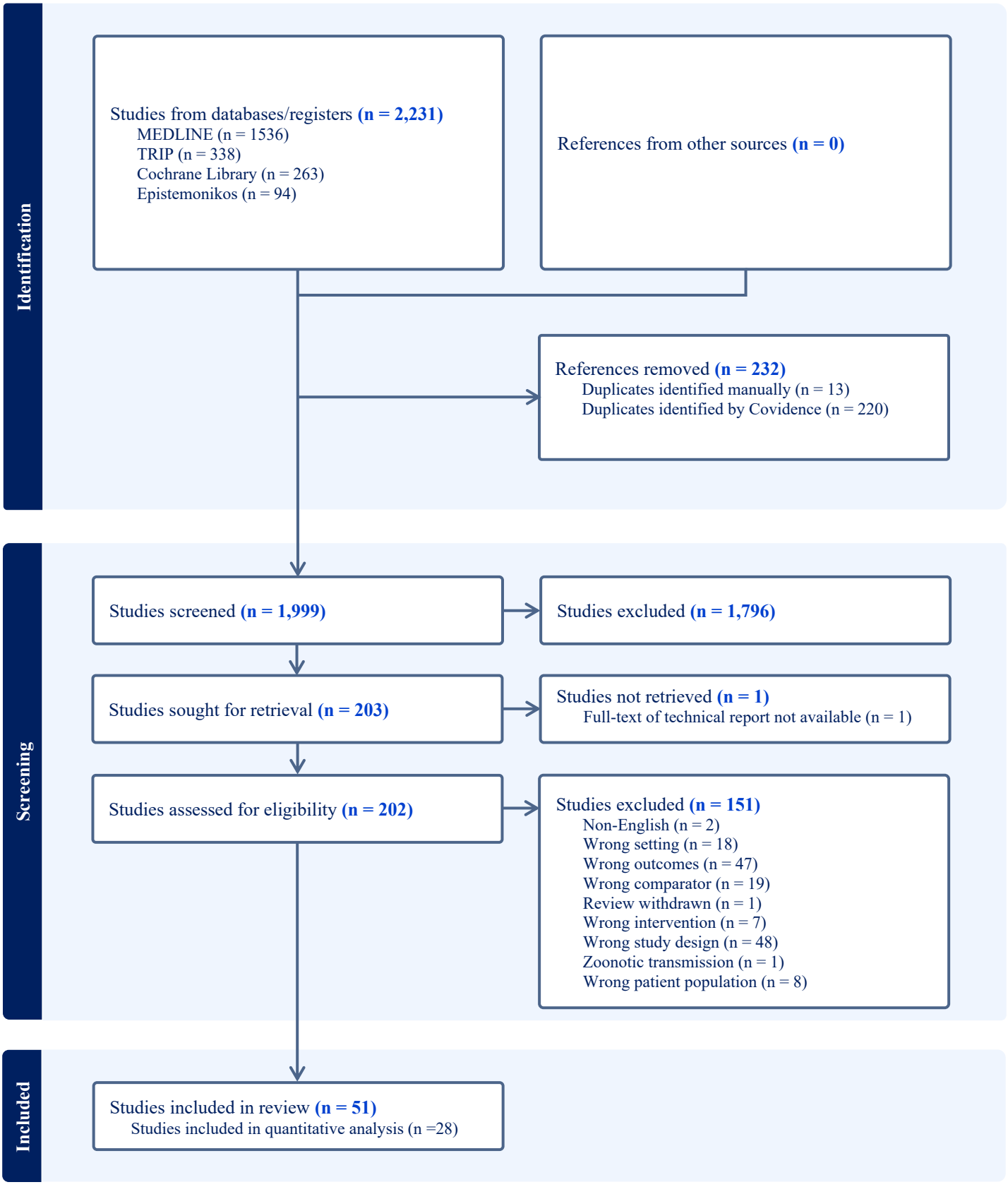


Figure 2: Risk of Bias for RCTs using the Cochrane Risk of Bias 2.0 Tool

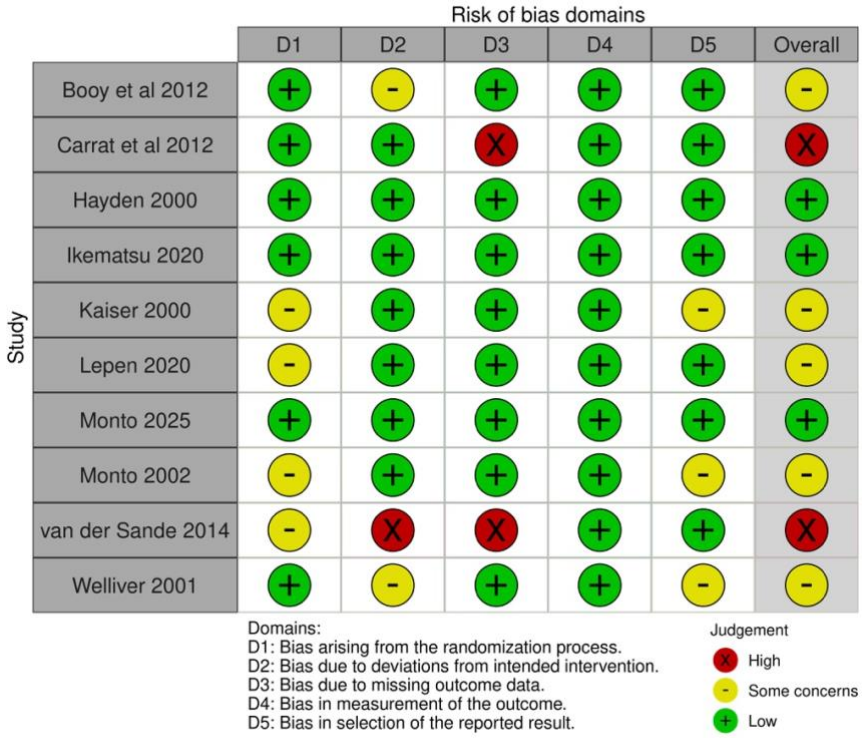


Figure 3: Risk of Bias for Non-Randomized Studies using the Newcastle Ottawa Scale

Study	Selection	Comparability	Outcome	Overall
Best 2024	★★★	-	★★	✗
Dronavalli 2020	★★★★	-	★★★	✗
Fujita 2020	★★★	-	★★★	✗
Goldstein 2010	★★★	-	★★	✗
Gorisek Miksic 2015	★★	-	★★★	✗
Higa 2012	★★★	-	★★★	✗
Hirotsu 2019	★★★★	★★	★★	+
Ikematsu 2024	★★★	★★	★★	+
Kojima 2025	★★★★	-	★★★	✗
Komeda 2021	★★★	★	★★★	+
Komiya 2010	★★★	-	★★★	✗
Nakano 2014	★★★	★	★★	✗
Nishiura 2011	★★	★	★★	–
Shah 2019	★★★★	★	★★★	+
Shapiro 2025	★★	★	★★★	✗
Shinjoh 2012	★★★	-	★★★	✗
Teh 2012	★★★★	-	★	✗
Umemura 2020	★★★★	★	★★★	+

Legend: ✗ Poor quality – Fair quality + Good quality

Results of Individual Studies

All extracted results regarding effects on eligible outcomes per included study are provided in *Appendix 4*.

Synthesis of Results

A total of 34 studies contributed to the synthesis for our primary outcome, secondary attack rate, including 28 studies in meta-analyses, and 6 modelling studies. See *Figures 4-18* for forest plots and *Tables 2-9* for the summary of findings.

For antiviral post-exposure prophylaxis compared with placebo or no antiviral prophylaxis, findings were broadly consistent across study designs, although effect estimates varied by setting and certainty of the evidence varied by study design and setting. Absolute effect estimates were dependent on the control group risk from the studies (baseline risk), and although this risk varied by study the overall baseline risk was around 20% for both RCTs and NRS. The effects from NRS were all very uncertain. Antiviral prophylaxis was associated with a lower secondary attack rate overall (RR 0.32, 95% CI 0.14 to 0.72; *Figure 4*) which translated into 128 fewer events per 1,000 persons (95% CI 161 fewer to 53 fewer; very low certainty; *Table 2*). In subgroup analyses, the pooled estimate showed a reduction among long-term care or healthcare facility residents (RR 0.42, 95% CI 0.13 to 1.38; *Figure 4*) which translated into 107 fewer events per 1,000 persons (95% CI 160 fewer to 70 more; very low certainty; *Table 2*), and among staff (RR 0.71, 95% CI 0.30 to 1.66; *Figure 4*) which translated into 128 fewer events per 1,000 persons (95% CI 308 fewer to 290 more; very low certainty; *Table 2*), as well as in household or community settings (RR 0.17, 95% CI 0.04 to 0.68; *Figure 4*) which translated into 184 fewer events per 1,000 (95% CI 213 fewer to 71 fewer; very low certainty; *Table 2*). The evidence from randomized trials was of higher certainty than that from NRS. Overall, RCTs showed a reduction in secondary attack rate with antiviral prophylaxis compared with placebo or no antiviral (RR 0.46, 95% CI 0.36 to 0.60; moderate certainty; *Figure 5*) which translated into 123 fewer events per 1,000 persons (95% CI 146 fewer to 91 fewer; moderate certainty; *Table 2*). A reduction was also seen in household or community settings (RR 0.41, 95% CI 0.33 to 0.50; *Figure 5*) which translated into 121 fewer events per 1,000 persons (95% CI 138 fewer to 103 fewer; high certainty; *Table 2*), among long-term care or healthcare facility staff (RR 0.63, 95% CI 0.44 to 0.91; *Figure 5*) which translated into 79 fewer events per 1,000 persons (95% CI 119 fewer to 19 fewer; moderate certainty; *Table 2*), and among residents (RR 0.62, 95% CI 0.49 to 0.79; *Figure 5*) which translated into 130 fewer events per 1,000 persons (95% CI 174 fewer to 72 fewer; low certainty; *Table 2*). In addition, one RCT found that antiviral prophylaxis reduced viral shedding compared with placebo or no antiviral (RR 0.16, 95% CI 0.06 to 0.47; *Figure 6*) which translated into 98 fewer events per 1,000 persons (95% CI 110 fewer to 62 fewer; moderate certainty; *Table 2*).

Evidence on treatment of index cases also suggested a reduction in onward transmission. In one RCT, antiviral treatment of index patients was associated with a lower secondary attack rate compared with no treatment (RR 0.70, 95% CI 0.55 to 0.91; *Figure 7*) which translated into 36 fewer events per 1,000 persons (95% CI 54 fewer to 11 fewer; moderate certainty; *Table 2*).

In terms of duration of post-exposure prophylaxis, one RCT comparing 5 versus 10 days of oseltamivir did not show a clear difference between the two treatment courses (RR 5.09, 95% CI 0.25 to 104.83; *Figure 8*) which translated into 18 more events per 1,000 persons with a 5-day course (95% CI not available; very low certainty; *Table 3*).

Several head-to-head comparisons of antiviral agents were identified, most from NRS. Compared with baloxavir marboxil, oseltamivir was associated with a higher secondary attack rate (RR 1.38, 95% CI 1.24

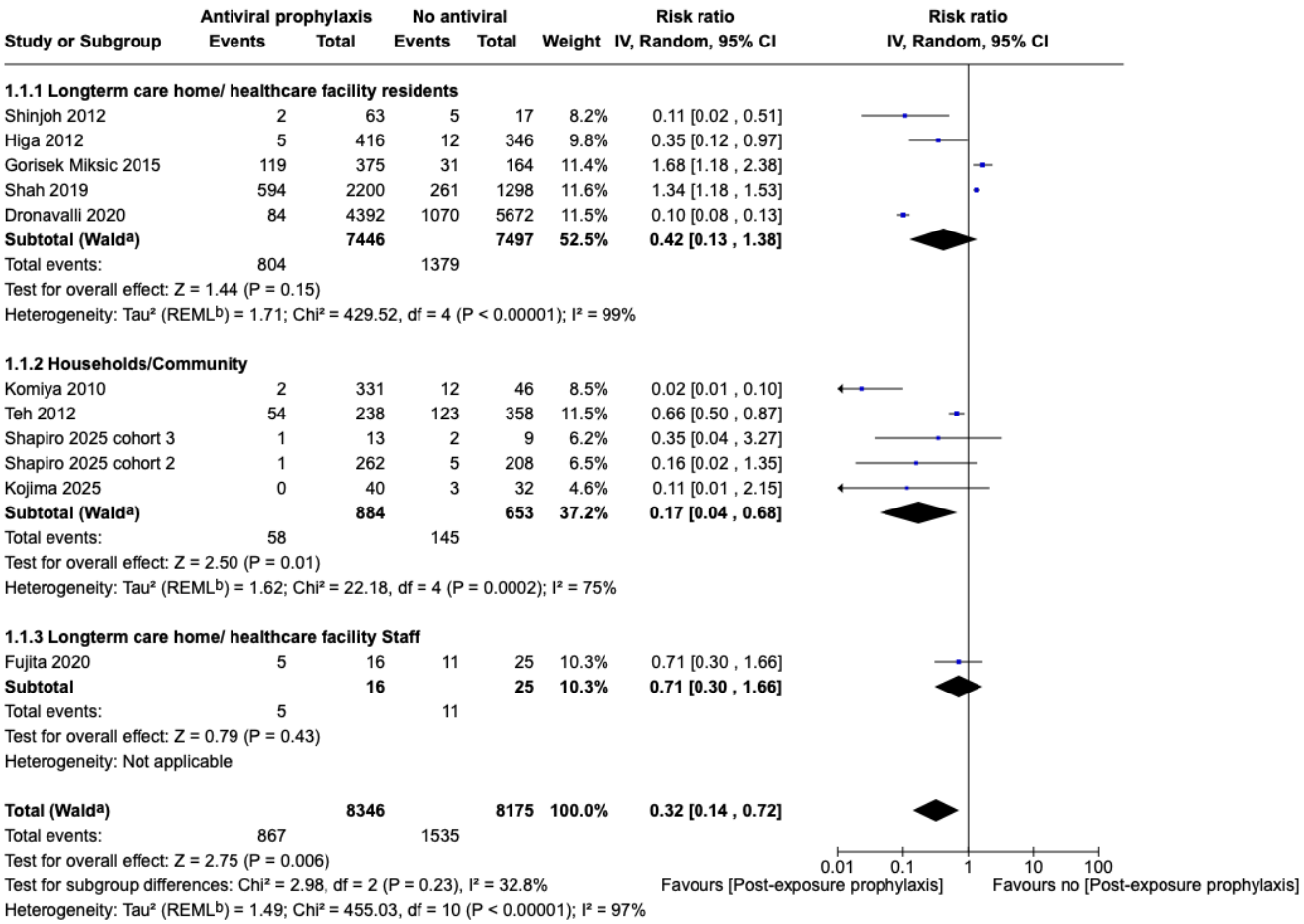
to 1.53; *Figure 9*) which translated into 68 more events per 1,000 persons (95% CI 43 more to 95 more; very low certainty; *Table 4*), whereas zanamivir did not differ importantly from baloxavir marboxil (RR 1.02, 95% CI 0.99 to 1.06; *Figure 10*) which translated into 4 more events per 1,000 persons (95% CI 2 fewer to 11 more; low certainty; *Table 5*). Zanamivir also did not differ importantly from peramivir (RR 0.93, 95% CI 0.69 to 1.24; *Figure 11*) which translated into 4 fewer events per 1,000 persons (95% CI 19 fewer to 15 more; very low certainty; *Table 6*).

Comparisons between oseltamivir and zanamivir showed mixed findings, all with very low certainty. In one RCT, index case treatment with oseltamivir and zanamivir did not differ importantly in their effect on secondary transmission (RR 0.94, 95% CI 0.56 to 1.58; *Figure 12*) which translated into 9 fewer events per 1,000 persons (95% CI 67 fewer to 88 more; very low certainty; *Table 7*). In contrast, NRS suggested that index case treatment with oseltamivir was associated with a higher secondary attack rate than zanamivir (RR 1.41, 95% CI 1.12 to 1.79; *Figure 13*) which translated into 64 more events per 1,000 persons (95% CI 19 more to 122 more; very low certainty; *Table 7*). For post-exposure prophylaxis, one NRS found no important difference between oseltamivir and zanamivir (RR 1.63, 95% CI 0.08 to 32.25; *Figure 14*) which translated into 42 more events per 1,000 persons (95% CI not available; very low certainty; *Table 7*). One NRS also found that index case treatment with oseltamivir was associated with a higher secondary attack rate than peramivir (RR 1.77, 95% CI 1.34 to 2.34; Figure 15), which translated into 47 more events per 1,000 persons (95% CI 21 more to 82 more; very low certainty; Table 8).

Additional analyses examined timing of antiviral treatment. One NRS found a lower probability of a household having at least one secondary transmission event after exposure with early vs late treatment (RR 0.66, 95% CI 0.33 to 1.31; *Figure 16*) which translated into 104 fewer events per 1,000 persons (95% CI 205 fewer to 95 more; very low certainty; *Table 2*). Also, pooling two comparisons from one study showed that early treatment initiated within 24 hours was associated with lower odds of secondary transmission compared with late treatment initiated after 48 hours or no treatment (OR 0.58, 95% CI 0.46 to 0.73; *Figure 17*) whereby the absolute effect could not be calculated (low certainty; *Table 9*). In contrast, early treatment combined with prophylaxis did not show a clear reduction in secondary transmission compared with late or no treatment combined with prophylaxis (OR 1.34, 95% CI 0.79 to 2.26; *Figure 18*) whereby the absolute effect could not be calculated (low certainty; *Table 9*).

In addition to the reported primary studies, six modelling studies also examined the effect of antivirals on influenza transmission. Overall, these modelling studies suggested that antiviral use may reduce influenza transmission, with larger effects when treatment was started earlier, used more widely, or combined with prophylaxis [21-26]. Across studies, baloxavir marboxil tended to show greater reductions in transmission-related outcomes than oseltamivir or no treatment [21, 23, 24, 26]. Several studies highlighted the importance of timing, showing that earlier treatment, particularly within 24 hours of symptom onset, was associated with greater reductions in onward transmission, while delayed treatment had smaller effects [24, 25]. One modelling study also found that higher treatment coverage was associated with larger population-level reductions in influenza incidence [26].

Figure 4: Antiviral Prophylaxis vs. No Antiviral (NRS) - Secondary Attack Rate

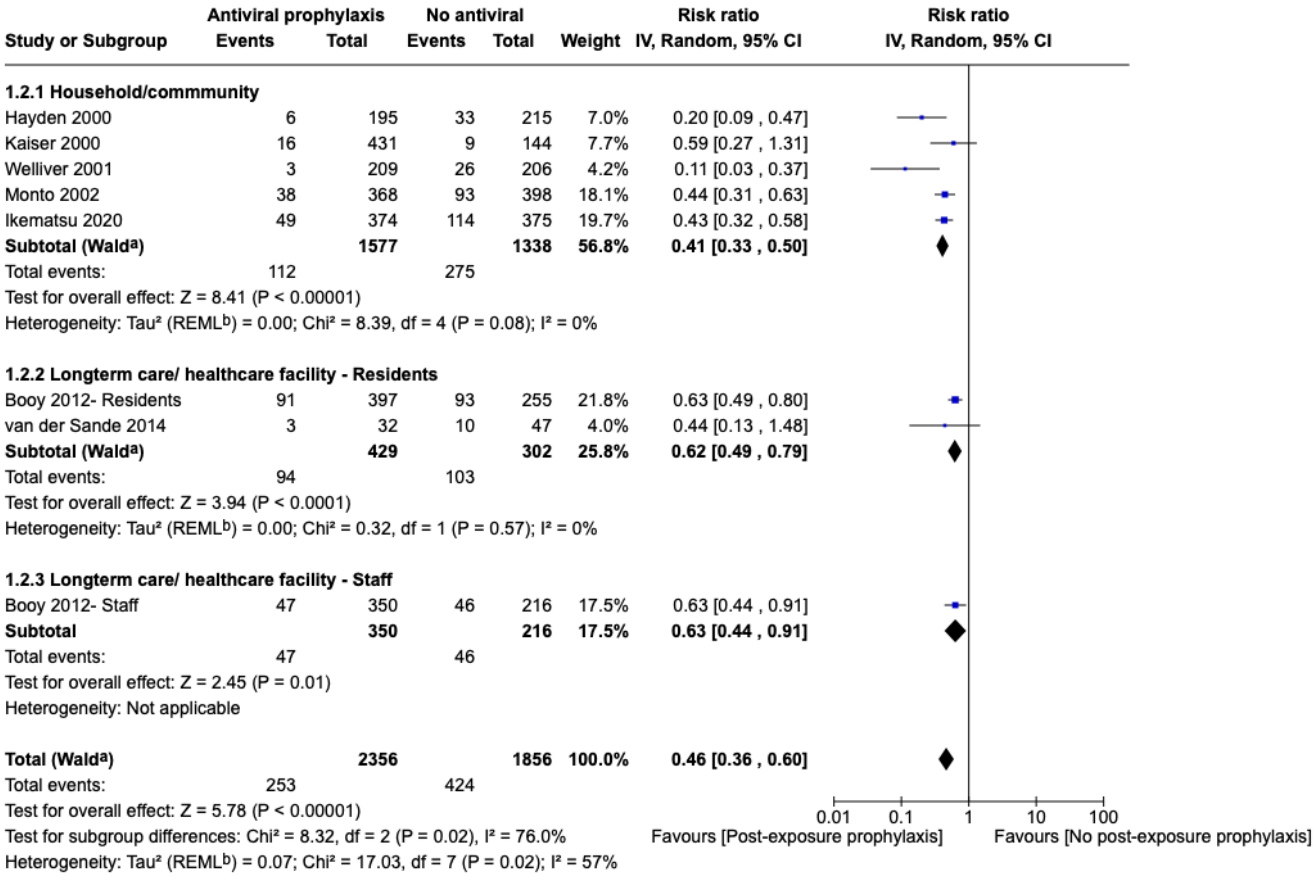


Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 5: Antiviral Prophylaxis vs. No Antiviral (RCT) - Secondary Attack Rate



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 6: Antiviral Prophylaxis vs. Placebo/No Antiviral (RCT) – Viral Shedding

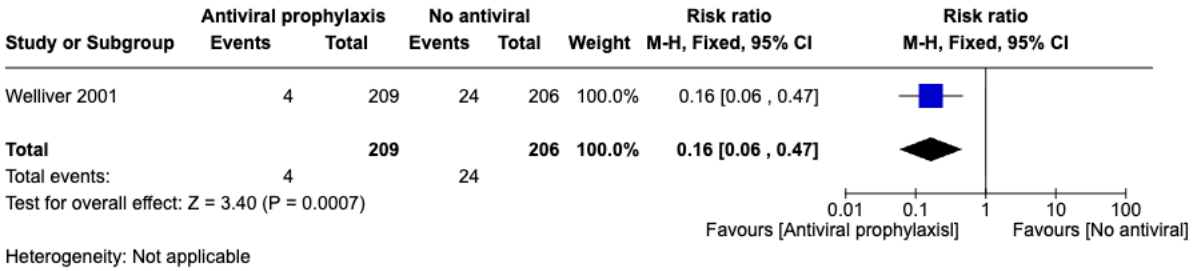


Figure 7: Antiviral Treatment of Index Patients vs. No Treatment (RCT) – Secondary Attack Rate

Study or Subgroup	Antiviral treatment Events	Total	No antiviral Events	Total	Weight	Risk ratio M-H, Fixed, 95% CI
Monto 2025	94	1118	131	1098	100.0%	0.70 [0.55 , 0.91]
Total		**1118**		**1098**	**100.0%**	**0.70 [0.55 , 0.91]**
Total events:	94		131			

Test for overall effect: Z = 2.73 (P = 0.006)

Heterogeneity: Not applicable

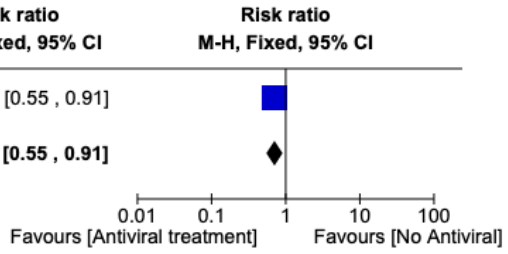


Figure 8: Duration of Oseltamivir Post-Exposure Prophylaxis – 5 days vs. 10 days (RCT) – Secondary Attack Rate

Study or Subgroup	5 days of antiviral Events	Total	10 days of antiviral Events	Total	Weight	Risk ratio IV, Fixed, 95% CI
Lepen 2020	2	110	0	112	100.0%	5.09 [0.25 , 104.83]
Total		**110**		**112**	**100.0%**	**5.09 [0.25 , 104.83]**
Total events:	2		0			

Test for overall effect: Z = 1.05 (P = 0.29)

Heterogeneity: Not applicable

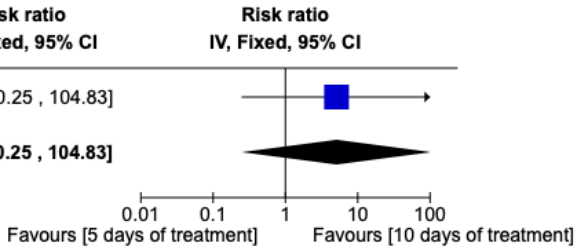
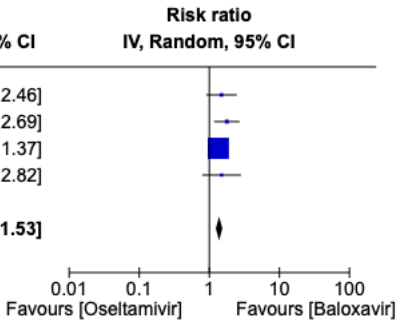


Figure 9: Oseltamivir vs. Baloxavir marboxil Treatment of Index Cases (NRS) – Secondary Attack Rate

Study or Subgroup	Oseltamivir Events	Total	Baloxavir Events	Total	Weight	Risk ratio IV, Random, 95% CI
Best 2024	52	196	16	90	4.4%	1.49 [0.90 , 2.46]
Ikematsu 2024	37	153	35	257	6.2%	1.78 [1.17 , 2.69]
Komeda 2021	14983	62004	15226	84672	86.6%	1.34 [1.32 , 1.37]
Umemura 2020	40	296	11	122	2.8%	1.50 [0.80 , 2.82]
Total (Wald[a])		**62649**		**85141**	**100.0%**	**1.38 [1.24 , 1.53]**
Total events:	15112		15288			

Test for overall effect: Z = 5.84 (P < 0.00001)

Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 1.99, df = 3 (P = 0.57); I² = 10%



Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 10: Zanamivir vs Baloxavir marboxil Treatment of Index Cases (NRS) – Secondary Attack Rate

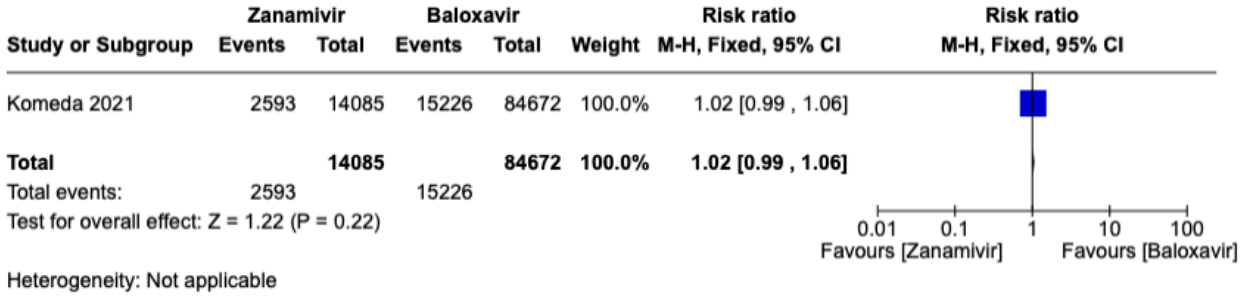


Figure 11: Zanamivir vs. Peramivir Treatment of Index Case (NRS) – Secondary Attack Rate

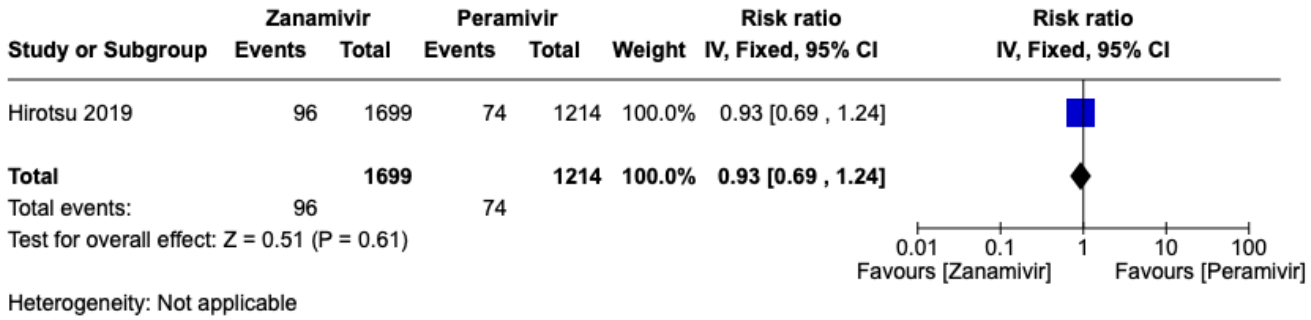


Figure 12: Oseltamivir vs. Zanamivir Treatment of Index Case (RCT) – Secondary Attack Rate

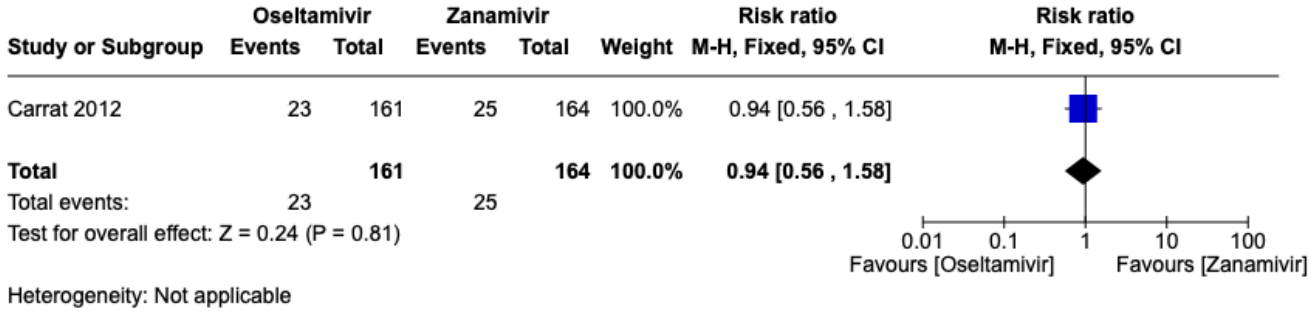
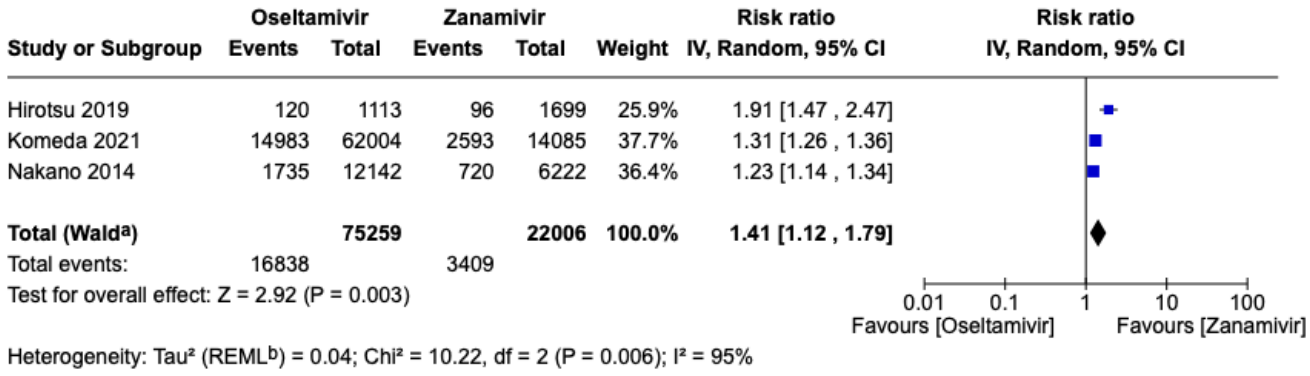


Figure 13: Oseltamivir vs. Zanamivir Treatment of Index Case (NRS) – Secondary Attack Rate



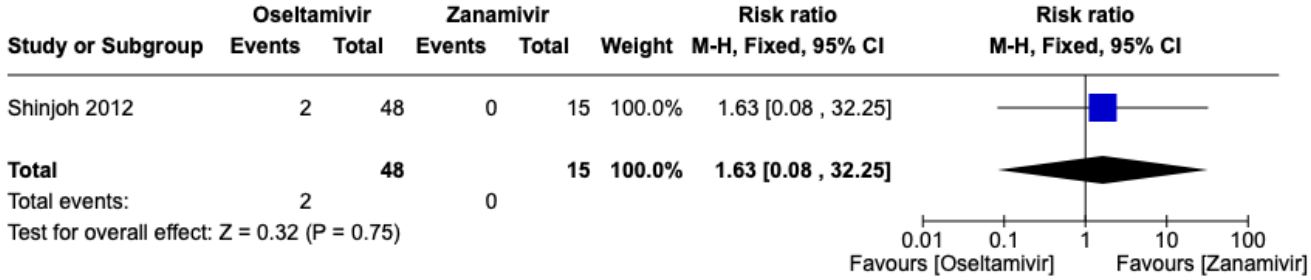
Heterogeneity: Tau² (REML[b]) = 0.04; Chi² = 10.22, df = 2 (P = 0.006); I² = 95%

Footnotes

[a]CI calculated by Wald-type method.

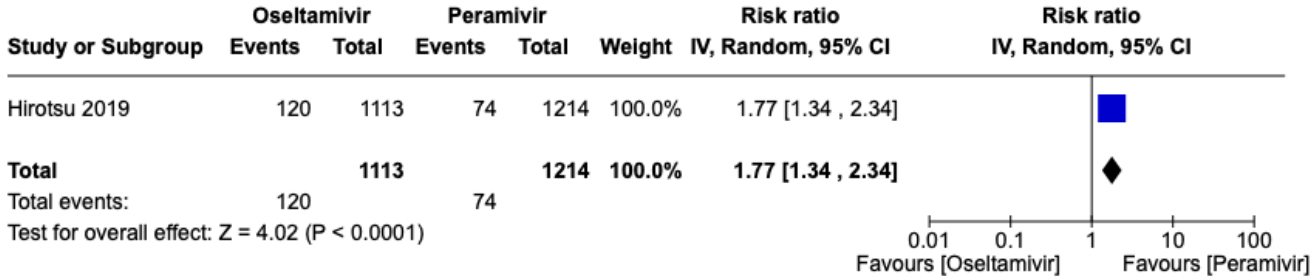
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 14: Oseltamivir vs Zanamivir Post-exposure Prophylaxis (NRS) – Secondary Attack Rate



Heterogeneity: Not applicable

Figure 15: Oseltamivir vs Peramivir Treatment of Index Case (NRS) – Secondary Attack Rate



Heterogeneity: Not applicable

Figure 16: Early vs Late Treatment, Household with ≥ 1 Secondary Transmission After Exposure (NRS)– Household Secondary Attack Rate

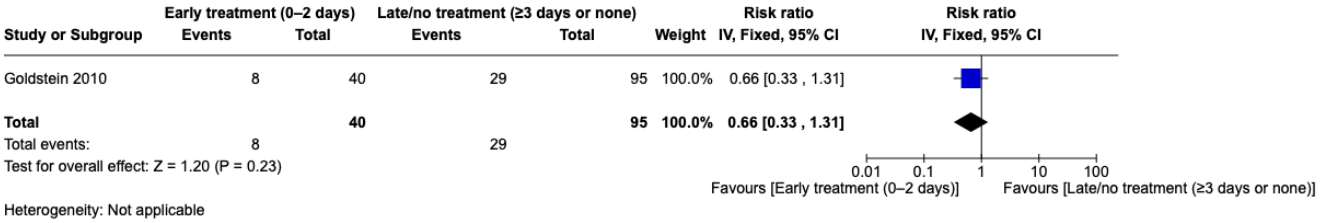


Figure 17: Early Treatment < 24 hour Vs Late > 48 hour/No Treatment – Secondary Attack Rate

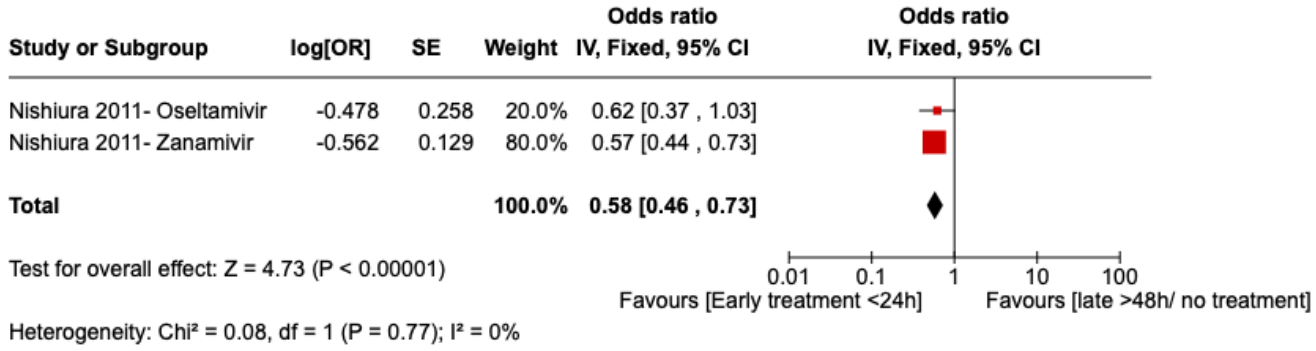


Figure 18: Early Treatment + Prophylaxis < 24 hour vs Late > 48 hour/No Treatment + Prophylaxis – Secondary Attack Rate

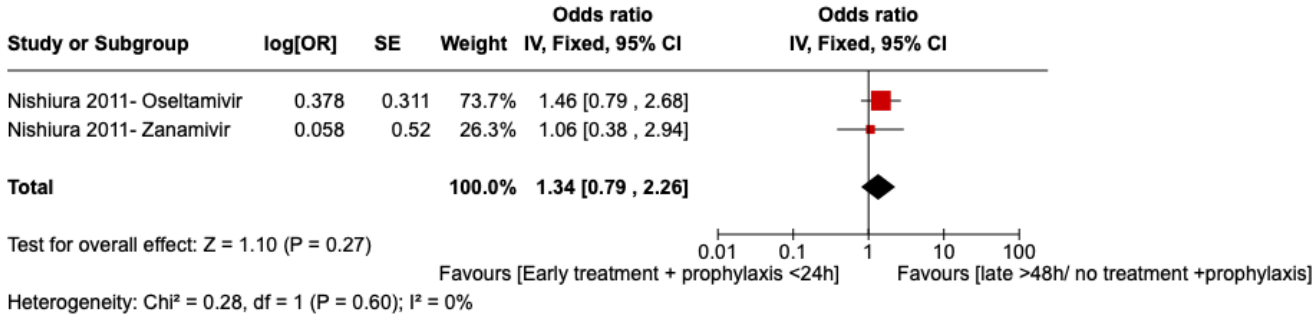


Table 2: Summary of Findings for Any Antiviral vs. No Antiviral

Influenza antiviral post-exposure prophylaxis or treatment compared to no antivirals for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: influenza antiviral post-exposure prophylaxis or treatment
Comparison: no antivirals

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no antivirals	Risk difference with influenza antiviral post-exposure prophylaxis or treatment
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (Observational) - Longterm care/healthcare facility - Residents	14943 (5 non-randomised studies)[1,2,3,4,5]	⨁◯◯◯ Very low[a,b,c]	**RR 0.42** (0.13 to 1.38)	184 per 1,000	**107 fewer per 1,000** (from 160 fewer to 70 more)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (Observational) - Longterm care/healthcare facility - Staff	41 (1 non-randomised study)[6]	⨁◯◯◯ Very low[a,d]	**RR 0.71** (0.30 to 1.66)	440 per 1,000	**128 fewer per 1,000** (from 308 fewer to 290 more)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (Observational) - Households/Community	1537 (5 non-randomised studies)[7,8,9,10,e]	⨁◯◯◯ Very low[f,g,h]	**RR 0.17** (0.04 to 0.68)	222 per 1,000	**184 fewer per 1,000** (from 213 fewer to 71 fewer)

Influenza antiviral post-exposure prophylaxis or treatment compared to no antivirals for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: influenza antiviral post-exposure prophylaxis or treatment
Comparison: no antivirals

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no antivirals	Risk difference with influenza antiviral post-exposure prophylaxis or treatment
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (Observational) - Total	16521 (11 non-randomised studies)[1,2,3,4,5,6,7,8,9,10,e]	⨁◯◯◯ Very low[a,b,i]	**RR 0.32** (0.14 to 0.72)	188 per 1,000	**128 fewer per 1,000** (from 161 fewer to 53 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (RCT) - Household/community	2915 (5 RCTs)[11,12,13,14,15]	⨁⨁⨁⨁ High	**RR 0.41** (0.33 to 0.50)	206 per 1,000	**121 fewer per 1,000** (from 138 fewer to 103 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (RCT) - Longterm care/healthcare facility - Staff	566 (1 RCT)[16]	⨁⨁⨁◯ Moderate[j]	**RR 0.63** (0.44 to 0.91)	213 per 1,000	**79 fewer per 1,000** (from 119 fewer to 19 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (RCT) - Longterm care/healthcare facility - Residents	731 (2 RCTs)[16,17]	⨁⨁◯◯ Low[h,k]	**RR 0.62** (0.49 to 0.79)	341 per 1,000	**130 fewer per 1,000** (from 174 fewer to 72 fewer)

Influenza antiviral post-exposure prophylaxis or treatment compared to no antivirals for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: influenza antiviral post-exposure prophylaxis or treatment
Comparison: no antivirals

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no antivirals	Risk difference with influenza antiviral post-exposure prophylaxis or treatment
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (RCT) - Total	4212 (8 RCTs)[11,12,13,14,15,16,17,l]	⨁⨁⨁◯ Moderate[m,n]	**RR 0.46** (0.36 to 0.60)	228 per 1,000	**123 fewer per 1,000** (from 146 fewer to 91 fewer)
Antiviral Treatment vs. Placebo/No Antiviral - Antiviral treatment of index patients vs no treatment (RCT) - Secondary attack rate	2216 (1 RCT)[18]	⨁⨁⨁◯ Moderate[h,o]	**RR 0.70** (0.55 to 0.91)	119 per 1,000	**36 fewer per 1,000** (from 54 fewer to 11 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Viral Shedding (RCT)	415 (1 RCT)[11]	⨁⨁⨁◯ Moderate[o]	**RR 0.16** (0.06 to 0.47)	117 per 1,000	**98 fewer per 1,000** (from 110 fewer to 62 fewer)
Household with ≥ 1 Secondary Transmission After Exposure (Observational) - Secondary attack rate	135 (1 non-randomised study)[19]	⨁◯◯◯ Very low[a,c]	**RR 0.66** (0.33 to 1.31)	305 per 1,000	**104 fewer per 1,000** (from 205 fewer to 95 more)
Basic reproduction number - not reported	-	-	-	-	-

Influenza antiviral post-exposure prophylaxis or treatment compared to no antivirals for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: influenza antiviral post-exposure prophylaxis or treatment
Comparison: no antivirals

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no antivirals	Risk difference with influenza antiviral post-exposure prophylaxis or treatment
Effective reproduction number - not reported	-	-	-	-	-
Serial interval - not reported	-	-	-	-	-
Bottleneck analysis - not reported	-	-	-	-	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Risk of bias was rated down by one level due to failure to match groups or adjust for key confounders in the study's design or analysis.
b. Inconsistency was rate down by two levels due to substantial heterogeneity.
c. Imprecision was rated down by three levels since the 95% CI of the absolute effect included substantial benefit and important harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
d. Imprecision was rated down by three levels since the 95% CI of the absolute effect included substantial benefit and substantial harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed

symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
e. Shapiro 2025: cohort 2 and cohort 3 counted as separate studies in the analysis.
f. Risk of bias was rated down by two levels due to failure to match groups or adjust for key confounders in the study's design or analysis.
g. Inconsistency was rated down by one level due to important heterogeneity.
h. Imprecision was rated down by one level since the 95% CI of the absolute effect included important benefit and substantial benefit. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
i. Imprecision was rated down by one level since the 95% CI of the absolute effect included close to important benefit and substantial benefit. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
j. Imprecision was rated down by one level since the 95% CI of the absolute effect included important benefit and trivial benefit. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel
k. Risk of bias was rated down by one level due to deviations from the intended intervention and missing outcome data.
l. Booy 2012: Residents and staff counted as separate studies in the analysis.
m. 1 RCT had High RoB, 5 RCTs had Some RoB concerns, and 2 RCTs had Low RoB. Sensitivity analysis excluding the RCT with High RoB showed a similar pooled RR of 0.46 (0.34-0.61). Sensitivity analysis only including the 2 RCTs with Low RoB showed a pooled RR of 0.33 (0.16-0.67). Therefore, the certainty of evidence was not rated down for risk of bias.
n. Potentially important inconsistency (I2 = 57%; Chi-square p-value = 0.02; varying point estimates; non-overlapping 95% confidence intervals) that cannot completely be explained based on study characteristics.
o. Imprecision was rated down by one level due to the evidence not meeting the optimal information size.

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Table 3 – Summary of Findings for Duration of Oseltamivir Post-Exposure Prophylaxis

5 days of influenza antiviral post-exposure prophylaxis compared to 10 days of influenza antiviral post-exposure prophylaxis for reducing influenza transmission among exposed (asymptomatic) individuals in community and high-risk settings

Patient or population: reducing influenza transmission among exposed (asymptomatic) individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: 5 days of influenza antiviral post-exposure prophylaxis
Comparison: 10 days of influenza antiviral post-exposure prophylaxis

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with 10 days of influenza antiviral post-exposure prophylaxis	Risk difference with 5 days of influenza antiviral post-exposure prophylaxis
Duration of Oseltamivir Post- Exposure Prophylaxis - 5 days vs. 10 days (RCT) - Secondary Attack Rate	222 (1 RCT)[1]	⨁◯◯◯ Very low[a]	**RR 5.09** (0.25 to 104.83)	0 per 1,000	**18 more per 1,000** (from -- to --)
Basic reproduction number - not reported	-	-	-	-	-
Effective reproduction number - not reported	-	-	-	-	-
Serial interval - not reported	-	-	-	-	-
Bottleneck analysis - not reported	-	-	-	-	-
Viral shedding - not reported	-	-	-	-	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

5 days of influenza antiviral post-exposure prophylaxis compared to 10 days of influenza antiviral post-exposure prophylaxis for reducing influenza transmission among exposed (asymptomatic) individuals in community and high-risk settings

Patient or population: reducing influenza transmission among exposed (asymptomatic) individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: 5 days of influenza antiviral post-exposure prophylaxis
Comparison: 10 days of influenza antiviral post-exposure prophylaxis

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with 10 days of influenza antiviral post-exposure prophylaxis	Risk difference with 5 days of influenza antiviral post-exposure prophylaxis

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Imprecision was downgraded by three levels due to the very large 95% confident interval of the RR which was calculated based on only 2 events.

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Table 4 – Summary of Findings for Oseltamivir vs Baloxavir marboxil

Oseltamivir treatment compared to baloxavir marboxil treatment for reducing influenza transmission among infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: oseltamivir treatment
Comparison: baloxavir treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with baloxavir treatment	Risk difference with oseltamivir treatment
Oseltamivir vs Baloxavir marboxil Treatment of Index Cases (Observational) - Secondary Attack Rate	147790 (4 non-randomised studies)[1,2,3,4]	⨁◯◯◯ Very low[a]	**RR 1.38** (1.24 to 1.53)	180 per 1,000	**68 more per 1,000** (from 43 more to 95 more)
Basic reproduction number - not reported	-	-	-	-	-
Effective reproduction number - not reported	-	-	-	-	-
Serial interval - not reported	-	-	-	-	-
Bottleneck analysis - not reported	-	-	-	-	-
Viral shedding - not reported	-	-	-	-	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Imprecision was rated down by one level since the 95% CI of the absolute effect includes trivial benefit and important benefit. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.

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Table 5 – Summary of Findings for Zanamivir vs. Baloxavir marboxil Treatment

Zanamivir treatment compared to baloxavir marboxil treatment for reducing influenza transmission among infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: zanamivir treatment
Comparison: baloxavir treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with baloxavir treatment	Risk difference with zanamivir treatment
Zanamivir vs Baloxavir Treatment of Index Cases (Observational) - Secondary Attack Rate	98757 (1 non-randomised study)[1]	⨁⨁◯◯ Low	**RR 1.02** (0.99 to 1.06)	180 per 1,000	**4 more per 1,000** (from 2 fewer to 11 more)
Basic reproduction number - not reported	-	-	-	-	-
Effective reproduction number - not reported	-	-	-	-	-
Serial interval - not reported	-	-	-	-	-
Bottleneck analysis - not reported	-	-	-	-	-
Viral shedding - not reported	-	-	-	-	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

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Table 6 – Summary of Findings for Zanamivir vs. Peramivir Treatment

Zanamivir treatment compared to peramivir treatment for reducing influenza transmission among infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: zanamivir treatment
Comparison: peramivir treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with peramivir treatment	Risk difference with zanamivir treatment
Zanamivir vs Peramivir Treatment of Index Cases (Observational) - Secondary Attack Rate	2913 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a]	**RR 0.93** (0.69 to 1.24)	61 per 1,000	**4 fewer per 1,000** (from 19 fewer to 15 more)
Basic reproduction number - not reported	-	-	-	-	-
Effective reproduction number - not reported	-	-	-	-	-
Serial interval - not reported	-	-	-	-	-
Bottleneck analysis - not reported	-	-	-	-	-
Viral Shedding - not reported	-	-	-	-	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Imprecision was rated down by one level due to the evidence not meeting the optimal information size.

References

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Table 7 – Summary of Findings for Oseltamivir vs. Zanamivir Post-Exposure Prophylaxis or Treatment

Patient or population: reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: oseltamivir post-exposure prophylaxis or treatment
Comparison: zanamivir post-exposure prophylaxis or treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with zanamivir post-exposure prophylaxis or treatment	Risk difference with oseltamivir post-exposure prophylaxis or treatment
Oseltamivir vs Zanamivir Treatment of Index Cases (RCT) - Secondary Attack Rate	325 (1 RCT)[1]	⨁◯◯◯ Very low[a,b]	**RR 0.94** (0.56 to 1.58)	152 per 1,000	**9 fewer per 1,000** (from 67 fewer to 88 more)
Oseltamivir vs Zanamivir Treatment of Index Cases (Observational) - Secondary Attack Rate	97265 (3 non-randomised studies)[2,3,4]	⨁◯◯◯ Very low[c,d]	**RR 1.41** (1.12 to 1.79)	155 per 1,000	**64 more per 1,000** (from 19 more to 122 more)
Oseltamivir vs Zanamivir Post-Exposure Prophylaxis (Observational) - Secondary Attack Rate	63 (1 non-randomised study)[5]	⨁◯◯◯ Very low[e,f]	**RR 1.63** (0.08 to 32.25)	0 per 1,000	**42 more per 1,000** (from 0 fewer to 0 fewer)
Basic reproduction number - not reported	-	-	-	-	-
Effective reproduction number - not reported	-	-	-	-	-
Serial interval - not reported	-	-	-	-	-
Bottleneck analysis - not reported	-	-	-	-	-
Viral shedding - not reported	-	-	-	-	-

Patient or population: reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: oseltamivir post-exposure prophylaxis or treatment
Comparison: zanamivir post-exposure prophylaxis or treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with zanamivir post-exposure prophylaxis or treatment	Risk difference with oseltamivir post-exposure prophylaxis or treatment

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Risk of bias was downgraded by one level due to missing outcome data.
b. Imprecision was rated down by two levels since the 95% CI of the absolute effect includes important benefit and important harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
c. Inconsistency was downgraded by two levels due to substantial heterogeneity.
d. Imprecision was rated down by one level since the 95% CI of the absolute effect includes trivial harm and important harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
e. Risk of bias was rated down by one level due to failure to match groups or adjust for key confounders in the study's design or analysis.
f. Imprecision was rated down by two levels due to the evidence not meeting the optimal information size.

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Table 8 – Summary of Findings for Oseltamivir vs. Peramivir Treatment

Oseltamivir treatment compared to peramivir treatment for reducing influenza transmission among infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: oseltamivir treatment
Comparison: peramivir treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with peramivir treatment	Risk difference with oseltamivir treatment
Oseltamivir vs Peramivir Treatment of Index Cases (Observational) - Secondary Attack Rate	2327 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a]	**RR 1.77** (1.34 to 2.34)	61 per 1,000	**47 more per 1,000** (from 21 more to 82 more)
Basic reproduction number - not reported	-	-	-	-	-
Effective reproduction number - not reported	-	-	-	-	-
Serial interval - not reported	-	-	-	-	-
Bottleneck analysis - not reported	-	-	-	-	-
Viral shedding - not reported	-	-	-	-	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Imprecision was rated down by one level since the 95% CI of the absolute effect included trivial harm and important harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.

References

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Table 9 – Summary of Findings for Early vs. Late Post-Exposure Prophylaxis or Treatment

Early (<24 h) influenza antiviral post-exposure prophylaxis or treatment compared to late (>48 h) or no antiviral post-exposure prophylaxis or treatment for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: early (<24 h) influenza antiviral post-exposure prophylaxis or treatment
Comparison: late (>48 h) or no antiviral post-exposure prophylaxis or treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with late (>48 h) or no antiviral post-exposure prophylaxis or treatment	Risk difference with early (<24 h) influenza antiviral post-exposure prophylaxis or treatment
Early Treatment <24h vs Late >48h/No treatment (Observational) - Secondary Attack Rate	(2 non-randomised studies)[1,a]	⨁⨁◯◯ Low	**OR 0.58** (0.46 to 0.73)[b]	0 per 1,000	**-- per 1,000** (from -- to --)
Early Treatment + Prophylaxis <24h vs Late >48h/No treatment + Prophylaxis (Observational) - Secondary Attack Rate	(2 non-randomised studies)[1,a]	⨁◯◯◯ Very low[c]	**OR 1.34** (0.79 to 2.26)[b]	0 per 1,000	**-- per 1,000** (from -- to --)
Basic reproduction number - not reported	-	-	-	-	-
Effective reproduction number - not reported	-	-	-	-	-
Serial interval - not reported	-	-	-	-	-
Bottleneck analysis - not reported	-	-	-	-	-
Viral shedding - not reported	-	-	-	-	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **OR:** odds ratio

Early (<24 h) influenza antiviral post-exposure prophylaxis or treatment compared to late (>48 h) or no antiviral post-exposure prophylaxis or treatment for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings

Patient or population: reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings
Intervention: early (<24 h) influenza antiviral post-exposure prophylaxis or treatment
Comparison: late (>48 h) or no antiviral post-exposure prophylaxis or treatment

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with late (>48 h) or no antiviral post-exposure prophylaxis or treatment	Risk difference with early (<24 h) influenza antiviral post-exposure prophylaxis or treatment

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Nishiura 2011: Oseltamivir cohort and Zanamivir cohort counted as separate studies in the analysis.
b. Pooled adjusted ORs for effect of <24h compared with >48h. Nominator and denominator for event rates were not provided.
c. Imprecision was rated down by one level due to the wide 95% confidence interval of the odds ratio including benefit and harm.

References

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Subgroup and Sensitivity Analyses

Appendix 5 contains forest plots of sensitivity analyses removing studies at high risk of bias from meta-analyses that included three or more studies. No meaningful changes were observed, except in the NRS meta-analysis of antivirals for post-exposure prophylaxis on secondary attacks, where all but one study were judged to be at high risk of bias.

Certainty of Evidence

GRADE evidence profiles for the reported analyses per outcome and subgroup with all certainty of evidence assessments and footnotes for explanation are shown in *Appendix 6*.

The certainty of the evidence varied across comparisons and was generally higher for RCT evidence than for NRS evidence. The most common reasons for rating down RCT evidence were some concerns about risk of bias, and imprecision or inconsistency. The most common reasons for rating down NRS evidence were risk of bias, imprecision, and inconsistency. The evidence for head-to-head comparison of antivirals was almost completely of very low certainty.

Discussion

Summary of Main Findings

This rapid systematic review synthesized evidence on the effects of influenza antivirals used for post-exposure prophylaxis or treatment on transmission-related outcomes in community and high-risk settings. Across the meta-analyses, antiviral prophylaxis compared with placebo or no antiviral was consistently associated with a lower secondary attack rate, with the most robust findings coming from randomized trials which indicated that the risk is approximately halved with antivirals. This effect was seen overall and across multiple settings, including households, community settings, and long-term care or healthcare facilities, although the effect size and certainty of evidence varied by subgroup. Antiviral prophylaxis was also associated with reduced viral shedding in one randomized trial.

Evidence on treatment of index cases was more limited, but the available RCT data suggested that antiviral treatment may reduce onward transmission compared with no treatment. This relative reduction was about 30%, although uncertainty remains around the precise magnitude of this effect despite a consistent direction of benefit across analyses, and further exploration may clarify to what extent this was already part of or may add to the ~50% relative reduction with post-exposure prophylaxis. Findings from analyses of treatment timing further supported the importance of early intervention, with treatment initiated within 24 hours associated with lower odds of secondary transmission than delayed treatment or no treatment. In contrast, combining early treatment with prophylaxis did not show a clear additional benefit in the available analysis, although this was of very low certainty. Data comparing different treatment durations were sparse and did not show a significant difference between 5 vs 10 days of oseltamivir.

Head-to-head comparisons between antiviral agents were available mostly from non-randomized studies. These analyses suggested that baloxavir marboxil, zanamivir, and peramivir were often associated with lower secondary attack rates than oseltamivir, while differences between several other

pairwise comparisons were small. Although these findings may indicate meaningful differences between agents, they should be interpreted cautiously because most were based on very low certainty evidence.

The modelling evidence complemented these findings. Overall, modelling studies suggested that antiviral use may reduce influenza transmission, with larger effects when treatment was initiated earlier, used more broadly, or combined with prophylaxis. Across these studies, baloxavir marboxil generally produced greater reductions in transmission-related outcomes than oseltamivir or no treatment.

Future research that may increase the certainty of evidence for this review includes additional high-quality RCTs assessing the effect of index case treatment on transmission, and quantification regarding how much index case treatment may add to the effect of post-exposure prophylaxis when combined. Most importantly, the low to very low certainty evidence for duration of treatment and head-to-head comparisons of antivirals require better quality evidence, by means of RCTs and/or well-designed NRS.

Strengths and Limitations

This rapid systematic review has several strengths and limitations. First, the control group risks from the included studies (baseline risk) for secondary attack rate varied, but overall, the risk from RCTs and NRS were both around 20% which is reassuring. This risk may be higher than reported in other reviews as we focused on post-exposure prophylaxis while others may have also included pre-exposure prophylaxis. The baseline risk influences the absolute effects that were reported, and effects based on a range of baseline risks (lower and higher end of the range) may be needed depending on the user of this report. Secondly, we used the MID from the paper by Zhao et al. who determined 5.5% in low-risk and 3.0% in high-risk persons as decision thresholds with a WHO panel [9]. The 5.5% threshold was chosen to be conservative, but another threshold may be preferred by users. Third, the literature search and screening only identified publications in English. Fourth, the rapid methods included data extraction and risk of bias assessments by one person with checking of results by a 2nd person, i.e., not independently in duplicate. Fifth, the evidence for comparison of specific antivirals was only assessed per pair, but with very low certainty evidence a network meta-analysis would not have been meaningful. Sixth, this review focused on outcomes of transmission to inform public health and outbreak measures and does not include beneficial and harmful consequences for individuals to decide whether to take an antiviral.

Conclusions

Influenza antivirals probably reduce transmission, particularly when used for post-exposure prophylaxis, when started early. The strongest evidence came from randomized trials showing that prophylaxis reduced secondary attack rate compared with placebo or no antiviral. Evidence for treatment of index cases and for differences between specific antiviral agents was more limited and less certain. Modelling studies supported the overall findings and suggested greater benefit with earlier treatment, broader coverage, and, in some scenarios, combined treatment and prophylaxis. However, important uncertainties remain regarding the comparative effectiveness of individual agents, the impact of treatment duration, and the extent to which findings generalize across settings and populations. Further well-designed large-scale randomized controlled trials are needed, especially for head-to-head antiviral comparisons and for transmission outcomes beyond secondary attack rate.

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Appendix 1: Search Strategies

Database: Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® <1946-Present>

Date Searched: February 19, 2026

Search Strategy:

1 exp Influenza, Human/ 62938
2 exp Influenza A virus/ 53373
3 exp Influenza B virus/ 5045
4 exp Influenza C virus/ 373
5 (Influenza or influenza* or flu or H1N1 or PH1N1 or H3N2 or AH1N1 or AH3N2 or H5N1 or H7N9).tw,kf. 166363
6 1 or 2 or 3 or 4 or 5 172768
7 Oseltamivir/ 3463
8 Zanamivir/ 1131
9 (oseltamivir or tamiflu or GS 4104 or GS4104 or GS-4104 or GS 4071 or GS4071 or GS-4071 or zanamivir or relenza or GG 167 or GG167 or GG-167 or peramivir or BCX 1812 or BCX1812 or BCX-1812 or RWJ 270201 or RWJ270201 or RWJ-270201 or Rapivab or rapiacta).tw,kf. 5575
10 cap-dependent endonuclease inhibitor*.tw,kf. 83
11 ("Baloxavir marboxil" or Baloxavir or S-033188 or Xofluza).tw,kf. 493
12 (neuraminidase inhibit* or NA inhibit*).tw,kf. 3554
13 7 or 8 or 9 or 10 or 11 or 12 8405
14 Disease transmission, infectious/ 10978
15 (transmi* or spread* or infectivit* or contagious* or "secondary attack rate*" or SAR or (household* adj3 (contact* or spread* or transmi*)) or shedding).tw,kf. 1126695
16 Post-exposure Prophylaxis/ 2066
17 Primary Prevention/ 20664
18 Infection control/ 30080
19 (prophyla* or prevent* or transmi* or post-exposure or IPC).tw,kf. 2873553
20 14 or 15 or 16 or 17 or 18 or 19 3244493
21 6 and 13 and 20 2326
22 (animals not (humans and animals)).sh. 5390838
23 21 not 22 2080
24 clinical trial.mp. or clinical trial.pt. or random$.mp. or tu.xs. 7332065
25 search?.tw. or meta analysis.mp,pt. or review.pt. or di.xs. or associated.tw. 12150307
26 exp cohort studies/ or exp epidemiologic studies/ or exp clinical trial/ or exp evaluation studies as topic/ or exp statistics as topic/ 7329494
27 ((control and (group? or study)) or (time and factors) or program or survey? or ci or cohort or comparative stud? or evaluation studies or follow-up?).mp. 9746079
28 modeling studies.mp. or exp Models, Biological/ 985387
29 24 or 25 or 26 or 27 or 28 22260807
30 23 and 29 1714
31 limit 30 to (english language and yr="2000 - 2026") 1536

Number of Records Retrieved: 1536

Database: Cochrane Library
Date Searched: March 11, 2026
Search Strategy:

ID	Search	Hits
#1	MeSH descriptor: [Influenza, Human] explode all trees	3766
#2	MeSH descriptor: [Influenza A virus] explode all trees	1165
#3	MeSH descriptor: [Influenza B virus] explode all trees	354
#4	MeSH descriptor: [Gammainfluenzavirus] explode all trees	0
#5	(influenza OR influenza* OR flu OR H1N1 OR PH1N1 OR H3N2 OR AH1N1 OR AH3N2 OR H5N1 OR H7N9):ti,ab,kw	13701
#6	#1 OR #2 OR #3 OR #4 OR #5	13701
#7	MeSH descriptor: [Oseltamivir] explode all trees	315
#8	MeSH descriptor: [Zanamivir] explode all trees	99
#9	(oseltamivir OR tamiflu OR "GS 4104" OR GS4104 OR GS-4104 OR "GS 4071" OR GS4071 OR GS-4071 OR zanamivir OR relenza OR "GG 167" OR GG167 OR GG-167 OR peramivir OR "BCX 1812" OR BCX1812 OR BCX-1812 OR "RWJ 270201" OR RWJ270201 OR RWJ-270201 OR Rapivab OR rapiacta):ti,ab,kw	812
#10	(cap-dependent NEAR/2 endonuclease NEAR/2 inhibit*):ti,ab,kw	15
#11	("baloxavir marboxil" OR baloxavir OR S-033188 OR Xofluza):ti,ab,kw	73
#12	(neuraminidase inhibit* OR NA inhibit*):ti,ab,kw	2186
#13	#7 OR #8 OR #9 OR #10 OR #11 OR #12	2862
#14	MeSH descriptor: [Disease Transmission, Infectious] explode all trees	1504
#15	(transmi* OR spread* OR infectivit* OR contagious* OR (secondary NEXT attack NEXT rate*) OR SAR OR (household* NEAR/3 (contact* OR spread* OR transmi*)) OR shedding):ti,ab,kw	32948
#16	MeSH descriptor: [Post-Exposure Prophylaxis] explode all trees	141
#17	MeSH descriptor: [Primary Prevention] explode all trees	7069
#18	MeSH descriptor: [Infection Control] explode all trees	1675
#19	(prophyla* OR prevent* OR transmi* OR post-exposure OR IPC):ti,ab,kw	344528
#20	#14 OR #15 OR #16 OR #17 OR #18 OR #19	356773
#21	#6 AND #13 AND #20	328
#22	(clinical trial OR random* OR meta-analysis OR review OR cohort OR (comparative NEXT stud*) OR (evaluation NEXT stud*) OR "follow-up" OR survey OR program OR modeling OR modelling):ti,ab,kw	1680933
#23	#21 and #22 with Cochrane Library publication date Between Jan 2000 and Jan 2026	265

Search Filters:
Publication Type = Cochrane Reviews, Trials
Number of Records Retrieved: 263

Database: Epistemonikos

Date Searched: March 11, 2026
Search Strategy:

(Influenza OR influenza* OR flu OR H1N1 OR PH1N1 OR H3N2 OR AH1N1 OR AH3N2 OR H5N1 OR H7N9)

AND
(oseltamivir OR tamiflu OR "GS 4104" OR GS4104 OR "GS-4104" OR "GS 4071" OR GS4071 OR "GS-4071" OR zanamivir OR relenza OR "GG 167" OR GG167 OR "GG-167" OR peramivir OR "BCX 1812" OR BCX1812 OR "BCX-1812" OR "RWJ 270201" OR RWJ270201 OR "RWJ-270201" OR Rapivab OR rapiacta OR "cap-dependent endonuclease inhibitor*" OR "baloxavir marboxil" OR baloxavir OR S-033188 OR Xofluza OR "neuraminidase inhibit*" OR "NA inhibit*")

AND
(transmi* OR spread* OR infectivit* OR contagious* OR "secondary attack rate*" OR SAR OR household* OR shedding OR prophyla* OR prevent* OR "post-exposure" OR "infection control" OR IPC)

AND

(systematic review OR meta-analysis OR "evidence synthesis" OR trial OR random* OR cohort OR comparative OR evaluation OR modeling)

Search Filters:

Publication Year = 2000-2026

Number of Records Retrieved: 94

Database: TRIP

Date Searched: March 12, 2026
Search Strategy:
(Influenza OR influenza* OR flu OR H1N1 OR pH1N1 OR H3N2 OR AH1N1 OR AH3N2 OR H5N1 OR H7N9)

AND

(oseltamivir OR Tamiflu OR GS-4104 OR GS4104 OR GS 4104 OR GS-4071 OR GS4071 OR GS 4071 OR zanamivir OR Relenza OR GG-167 OR GG167 OR GG 167 OR peramivir OR BCX-1812 OR BCX1812 OR BCX 1812 OR RWJ-270201 OR RWJ270201 OR RWJ 270201 OR Rapivab OR Rapiacta OR "baloxavir marboxil" OR baloxavir OR S-033188 OR Xofluza OR "cap-dependent endonuclease inhibitor*" OR "neuraminidase inhibitor*" OR "NA inhibitor*")

AND

(transmi* OR spread* OR infectivit* OR contagious* OR "secondary attack rate" OR "secondary attack rates" OR SAR OR household* OR shedding OR prophyla* OR prevent* OR "post-exposure" OR "infection control" OR IPC)

AND

("clinical trial" OR random* OR cohort OR "comparative study" OR "evaluation study" OR "follow-up" OR survey OR "modeling study" OR "modelling study" OR "systematic review" OR "meta-analysis")

Search Filters:

Publication date = 2000–2026

Publication type = Systematic Reviews, Guidelines, Evidence Based Synopses

Number of Records Retrieved: 338

Appendix 2: List of Excluded Studies

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Clinical efficacy of baloxavir marboxil versus oseltamivir in kidney transplant recipients with influenza.	Jiang, Jiali; Wang, Jianping; Hou, Wenjing; Hu, Bangqin; Chen, Pan; Zeng, Fang; Zhang, Yan; Qian, Qing; Ma, Kuifen	2025	Microbiology spectrum	13	7	e0295424	https://dx.doi.org/10.1128/spectrum.02954-24	Wrong patient population
A noninferiority randomized open-label pilot study of 3- versus 7-day influenza postexposure prophylaxis with oseltamivir in hospitalized children.	Wrotek, August; Jackowska, Teresa	2024	Scientific reports	14	1	14192	https://dx.doi.org/10.1038/s41598-024-65244-5	Wrong outcomes
The effectiveness of interventions to reduce the transmission of acute respiratory infections in care homes: a systematic review.	Willcox, Merlin L; Lavu, Deepthi; Yousaf, Usaid; Dalton, Sam; Roberts, Nia; Pluddemann, Annette	2024	Journal of public health (Oxford, England)	46	4	551-563	https://dx.doi.org/10.1093/pubmed/fdae178	Wrong outcomes
Evaluating the Public Health and Health Economic Impacts of Baloxavir Marboxil and Oseltamivir for Influenza Pandemic Control in China: A Cost-Effectiveness Analysis Using a Linked Dynamic	Jiang, Yawen; Wen, Jiaxin; Sun, Jiatong; Shu, Yuelong	2024	PharmacoEconomics	42	10	1111-1125	https://dx.doi.org/10.1007/s40273-024-01412-9	Wrong setting

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Transmission-Economic Evaluation Model.								
Design and Evaluation of Prophylactic Interventions Using Infectious Disease Incidence Data from Close Contact Groups.	Yang, Yang; Longini, Ira M Jr; Halloran, M Elizabeth	2006	Journal of the Royal Statistical Society. Series C, Applied statistics	55	3	317-330	https://dx.doi.org/10.1111/j.1467-9876.2006.00539.x	Wrong study design
A Data-Augmentation Method for Infectious Disease Incidence Data from Close Contact Groups.	Yang, Yang; Longini, Ira M; Halloran, M Elizabeth	2007	Computational statistics & data analysis	51	12	6582-6595	https://dx.doi.org/10.1016/j.csda.2007.03.007	Wrong study design
Clinical and Virologic Outcomes of Baloxavir Compared with Oseltamivir in Pediatric Patients with Influenza in Japan.	Ishiguro, Nobuhisa; Morioka, Ichiro; Nakano, Takashi; Manabe, Atsushi; Kawaguchi, Keiko; Tanaka, Shintaro; Kinoshita, Masahiro	2025	Infectious diseases and therapy	14	4	833-846	https://dx.doi.org/10.1007/s40121-025-01131-4	Wrong outcomes
Real-world effectiveness and safety of Baloxavir Marboxil or Oseltamivir in outpatients with uncomplicated influenza A: an ambispective, observational, multi-center study.	Cai, Jianpeng; Wang, Hongyu; Ye, Xiaoting; Lu, Shengjia; Tan, Zhili; Li, Zhonghua; Lin, Dan; Qian, Jiancheng; Lu, Xiaoxian; Wan, Jiaolong; Wang, Jie; Ai, Jingwen; Pu, Yonglan; Qu, Lihong; Wang, Sen	2024	Frontiers in microbiology	15	10154 8977	1428095	https://dx.doi.org/10.3389/fmicb.2024.1428095	Wrong study design

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Factors associated with viral RNA shedding and evaluation of potential viral infectivity at returning to school in influenza outpatients after treatment with baloxavir marboxil and neuraminidase inhibitors during 2013/2014-2019/2020 seasons in Japan: an o	Li, Jiaming; Wagatsuma, Keita; Sun, Yuyang; Sato, Isamu; Kawashima, Takashi; Saito, Tadashi; Shimada, Yasushi; Ono, Yasuhiko; Kakuya, Fujio; Nagata, Nobuo; Minato, Michiyoshi; Kodo, Naoki; Suzuki, Eitaro; Kitano, Akito; Tanaka, Toshihiro; Aoki, Satoshi; Chon, Irina; Phyu, Wint Wint; Watanabe, Hisami; Saito, Reiko	2023	BMC infectious diseases	23	1	188	https://dx.doi.org/10.1186/s12879-023-08140-z	Wrong outcomes
Investigating the transmission of baloxavir-resistant influenza viruses from treated index patients to untreated household contacts in the BLOCKSTONE study.	Harding, Joanne; Bernasconi, Corrado; Williams, Sarah; Wildum, Steffen; Kinoshita, Masahiro; Uehara, Takeki; Hurt, Aeron C	2023	Influenza and other respiratory viruses	17	1	e13079	https://dx.doi.org/10.1111/irv.13079	Wrong patient population
Influenza antivirals and their role in pandemic preparedness.	Jones, Jeremy C; Yen, Hui-Ling; Adams, Peter; Armstrong, Kimberly; Govorkova, Elena A	2023	Antiviral research	210	6i7, 8109699	105499	https://dx.doi.org/10.1016/j.antiviral.2022.105499	Wrong study design
Effects of baloxavir and oseltamivir antiviral therapy on the transmission of seasonal influenza in China: A	Jiang, Yawen; Lin, Yi-Fan; Shi, Si; Chen, Daqin; Shu, Yuelong	2022	Journal of medical virology	94	11	5425-5433	https://dx.doi.org/10.1002/jmv.27969	Wrong setting

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
mathematical modeling analysis.								
Is it possible to hospitalize patients in multiple-bed room without increasing the risk of hospital-acquired influenza? Description of a pragmatic preventive strategy in a French university hospital.	Cazzorla, Fabiana; Azzam, Othmane; Buet, Emeline; Gallouche, Meghann; Larrat, Sylvie; Giner, Celine; Mallaret, Marie Reine; Morand, Patrice; Landelle, Caroline	2022	American journal of infection control	50	2	155-158	https://dx.doi.org/10.1016/j.ajic.2021.09.016	Wrong comparator
Reducing Influenza Virus Transmission: The Potential Value of Antiviral Treatment.	Hayden, Frederick G; Asher, Jason; Cowling, Benjamin J; Hurt, Aeron C; Ikematsu, Hideyuki; Kuhlbusch, Klaus; Lemenuel-Diot, Annabelle; Du, Zhanwei; Meyers, Lauren Ancel; Piedra, Pedro A; Takazono, Takahiro; Yen, Hui-Ling; Monto, Arnold S	2022	Clinical infectious diseases : an official publication of the Infectious Diseases Society of America	74	3	532-540	https://dx.doi.org/10.1093/cid/ciab625	Wrong study design
Interventions for preventing influenza: An overview of Cochrane systematic reviews and a Bayesian network meta-analysis.	Yuan, Yi; Wang, Rui-Ting; Xia, Jun; Cao, Hui-Juan	2021	Journal of integrative medicine	19	6	503-514	https://dx.doi.org/10.1016/j.joim.2021.09.001	Wrong study design
Influenza A (H1N1): outbreak management in a	Ventura, Carlucci Gualberto; Roque, Felicio Lopes; Sousa,	2020	Jornal brasileiro de nefrologia	42	2	182-190	https://dx.doi.org/10.1590/2	Wrong setting

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
dialysis unit and clinical outcomes of infection in chronic hemodialysis patients.	Itanilton Queiroz de; Lobo, Renata Desordi; Luders, Claudio						175-8239-jbn-2019-0180	
Examining the use of antiviral prophylaxis for influenza outbreaks in residential aged care facilities in NSW, Australia.	Meshreky, Wedyan; Hennessy, Daneeta; Gilmour, Robin; Tobin, Sean; Sheppeard, Vicky	2020	Public health research & practice	30	1		https://dx.doi.org/10.17061/phrp29121904	Wrong outcomes
A network meta-analysis of the efficacy and safety of baloxavir marboxil versus neuraminidase inhibitors for the treatment of influenza in otherwise healthy patients.	Taieb, Vanessa; Ikeoka, Hidetoshi; Ma, Fang-Fang; Borkowska, Katarzyna; Aballea, Samuel; Tone, Keiko; Hirotsu, Nobuo	2019	Current medical research and opinion	35	8	1355-1364	https://dx.doi.org/10.1080/03007995.2019.1584505	Wrong outcomes
Common cold in Team Finland during 2018 Winter Olympic Games (PyeongChang): epidemiology, diagnosis including molecular point-of-care testing (POCT) and treatment.	Valtonen, Maarit; Waris, Matti; Vuorinen, Tytti; Eerola, Erkki; Hakanen, Antti J; Mjosund, Katja; Gronroos, Wilma; Heinonen, Olli J; Ruuskanen, Olli	2019	British journal of sports medicine	53	17	1093-1098	https://dx.doi.org/10.1136/bjsports-2018-100487	Wrong outcomes
Oseltamivir for prophylaxis of influenza in vaccinated	Van Praet, Jens T; Steyaert, Sanne; Demesmaecker, Mirjam; Grootaert, Veerle; Reynders, Marijke	2019	Infection control and hospital epidemiology	40	4	497-498	https://dx.doi.org/10.1017/ice.2019.11	Wrong comparator

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
hemodialysis patients.								
Influenza Transmission Dynamics in Urban Households, Managua, Nicaragua, 2012-2014.	Gordon, Aubree; Tsang, Tim K; Cowling, Benjamin J; Kuan, Guillermina; Ojeda, Sergio; Sanchez, Nery; Gresh, Lionel; Lopez, Roger; Balmaseda, Angel; Harris, Eva	2018	Emerging infectious diseases	24	10	1882-1888	https://dx.doi.org/10.3201/eid2410.161258	Wrong setting
The Prophylactic Effect of Anti-influenza Agents for an Influenza Outbreak in a University Hospital.	Hagihara, Mao; Kato, Yukiko; Kurumiya, Ai; Takahashi, Tomoko; Sakata, Miki; Kato, Hideo; Sakanashi, Daisuke; Yamada, Atsuko; Suematsu, Hiroyuki; Hirai, Jun; Nishiyama, Naoya; Koizumi, Yusuke; Yamagishi, Yuka; Mikamo, Hiroshige	2018	Internal medicine (Tokyo, Japan)	57	4	497-501	https://dx.doi.org/10.2169/internalmedicine.8854-17	Wrong study design
Combined interventions for mitigation of an influenza A (H1N1) 2009 outbreak in a physical training camp in Beijing, China.	Chu, Chen-Yi; de Silva, U Chandimal; Guo, Jin-Peng; Wang, Yong; Wen, Liang; Lee, Vernon J; Li, Shen-Long; Huang, Liu-Yu	2017	International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases	60	c3r, 9610933	77-82	https://dx.doi.org/10.1016/j.ijid.2017.04.021	Wrong comparator
Interdisciplinary pharmacometrics linking oseltamivir pharmacology, influenza epidemiology and	Kamal, Mohamed A; Smith, Patrick F; Chaiyakunapruk, Nathorn; Wu, David B C; Pratoomsoot, Chayanin; Lee, Kenneth K C; Chong,	2017	British journal of clinical pharmacology	83	7	1580-1594	https://dx.doi.org/10.1111/bcp.13229	Wrong patient population

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
health economics to inform antiviral use in pandemics.	Huey Yi; Nelson, Richard E; Nieforth, Keith; Dall, Georgina; Toovey, Stephen; Kong, David C M; Kamauu, Aaron; Kirkpatrick, Carl M; Rayner, Craig R							
Successful use of oseltamivir prophylaxis in managing a nosocomial outbreak of influenza A in a hematology and allogeneic stem cell transplant unit.	Yue, Mimi C; Collins, Joel T; Subramoniapillai, Elango; Kennedy, Glen A	2017	Asia-Pacific journal of clinical oncology	13	1	37-43	https://dx.doi.org/10.1111/ajco.12565	Wrong comparator
Control of an H1N1 outbreak in a correctional facility in central Taiwan.	Chao, Wen-Cheng; Liu, Po-Yu; Wu, Chieh-Liang	2017	Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi	50	2	175-182	https://dx.doi.org/10.1016/j.jmii.2015.05.005	Wrong setting
Evaluation of the use of oseltamivir prophylaxis in the control of influenza outbreaks in long-term care facilities in Alberta, Canada: a retrospective provincial database analysis.	Ye, Ming; Jacobs, Angela; Khan, Muhammad Naeem; Jaipaul, Joy; Oda, Joanna; Johnson, Marcia; Doroshenko, Alexander	2016	BMJ open	6	7	e011686	https://dx.doi.org/10.1136/bmjopen-2016-011686	Wrong outcomes
Three-day regimen of oseltamivir for postexposure prophylaxis of influenza in wards.	Ishiguro, N; Oyamada, R; Nasuhara, Y; Yamada, T; Miyamoto, T; Imai, S; Akizawa, K; Fukumoto, T;	2016	The Journal of hospital infection	94	2	150-3	https://dx.doi.org/10.1016/j.jhin.2016.05.012	Wrong comparator

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	Iwasaki, S; Iijima, H; Ono, K							
Influenza in the Emergency Department: Vaccination, Diagnosis, and Treatment: Clinical Practice Paper Approved by American Academy of Emergency Medicine Clinical Guidelines Committee.	Abraham, Michael K; Perkins, Jack; Vilke, Gary M; Coyne, Christopher J	2016	The Journal of emergency medicine	50	3	536-42	https://dx.doi.org/10.1016/j.jemermed.2015.10.013	Wrong study design
Association of Oseltamivir Treatment With Virus Shedding, Illness, and Household Transmission of Influenza Viruses.	Cheung, Doug H; Tsang, Tim K; Fang, Vicky J; Xu, Jiajing; Chan, Kwok-Hung; Ip, Dennis K M; Peiris, Joseph Sriyal Malik; Leung, Gabriel M; Cowling, Benjamin J	2015	The Journal of infectious diseases	212	3	391-6	https://dx.doi.org/10.1093/infdis/jiv058	Wrong study design
Oseltamivir in influenza outbreaks in care homes: challenges and benefits of use in the real world.	Millership, S; Cummins, A	2015	The Journal of hospital infection	90	4	299-303	https://dx.doi.org/10.1016/j.jhin.2015.04.019	Wrong study design
Prevention of nosocomial transmission of influenza A (H7N9) in Hong Kong.	Cheng, V C C; Lee, W M; Sridhar, S; Ho, P L; Yuen, K Y	2015	The Journal of hospital infection	90	4	355-6	https://dx.doi.org/10.1016/j.jhin.2015.04.016	Wrong study design
Effects of oseltamivir treatment of index patients with	Fry, Alicia M; Goswami, Doli; Nahar, Kamrun; Sharmin, Amina T; Rahman, Mustafizur;	2015	The Lancet. Infectious diseases	15	6	654-62	https://dx.doi.org/10.1016/S1473-	Wrong setting

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
influenza on secondary household illness in an urban setting in Bangladesh: secondary analysis of a randomised, placebo-controlled trial.	Gubareva, Larisa; Trujillo, Alma; Barnes, John; Azim, Tasnim; Bresee, Joseph; Luby, Stephen P; Brooks, W Abdullah						3099(15)70041-1	
Infection control preparedness for human infection with influenza A H7N9 in Hong Kong.	Cheng, Vincent C C; Tai, Josepha W M; Lee, W M; Chan, W M; Wong, Sally C Y; Chen, Jonathan H K; Poon, Rosana W S; To, Kelvin K W; Chan, Jasper F W; Ho, P L; Chan, K H; Yuen, K Y	2015	Infection control and hospital epidemiology	36	1	87-92	https://dx.doi.org/10.1017/ice.2014.2	Wrong outcomes
Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children.	Toniolo Neto, Joao	2014	Sao Paulo medical journal = Revista paulista de medicina	132	4	256-7	https://dx.doi.org/10.1590/1516-3180.201441324t2	Wrong study design
The value of neuraminidase inhibitors for the prevention and treatment of seasonal influenza: a systematic review of systematic reviews.	Michiels, Barbara; Van Puyenbroeck, Karolien; Verhoeven, Veronique; Vermeire, Etienne; Coenen, Samuel	2013	PloS one	8	4	e60348	https://dx.doi.org/10.1371/journal.pone.0060348	Wrong outcomes
Management of influenza infection in solid-organ transplant recipients: consensus	Lopez-Medrano, Francisco; Cordero, Elisa; Gavalda, Joan; Cruzado, Josep M; Marcos, M Angeles; Perez-Romero, Pilar;	2013	Enfermedades infecciosas y microbiologia clinica	31	8	526.e1-526.e20	https://dx.doi.org/10.1016/j.eimc.2013.01.013	Wrong study design

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
statement of the Group for the Study of Infection in Transplant Recipients (GESITRA) of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) and the	Sabe, Nuria; Gomez-Bravo, Miguel Angel; Delgado, Juan Francisco; Cabral, Evelyn; Carratala, Jordi							
Oseltamivir for control of influenza at mass gatherings.	Tashani, Mohamed; Rashid, Harunor; Ridda, Iman; Heron, Leon; Memish, Ziad A; Haworth, Elizabeth; Booy, Robert	2013	Infectious disorders drug targets	13	1	46-52	https://dx.doi.org/10.2174/187152651212999007	Wrong study design
The spread of influenza A(H1N1)pdm09 in Victorian school children in 2009: implications for revised pandemic planning.	Fielding, James E; Bergeri, Isabel; Higgins, Nasra; Kelly, Heath A; Meagher, Julian; McBryde, Emma S; Moran, Rodney; Hellard, Margaret E; Lester, Rosemary A	2013	PloS one	8	2	e57265	https://dx.doi.org/10.1371/journal.pone.0057265	Wrong outcomes
Two aircraft carriers' perspectives: a comparative of control measures in shipboard H1N1 outbreaks.	Harwood, Jared L; LaVan, Joseph T; Brand, George J 2nd	2013	Disaster medicine and public health preparedness	7	1	29-35	https://dx.doi.org/10.1001/dmp.2012.53	Wrong intervention
High morbidity and mortality associated with an outbreak of influenza A(H3N2) in a psycho-geriatric facility.	Sayers, G; Igoe, D; Carr, M; Cosgrave, M; Duffy, M; Crowley, B; O'Herlihy, B	2013	Epidemiology and infection	141	2	357-65	https://dx.doi.org/10.1017/S0950268812000659	Wrong comparator

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Mass oseltamivir prophylaxis halts pandemic influenza A H1N1 2009 outbreak in a secondary school in Ashanti Region, Ghana.	Asiedu-Bekoe, F; Adu, D A; Offei, A	2012	Ghana medical journal	46	4	219-24		Wrong setting
Case characteristics and use of oseltamivir in children and household contacts.	Fallo, Aurelia A; Contrini, Maria Marta; Neyro, Silvina; Lopez, Eduardo Luis	2012	The Pediatric infectious disease journal	31	7	781-3	https://dx.doi.org/10.1097/INF.0b013e318256c06b	Wrong study design
Pandemic (H1N1) 2009 influenza in Canadian pediatric cancer and hematopoietic stem cell transplant patients.	Tran, Dat; Science, Michelle; Dix, David; Portwine, Carol; Zelcer, Shayna; Johnston, Donna L; Yanofsky, Rochelle; Gassas, Adam; Ethier, Marie-Chantal; Sung, Lillian	2012	Influenza and other respiratory viruses	6	6	e105-13	https://dx.doi.org/10.1111/j.1750-2659.2012.00352.x	Wrong outcomes
Neuraminidase inhibitors for preventing and treating influenza in healthy adults.	Jefferson, Tom; Jones, Mark; Doshi, Peter; Del Mar, Chris; Dooley, Liz; Foxlee, Ruth	2010	The Cochrane database of systematic reviews		2	CD001265	https://dx.doi.org/10.1002/14651858.CD001265.pub3	Review withdrawn
An influenza outbreak among pilgrims sleeping at a school without purpose built overnight accommodation facilities.	Staff, Michael; Torres, Maria I	2011	Communicable diseases intelligence quarterly report	35	1	05-Oct	https://dx.doi.org/10.33321/cdi.2011.35.3	Wrong outcomes
Effects of oseltamivir	Ng, Sophia; Cowling, Benjamin J; Fang, Vicky J;	2010	Clinical infectious	50	5	707-14	https://dx.doi.org/1	Wrong study design

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
treatment on duration of clinical illness and viral shedding and household transmission of influenza virus.	Chan, Kwok Hung; Ip, Dennis K M; Cheng, Calvin K Y; Uyeki, Timothy M; Houck, Peter M; Malik Peiris, J S; Leung, Gabriel M		diseases : an official publication of the Infectious Diseases Society of America				0.1086/650458	
Does treatment with oseltamivir prevent transmission of influenza to household contacts?.	Hayward, Andrew	2010	Clinical infectious diseases : an official publication of the Infectious Diseases Society of America	50	5	715-6	https://dx.doi.org/10.1086/650459	Wrong study design
Post-exposure prophylaxis for H1N1 with oseltamivir in renal allograft recipient--safe and effective without any immunosuppresive drug interaction.	Kute, Vivek; Goplani, K R; Godara, S M; Shah, P R; Vanikar, A V; Trivedii, H L	2011	The Journal of the Association of Physicians of India	59	hg7, 7505585	49-51		Wrong setting
How we optimized prevention and control of pandemic 2009 influenza A (H1N1) in a resource-limited nation's pediatric oncology unit.	Melgar, Mario; De-Leon, Rosa Elvira; Geronimo, Mariana; Ramirez, Marilyn; Asturias, Edwin J; Antillon-Klussmann, Federico; Guimera, Don; Caniza, Miguela A	2011	American journal of infection control	39	6	534-5	https://dx.doi.org/10.1016/j.ajic.2010.10.012	Wrong setting
Pandemic influenza A(H1N1) 2009 virus outbreak among boarding school pupils in Madagascar:	Rajatonirina, Soatiana; Heraud, Jean-Michei; Randrianasolo, Laurence; Razanajatovo, Norosoa; Ramandimbisoa, Tombo;	2011	Journal of infection in developing countries	5	3	156-62	https://dx.doi.org/10.3855/jidc.1318	Wrong setting

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
compliance and adverse effects of prophylactic oseltamivir treatment.	Ratsitorahina, Maherisoa; Richard, Vincent							
Monitoring and characterization of oseltamivir-resistant pandemic (H1N1) 2009 virus, Japan, 2009-2010.	Ujike, Makoto; Ejima, Miho; Anraku, Akane; Shimabukuro, Kozue; Obuchi, Masatsugu; Kishida, Noriko; Hong, Xu; Takashita, Emi; Fujisaki, Seiichiro; Yamashita, Kazuyo; Horikawa, Hiroshi; Kato, Yumiko; Oguchi, Akio; Fujita, Nobuyuki; Tashiro, Masato; Odagiri, Takato	2011	Emerging infectious diseases	17	3	470-9	https://dx.doi.org/10.3201/eid1703.101188	Wrong outcomes
Investigation of causes of oseltamivir chemoprophylaxis failures during influenza A (H1N1-2009) outbreaks.	Lee, Vernon J; Yap, Jonathan; Maurer-Stroh, Sebastian; Lee, Raphael T C; Eisenhaber, Frank; Tay, Joshua K; Ting, Pei Jun; Loh, Jin Phang; Wong, Christopher W; Tan, Boon Huan; Koay, Evelyn S C; Kelly, Paul M; Hibberd, Martin L	2011	Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology	50	2	104-8	https://dx.doi.org/10.1016/j.jcv.2010.10.004	Wrong setting
A school outbreak of pandemic (H1N1) 2009 infection: assessment of secondary household transmission and the protective role of oseltamivir.	Leung, Y H; Li, M P; Chuang, S K	2011	Epidemiology and infection	139	1	Apr-41	https://dx.doi.org/10.1017/S0950268810001445	Wrong setting

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Effectiveness of antiviral treatment in human influenza A(H5N1) infections: analysis of a Global Patient Registry.	Adisasmito, Wiku; Chan, Paul K S; Lee, Nelson; Oner, Ahmet Faik; Gasimov, Viktor; Aghayev, Faik; Zaman, Mukhtiar; Bamgboye, Ebun; Dogan, Nazim; Coker, Richard; Starzyk, Kathryn; Dreyer, Nancy A; Toovey, Stephen	2010	The Journal of infectious diseases	202	8	1154-60	https://dx.doi.org/10.1086/656316	Wrong outcomes
Community transmission of pandemic influenza A (H1N1) in China.	Liu, Wei; Jiang, Tao; Li, Xiao-Feng; Tang, Fang; Wei, Mao-Ti; Yu, Man; Zhao, Hui; Yu, Xue-Dong; Liu, Li-Juan; Qin, Cheng-Feng; Cao, Wu-Chun	2010	Infection control and hospital epidemiology	31	9	961-3	https://dx.doi.org/10.1086/655020	Wrong setting
Transmission of novel influenza A(H1N1) in households with post-exposure antiviral prophylaxis.	van Boven, Michiel; Donker, Tjibbe; van der Lubben, Mariken; van Gageldonk-Lafeber, Rianne B; te Beest, Dennis E; Koopmans, Marion; Meijer, Adam; Timen, Aura; Swaan, Corien; Dalhuijsen, Anton; Hahne, Susan; van den Hoek, Anneke; Teunis, Peter; van der Sande, Marianne A B; Wallinga, Jacco	2010	PloS one	5	7	e11442	https://dx.doi.org/10.1371/journal.pone.0011442	Wrong comparator
Oseltamivir ring prophylaxis for containment of 2009 H1N1 influenza outbreaks.	Lee, Vernon J; Yap, Jonathan; Cook, Alex R; Chen, Mark I; Tay, Joshua K; Tan, Boon Huan; Loh, Jin Phang; Chew, Seok Wei; Koh, Wee Hong; Lin, Raymond; Cui, Lin; Lee, Charlie W H; Sung, Wing-	2010	The New England journal of medicine	362	23	2166-74	https://dx.doi.org/10.1056/NEJMoa0908482	Wrong setting

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
	Kin; Wong, Christopher W; Hibberd, Martin L; Kang, Wee Lee; Seet, Benjamin; Tambyah, Paul A							
An outbreak of novel influenza A (H1N1) in the English Language Institute.	Kim, Joon Hyung; Lee, Han Sung; Park, Hye Kyung; Kim, Jin Seok; Lee, Sang Won; Kim, Seong Sun; Lee, Jong Koo	2010	Journal of preventive medicine and public health = Yebang Uihakhoe chi	43	3	274-8	https://dx.doi.org/10.3961/jpmph.2010.43.3.274	Wrong study design
Influenza A(H1N1) outbreak in a long-term care facility for severely handicapped residents, Slovenia, March-April 2009.	Socan, M; Prosenc, K; Tevz-Cizej, N	2010	Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin	15	21	19577	https://dx.doi.org/10.2807/ese.15.21.19577-en	Wrong comparator
Household transmissibility and other characteristics of seasonal oseltamivir-resistant influenza A(H1N1) viruses, Germany, 2007-8.	Buchholz, U; Brockmann, S; Duwe, S; Schweiger, B; an der Heiden, M; Reinhardt, B; Buda, S	2010	Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin	15	6			Wrong patient population
The natural viral load profile of patients with pandemic 2009 influenza A(H1N1) and the effect of oseltamivir treatment.	Li, Iris W; Hung, Ivan F; To, Kelvin K; Chan, Kwok-Hung; Wong, Samson S Y; Chan, Jasper F; Cheng, Vincent C; Tsang, Owen T; Lai, Sik-To; Lau, Yu-Lung; Yuen, Kwok-Yung	2010	Chest	137	4	759-68	https://dx.doi.org/10.1378/chest.09-3072	Wrong outcomes
Pandemic (H1N1) 2009 virus outbreak	Calatayud, L; Kurkela, S; Neave, P E; Brock, A;	2010	Epidemiology and infection	138	2	183-91	https://dx.doi.org/1	Wrong comparator

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
in a school in London, April-May 2009: an observational study.	Perkins, S; Zuckerman, M; Sudhanva, M; Bermingham, A; Ellis, J; Pebody, R; Catchpole, M; Heathcock, R; Maguire, H						0.1017/S0950268809991191	
Systematic review: safety and efficacy of extended-duration antiviral chemoprophylaxis against pandemic and seasonal influenza.	Khazeni, Nayer; Bravata, Dena M; Holty, Jon-Erik C; Uyeki, Timothy M; Stave, Christopher D; Gould, Michael K	2009	Annals of internal medicine	151	7	464-73	https://dx.doi.org/10.7326/0003-4819-151-7-200910060-00143	Wrong outcomes
Amantadine and rimantadine for influenza A in children and the elderly.	Alves Galvao, M G; Rocha Crispino Santos, M A; Alves da Cunha, A J L	2008	The Cochrane database of systematic reviews		1	CD002745	https://dx.doi.org/10.1002/14651858.CD002745.pub2	Wrong intervention
A Bayesian model for evaluating influenza antiviral efficacy in household studies with asymptomatic infections.	Yang, Yang; Halloran, M Elizabeth; Longini, Ira M Jr	2009	Biostatistics (Oxford, England)	10	2	390-403	https://dx.doi.org/10.1093/biostatistics/kxn045	Wrong study design
Antiviral treatment and prevention of seasonal influenza: a comparative review of recommendations in the European Union.	Stephenson, Iain; Clark, Tristan W; Pareek, Manish	2008	Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology	42	3	244-8	https://dx.doi.org/10.1016/j.jcv.2008.04.001	Wrong study design
Antiviral treatment and prophylaxis of	Nayak, Jennifer L; Treanor, John J	2009	Pediatric annals	38	12	667-74	https://dx.doi.org/10.3928/0	Wrong study design

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
influenza virus in children.							0904481-20091117-07	
Outbreak of antiviral drug-resistant influenza a in long-term care facility, Illinois, USA, 2008.	Dharan, Nila J; Patton, Monica; Siston, Alicia M; Morita, Julie; Ramirez, Enrique; Wallis, Teresa R; Deyde, Varough; Gubareva, Larisa V; Klimov, Alexande I; Bresee, Joseph S; Fry, Alicia M	2009	Emerging infectious diseases	15	12	Jun-73	https://dx.doi.org/10.3201/eid1512.081644	Wrong study design
Novel influenza A (H1N1) outbreak on board a US navy vessel.	Dill, Curt E; Favata, Michael A	2009	Disaster medicine and public health preparedness	3 Suppl 2	10129 7401	S117-20	https://dx.doi.org/10.1097/DMP.0b013e3181bf249b	Wrong study design
Emergence of oseltamivir-resistant pandemic H1N1 virus during prophylaxis.	Baz, Mariana; Abed, Yacine; Papenburg, Jesse; Bouhy, Xavier; Hamelin, Marie-Eve; Boivin, Guy	2009	The New England journal of medicine	361	23	Jul-96	https://dx.doi.org/10.1056/NEJMc0910060	Wrong study design
A model-based assessment of oseltamivir prophylaxis strategies to prevent influenza in nursing homes.	van den Dool, Carline; Hak, Eelko; Bonten, Marc J M; Wallinga, Jacco	2009	Emerging infectious diseases	15	10	1547-55	https://dx.doi.org/10.3201/eid1510.081129	Wrong study design
Oseltamivir for influenza postexposure prophylaxis: economic evaluation for children aged 1-12 years in the U.S.	Talbird, Sandra E; Brogan, Anita J; Winiarski, Aleksander P	2009	American journal of preventive medicine	37	5	381-8	https://dx.doi.org/10.1016/j.amepre.2009.08.012	Wrong outcomes

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England.	Wallensten, A; Oliver, I; Lewis, D; Harrison, S	2009	Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin	14	30	19285	https://dx.doi.org/10.2807/ese.14.30.19285-en	Wrong outcomes
The use of oseltamivir during an influenza B outbreak in a chronic care hospital.	Seale, Holly; Weston, Kathryn M; Dwyer, Dominic E; Zhu, Mengzhi; Allchin, Lisa; Booy, Robert; MacIntyre, C Raina	2009	Influenza and other respiratory viruses	3	1	15-20	https://dx.doi.org/10.1111/j.1750-2659.2008.00063.x	Wrong comparator
Influenza outbreak management on a locked behavioral health unit.	Risa, Kathleen J; McAndrew, Janet M; Muder, Robert R	2009	American journal of infection control	37	1	Aug-76	https://dx.doi.org/10.1016/j.ajic.2008.05.008	Wrong outcomes
Summer influenza outbreak in a home for the elderly: application of preventive measures.	Gaillat, J; Dennetiere, G; Raffin-Bru, E; Valette, M; Blanc, M C	2008	The Journal of hospital infection	70	3	272-7	https://dx.doi.org/10.1016/j.jhin.2008.07.009	Wrong outcomes
Use of oseltamivir during an outbreak of influenza A in a long-term care facility in Taiwan.	Chang, Y-M; Li, W-C; Huang, C-T; Huang, C-G; Tsao, K-C; Cheng, Y-H; Chiang, S-L; Yang, S-Y; Chen, C-H; Huang, Y-C	2008	The Journal of hospital infection	68	1	Jul-83	https://dx.doi.org/10.1016/j.jhin.2007.08.022	Wrong setting
Antivirals for influenza in healthy adults: systematic review.	Jefferson, T; Demicheli, V; Rivetti, D; Jones, M; Di Pietrantonj, C; Rivetti, A	2006	Lancet (London, England)	367	9507	303-13	https://dx.doi.org/10.1016/S0140-6736(06)67970-1	Wrong patient population

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Observations on managing an outbreak of influenza A infection in an aged care facility.	McCall, Bradley J; Mohr, Christine M; Jarvinen, Kari A J	2007	Communicable diseases intelligence quarterly report	31	4	410-2	https://dx.doi.org/10.33321/cdi.2007.31.46	Wrong comparator
Post-exposure influenza prophylaxis with oseltamivir: cost effectiveness and cost utility in families in the UK.	Sander, Beate; Hayden, Frederick G; Gyldmark, Marlene; Garrison, Louis P Jr	2006	PharmacoEconomics	24	4	373-86	https://dx.doi.org/10.2165/00019053-200624040-00007	Wrong study design
Safety and tolerability of oseltamivir prophylaxis in hematopoietic stem cell transplant recipients: a retrospective case-control study.	Vu, Debie; Peck, Angela J; Nichols, W Garrett; Varley, Cara; Englund, Janet A; Corey, Lawrence; Boeckh, Michael	2007	Clinical infectious diseases : an official publication of the Infectious Diseases Society of America	45	2	187-93	https://dx.doi.org/10.1086/518985	Wrong comparator
Effectiveness of neuraminidase inhibitors for preventing staff absenteeism during pandemic influenza.	Lee, Vernon J; Chen, Mark I	2007	Emerging infectious diseases	13	3	449-57	https://dx.doi.org/10.3201/eid1303.060309	Wrong setting
Antiviral therapy and prophylaxis for influenza in children.	Anonymous	2007	Pediatrics	119	4	852-60	https://dx.doi.org/10.1542/peds.2007-0224	Wrong outcomes
Protective measures and human antibody response during an avian influenza H7N3 outbreak in	Skowronski, Danuta M; Li, Yan; Tweed, S Aleina; Tam, Theresa W S; Petric, Martin; David, Samara T; Marra,	2007	CMAJ : Canadian Medical Association journal = journal de l'Association	176	1	47-53	https://dx.doi.org/10.1503/cmaj.060204	Wrong outcomes

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poultry in British Columbia, Canada.	Fawziah; Bastien, Nathalie; Lee, Sandra W; Krajden, Mel; Brunham, Robert C		medicale canadienne					
Use of oseltamivir in Dutch nursing homes during the 2004-2005 influenza season.	van der Sande, Marianne A B; Ruijs, Wilhelmina L M; Meijer, Adam; Cools, Herman J M; van der Plas, Simone M	2006	Vaccine	24	44-46	Sep-64	https://dx.doi.org/10.1016/j.vaccine.2006.05.049	Wrong comparator
Antiviral drugs in influenza: an adjunct to vaccination in some situations.	Anonymous	2006	Prescrire international	15	81	21-30		Wrong study design
Influenza, Winter Olympiad, 2002.	Gundlapalli, Adi V; Rubin, Michael A; Samore, Matthew H; Lopansri, Bert; Lahey, Timothy; McGuire, Heather L; Winthrop, Kevin L; Dunn, James J; Willick, Stuart E; Vosters, Randal L; Waeckerle, Joseph E; Carroll, Karen C; Gwaltney, Jack M Jr; Hayden, Frederick G; Elstad, Mark R; Sande, Merle A	2006	Emerging infectious diseases	12	1	144-6	https://dx.doi.org/10.3201/eid1201.050645	Wrong outcomes
Efficacy and tolerability of the oral neuraminidase inhibitor peramivir in experimental human influenza: randomized, controlled trials for	Barroso, Luis; Treanor, John; Gubareva, Larisa; Hayden, Frederick G	2005	Antiviral therapy	10	8	901-10		Wrong study design

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
prophylaxis and treatment.								
Inhaled zanamivir versus rimantadine for the control of influenza in a highly vaccinated long-term care population.	Gravenstein, Stefan; Drinka, Paul; Osterweil, Dan; Schilling, Margo; Krause, Peggy; Elliott, Michael; Shult, Peter; Ambrozaitis, Arvydas; Kandel, Ruth; Binder, Ellen; Hammond, Janet; McElhaney, Janet; Flack, Nancy; Daly, Janet; Keene, Oliver	2005	Journal of the American Medical Directors Association	6	6	359-66	https://dx.doi.org/10.1016/j.jamda.2005.08.006	Wrong outcomes
Inhaled zanamivir versus placebo for the prevention of influenza outbreaks in an unvaccinated long-term care population.	Ambrozaitis, Arvydas; Gravenstein, Stefan; van Essen, Gerrit A; Rubinstein, Ethan; Balciuniene, Ligita; Stikleryte, Ausra; Crawford, Catriona; Elliott, Michael; Shult, Peter	2005	Journal of the American Medical Directors Association	6	6	367-74	https://dx.doi.org/10.1016/j.jamda.2005.08.007	Wrong outcomes
Viral shedding in children with influenza virus infections treated with neuraminidase inhibitors.	Sato, Masatoki; Hosoya, Mitsuaki; Kato, Kazuo; Suzuki, Hitoshi	2005	The Pediatric infectious disease journal	24	10	931-2	https://dx.doi.org/10.1097/01.inf.0000180976.81055.ce	Wrong setting
Antiviral prophylaxis in the management of an influenza outbreak in an aged care facility.	Bush, Kym A; McAnulty, Jeremy; McPhie, Ken; Reynolds, Roderick; Boomer, Melanie; Clarkson, Lisa M; Quaine, Julianne; Dwyer, Dominic E	2004	Communicable diseases intelligence quarterly report	28	3	396-400	https://dx.doi.org/10.33321/cdi.2004.28.45	Wrong study design
Influenza infections after hematopoietic stem cell	Nichols, W Garrett; Guthrie, Katherine A;	2004	Clinical infectious diseases : an	39	9	1300-6	https://dx.doi.org/1	Wrong outcomes

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
transplantation: risk factors, mortality, and the effect of antiviral therapy.	Corey, Lawrence; Boeckh, Michael		official publication of the Infectious Diseases Society of America				0.1086/425004	
Detection and control of influenza outbreaks in well-vaccinated nursing home populations.	Monto, Arnold S; Rotthoff, Judy; Teich, Esther; Herlocher, M Louise; Truscon, Rachel; Yen, Hui-Ling; Elias, Stephanie; Ohmit, Suzanne E	2004	Clinical infectious diseases : an official publication of the Infectious Diseases Society of America	39	4	459-64	https://dx.doi.org/10.1086/422646	Wrong comparator
Risk factors of influenza transmission in households.	Viboud, Cecile; Boelle, Pierre-Yves; Cauchemez, Simon; Lavenu, Audrey; Valleron, Alain-Jacques; Flahault, Antoine; Carrat, Fabrice	2004	The British journal of general practice : the journal of the Royal College of General Practitioners	54	506	684-9		Wrong intervention
Influenza outbreaks in aged-care facilities: staff vaccination and the emerging use of antiviral therapy.	Guy, Rebecca J; Di Natale, Richard; Kelly, Heath A; Lambert, Stephen B; Tobin, Sean; Robinson, Priscilla M; Tallis, Graham; Hampson, Alan W	2004	The Medical journal of Australia	180	12	640-2	https://dx.doi.org/10.5694/j.1326-5377.2004.tb06129.x	Wrong study design
Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands.	Koopmans, Marion; Wilbrink, Berry; Conyn, Marina; Natrop, Gerard; van der Nat, Hans; Vennema, Harry; Meijer, Adam; van Steenbergen, Jim; Fouchier, Ron; Osterhaus, Albert; Bosman, Arnold	2004	Lancet (London, England)	363	9409	587-93	https://dx.doi.org/10.1016/S0140-6736(04)15589-X	Zoonotic transmission

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Management of influenza in households: a prospective, randomized comparison of oseltamivir treatment with or without postexposure prophylaxis.	Hayden, Frederick G; Belshe, Robert; Villanueva, Catalina; Lanno, Riin; Hughes, Claire; Small, Ian; Dutkowski, Regina; Ward, Penelope; Carr, Jackie	2004	The Journal of infectious diseases	189	3	440-9	https://dx.doi.org/10.1086/381128	Wrong comparator
Safety and efficacy of nebulized zanamivir in hospitalized patients with serious influenza.	Ison, Michael G; Gnann, John W Jr; Nagy-Agren, Stephanie; Treannor, John; Paya, Carlos; Steigbigel, Roy; Elliott, Michael; Weiss, Heidi L; Hayden, Frederick G	2003	Antiviral therapy	8	3	183-90		Wrong intervention
Treatment and prevention of influenza: Swedish recommendations.	Uhnoo, Ingrid; Linde, Annika; Pauksens, Karlis; Lindberg, Anders; Eriksson, Margareta; Norrby, Ragnar	2003	Scandinavian journal of infectious diseases	35	1	11-Mar	https://dx.doi.org/10.1080/00365540210000269 99	Wrong study design
A population-dynamic model for evaluating the potential spread of drug-resistant influenza virus infections during community-based use of antivirals.	Ferguson, Neil M; Mallett, Susan; Jackson, Helen; Roberts, Noel; Ward, Penelope	2003	The Journal of antimicrobial chemotherapy	51	4	977-90	https://dx.doi.org/10.1093/jac/dkg136	Wrong patient population
Neuraminidase inhibitors for preventing and treating influenza in healthy adults.	Jefferson, T; Demicheli, V; Deeks, J; Rivetti, D	2000	The Cochrane database of systematic reviews		2	CD001265	https://dx.doi.org/10.1002/14651858.	Wrong outcomes

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
							CD001265	
Prevention and early treatment of influenza in healthy adults.	Demicheli, V; Jefferson, T; Rivetti, D; Deeks, J	2000	Vaccine	18	12-Nov	957-1030	https://dx.doi.org/10.1016/s0264-410x(99)00332-1	Wrong outcomes
Utility of zanamivir for chemoprophylaxis of concomitant influenza A and B in a complex continuing care population.	Hirji, Z; O'Grady, S; Bonham, J; Mak, M; Takata-Shewchuk, J; Hawkins, K; Gardam, M; Law, L; Mazzulli, T; Conly, J	2002	Infection control and hospital epidemiology	23	10	604-8	https://dx.doi.org/10.1086/501979	Wrong intervention
Economic analysis of influenza vaccination and antiviral treatment for healthy working adults.	Lee, Patrick Y; Matchar, David B; Clements, Dennis A; Huber, Joel; Hamilton, John D; Peterson, Eric D	2002	Annals of internal medicine	137	4	225-31	https://dx.doi.org/10.7326/0003-4819-137-4-20020820-00005	Wrong outcomes
Experience with oseltamivir in the control of nursing home influenza A outbreak.	Shijubo, Noriharu; Yamada, Gen; Takahashi, Mamoru; Tokunoh, Tetsuya; Suzuki, Takashi; Abe, Shosaku	2002	Internal medicine (Tokyo, Japan)	41	5	366-70	https://dx.doi.org/10.2169/internalmedicine.41.366	Wrong comparator
Use of oseltamivir during influenza outbreaks in Ontario nursing homes, 1999-2000.	Bowles, Susan K; Lee, Wayne; Simor, Andrew E; Vearncombe, Mary; Loeb, Mark; Tamblyn, Susan; Fearon, Margaret; Li, Yan; McGeer, Allison	2002	Journal of the American Geriatrics Society	50	4	608-16	https://dx.doi.org/10.1046/j.1532-5415.2002.50153.x	Wrong comparator
Is oral oseltamivir safe and effective	Sturpe, Deborah; Seaton, Terry L	2002	The Journal of family practice	51	1	87		Wrong study design

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
for the prevention of influenza and its complications in frail elderly long-term care residents who have received influenza vaccine?.								
Rapid pharmacotherapeutic intervention for an influenza A outbreak in the Canadian Arctic: lessons from the Sanikiluaq experience.	Van Caeseele, P; Macaulay, A; Orr, P; Aoki, F; Martin, B	2001	International journal of circumpolar health	60	4	640-8		Wrong outcomes
Long-term use of oseltamivir for the prophylaxis of influenza in a vaccinated frail older population.	Peters, P H Jr; Gravenstein, S; Norwood, P; De Bock, V; Van Couter, A; Gibbens, M; von Planta, T A; Ward, P	2001	Journal of the American Geriatrics Society	49	8	1025-31	https://dx.doi.org/10.1046/j.1532-5415.2001.49204.x	Wrong patient population
Experience with oseltamivir in the control of a nursing home influenza B outbreak.	Parker, R; Loewen, N; Skowronski, D	2001	Canada communicable disease report = Releve des maladies transmissibles au Canada	27	5	37-40		Wrong comparator
Zanamivir to prevent influenza.	Feder, H M Jr	2001	The New England journal of medicine	344	7	528-30		Wrong study design
Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP).	Bridges, C B; Winquist, A G; Fukuda, K; Cox, N J; Singleton, J A; Strikas, R A	2000	MMWR. Recommendations and reports : Morbidity and mortality weekly report.	49	RR-3	07-Jan		Wrong setting

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
			Recommendations and reports					
Zanamivir use during transmission of amantadine-resistant influenza A in a nursing home.	Lee, C; Loeb, M; Phillips, A; Nesbitt, J; Smith, K; Fearon, M; McArthur, M A; Mazzulli, T; Li, Y; McGeer, A	2000	Infection control and hospital epidemiology	21	11	700-4	https://dx.doi.org/10.1086/501727	Wrong comparator
Oral oseltamivir in human experimental influenza B infection.	Hayden, F G; Jennings, L; Robson, R; Schiff, G; Jackson, H; Rana, B; McClelland, G; Ipe, D; Roberts, N; Ward, P	2000	Antiviral therapy	5	3	205-13		Wrong outcomes
Oseltamivir for flu prevention.	Johnson, J M; Force, R W	2000	The Journal of family practice	49	2	183-4		Wrong outcomes
Economic and Social Benefits of Treating and Preventing Influenza in Aged Care Facilities	Actrn,	2006	http://www.who.int/trialsearch/Trial2.aspx?TrialID=ACTRN12606000278538					Wrong study design
The Role of Oseltamivir During Influenza Outbreaks in Aged-care Facilities in the Context of Optimal Influenza Vaccination and Infection Control	Actrn,	2015	http://www.who.int/trialsearch/Trial2.aspx?TrialID=ACTRN12615000638538					Wrong study design
A Study of Baloxavir Marboxil for the Reduction of Direct Transmission of Influenza from Otherwise Healthy Patients to Household Contacts	Euctr, E. S.	2019	https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2018-004056-37-ES					Wrong outcomes

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Use of the selective oral neuraminidase inhibitor oseltamivir to prevent influenza	Hayden, F. G.; Atmar, R. L.; Schilling, M.; Johnson, C.; Poretz, D.; Paar, D.; Huson, L.; Ward, P.; Mills, R. G.	1999	New England journal of medicine	341	18	1336,Äê1343	10.1056/NEJM199910283411802	Wrong outcomes
Efficacy and safety of the selective oral neuraminidase inhibitor oseltamivir for prophylaxis against influenza--placebo-controlled double-blind multicenter phase III trial	Kashiwagi, S.; Kudoh, S.; Watanabe, A.; Yoshimura, I.	2000	Kansenshogaku zasshi. The Journal of the Japanese Association for Infectious Diseases	74	12	1062,Äê1076	10.11150/kansenshogakuzasshi1970.74.1062	Non-English
A Randomised Controlled Trial on the Effect of Post-exposure Oseltamivir Prophylaxis on Influenza Transmission in Nursing Homes	Nct,	2010	https://clinicaltrials.gov/show/NCT01053377					Wrong study design
ED Influenza Therapeutic Pilot Study: oseltamivir vs. Peramivir	Nct,	2015	https://clinicaltrials.gov/show/NCT02609399					Wrong patient population
Study to Assess the Efficacy of Baloxavir Marboxil Versus Placebo to Reduce Onward Transmission of Influenza A or B in Households	Nct,	2019	https://clinicaltrials.gov/ct2/show/NCT03969212					Wrong study design
Baloxavir Versus Oseltamivir for	Nct,	2021	https://clinicaltrials.gov/show/NCT05012189					Wrong outcomes

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Nursing Home Influenza Outbreaks								
Oseltamivir and Baloxavir Marboxil for Prophylaxis Against Influenza Under a Hospital-based Setting	Nct,	2024	https://clinicaltrials.gov/ct2/show/NCT06762587					Wrong outcomes
A randomised controlled trial on the effectiveness of post-exposure prophylaxis (PEP) with oseltamivir in preventing influenza transmission in nursing home units	Nl, Omon	2009	https://trialsearch.who.int/Trial2.aspx?TrialID=NL-OMON33181					Wrong study design
Antivirals for influenza Like Illness? An rCt of Clinical and Cost effectiveness in primary CarE (ALICE)	Nl, Omon	2015	https://trialsearch.who.int/Trial2.aspx?TrialID=NL-OMON45203					Wrong study design
Is Tamiflu (oseltamivir) effective in preventing influenza in household contacts of patients with influenza?...commentary on Welliver R, Monto AS, Carewicz O et al. Effectiveness of oseltamivir in preventing influenza	Slawson, D. C.	2001	Evidence-based practice	4	5	3,Äê4		Wrong study design

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
in household contacts: a randomized controlled trial. JAMA 2001;285:748-54								
Prevention of influenza in the general population: systematic review and recommendations		2003	Health Technology Assessment (HTA) Database.					Full-text not available
Systematic review and economic decision modelling for the prevention and treatment of influenza A and B: neuraminidase inhibitors for treatment		2003	DARE.					Wrong outcomes
Systematic review and economic decision modelling for the prevention and treatment of influenza A and B: neuraminidase inhibitors for prevention		2003	DARE.					Wrong outcomes
Expert opinion on neuraminidase inhibitors for the prevention and treatment of influenza - review of recent systematic reviews and meta-analyses		2017	European Centre for Disease Prevention and Control - Expert Opinion					Wrong study design
Influenza post exposure prophylaxis and treatment: PGD templates		2019	Public Health England					Wrong study design
Baloxavir marboxil for reducing direct transmission of influenza ,Äí Horizon Scanning		2024	NIHR Innovation Observatory					Wrong study design
Antivirals for post-exposure prophylaxis of influenza: a systematic review and network meta-analysis ,Äí Findings		2024	medRxiv (Cold Spring Harbor Laboratory)				10.1101/2024.05.28.24307995	Wrong study design
Antivirals for treatment of severe influenza: a systematic review and network meta-analysis of randomized controlled trials ,Äí Discussion and Implications		2024	medRxiv (Cold Spring Harbor Laboratory)				10.1101/2024.05.28.24307938	Wrong outcomes
Antivirals for treatment of non-severe influenza: a systematic review and network meta-analysis of randomized controlled trials ,Äí Discussion and Implications		2024	medRxiv (Cold Spring Harbor Laboratory)				10.1101/2024.05.28.24307936	Wrong outcomes

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Clinical practice guidelines for influenza ,Äí Practical Information on Antivirals for Zoonotic Influenza ,Äí Evidence to Decision for Zanamivir		2024	World Health Organisation Guidelines					Wrong outcomes
Infectious and incubation period, and pre-symptomatic and asymptomatic transmission of influenza A H1N1pdm09 subtype: a rapid evidence summary ,Äí Final Summary of Findings		2025	AWS Test					Wrong intervention
Antiviral Treatment in Patients with Influenza Infection: A Systematic Review	Andhira Prilialoka, Dhea	2023	Journal of Advanced Research in Medical and Health science (ISSN 2208-2425)	9	10	21-25	10.53555/cpzr5184	Wrong outcomes
Antiviral drugs for the treatment of influenza: a systematic review and economic evaluation	Burch, J.; Paulden, M.; Conti, S.; Stock, C.; Corbett, M.; Welton, N. J.; Ades, A. E.; Sutton, A.; Cooper, N.; Elliot, A. J.; Nicholson, K.; Duffy, S.; McKenna, C.; Stewart, L.; Westwood, M.; Palmer, S.	2009	Health Technol Assess	13	58	1-265, iii-iv	10.3310/hta13580	Wrong outcomes
Zanamivir for the treatment of influenza in adults: a systematic review and economic evaluation	Burls, A.; Clark, W.; Stewart, T.; Preston, C.; Bryan, S.; Jefferson, T.; Fry-Smith, A.	2002	Health Technol Assess	6	9	1-87	10.3310/hta6090	Wrong outcomes
Recommendations for Prevention and Control of Influenza in Children, 2019-2020	Committee On Infectious, Diseases	2019	Pediatrics	144	4		10.1542/peds.2019-2478	Wrong study design
Clinical management and supervision of	G≈Çodzik, Micha≈Ç; Mi≈õkiewicz, Marek; ≈Åfôcka, Martyna; Ogieg≈Ço-Kowalczyk,	2024	Journal of Education, Health and Sport	54		32-42	10.12775/jehs.2024.54.003	Wrong intervention

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Influenza ‚Äì systematic review	Aleksandra; Samborska, Julia; Stelmaszak, Karina; Stencel, Katarzyna; Wifôckowiak, Pawe≈Ç; Wojtasik, Monika; ≈ºak, Katarzyna							
Evaluation of Influenza Antiviral Prophylaxis for Long-term Care Residents: A Systematic Review and Meta-Analysis	Hanula, R.; Glugosh, J.; Van Leer, E.; Bortolussi-Courval, E.; Prosty, C.	2026	Clin Infect Dis	82	3	484-493	10.1093/cid/ciaf101	Wrong study design
Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies	Hsu, J.; Santesso, N.; Mustafa, R.; Brozek, J.; Chen, Y. L.; Hopkins, J. P.; Cheung, A.; Hovhannisyan, G.; Ivanova, L.; Flottorp, S. A.; Saeterdal, I.; Wong, A. D.; Tian, J.; Uyeki, T. M.; Akl, E. A.; Alonso-Coello, P.; Smaill, F.; Schunemann, H. J.	2012	Ann Intern Med	156	7	512-24	10.7326/0003-4819-156-7-201204030-00411	Wrong outcomes
Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenzaa	Uyeki, T. M.; Bernstein, H. H.; Bradley, J. S.; Englund, J. A.; File, T. M.; Fry, A. M.; Gravenstein, S.; Hayden, F. G.; Harper, S. A.; Hirshon, J. M.; Ison, M. G.; Johnston, B. L.; Knight, S. L.; McGeer, A.; Riley, L. E.; Wolfe, C. R.; Alexander, P. E.; Pavia, A. T.	2019	Clin Infect Dis	68	6	e1-e47	10.1093/cid/ciy866	Wrong study design

Title	Authors	Published Year	Journal	Volume	Issue	Pages	DOI	Exclusion Reason
Evaluation of Influenza Antiviral Prophylaxis for Long-term Care Residents: A Systematic Review and Meta-Analysis	Hanula, R.; Glugosh, J.; Van Leer, E.; Bortolussi-Courval, √â; Prosty, C.	2025	Clinical infectious diseases : an official publication of the Infectious Diseases Society of America				10.1093/cid/ciaf101	Wrong outcomes
Review: antiviral agents reduce risk of influenza in health adults and alleviate symptoms faster than placebo	Moralejo, D.	2006	Evidence Based Nursing	9	4	108-108	10.1136/ebn.9.4.108	Wrong study design
Effect of Oseltamivir (Tamiflu¬Æ) for the Prevention and Treatment of Influenza During an Influenza Pandemic	M√∏rland, B.; Brants√¶ter, A. B.; Fuglesang, J. E.; Haaheim, L. R.; L√∏voll, √ò; Salm√©n, R.; Sjursen, H.; Kristiansen, I. S.; Wisl√∏ff, T.; √òrjas√¶ter Elvsaas, I. K.; Nilsen, E.	2005	NIPH Systematic Reviews: Executive Summaries					Non-English

Appendix 3: Summary of Study Characteristics

Table 1: RCT, NRS, and Mathematical Modelling Study Characteristics

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
RCTs - Oseltamivir (n=4)												
Booy 2012 [27]	Australia	Cluster RCT	Residents and staff in aged care facilities during influenza outbreaks	Residents: 652 (255 T, 397 T&P); Staff: 566 (216 T, 350 T&P)	Residents F:M ≈ 1.7–2.4. Staff 9:1- 10.8	81 years	Residents: T: 83.6% T&P: 84.8%. Staff: T: 50%, T&P: 34.8%	Treatment + prophylaxis vs treatment only	Treatment: 75 mg twice daily; Prophylaxis: 75 mg once daily	Treatment: 5 days; Prophylaxis: 10 days	Treatment only (oseltamivir treatment without prophylaxis)	Low statistical power due to only 9 influenza outbreaks; imbalance in outbreak numbers across arms; incomplete consent and treatment coverage; lack of blinding; potential delays in outbreak detection affecting intervention timing
Lepen 2020 [28]	Slovenia	Open-label, RCT	Adult hospitalized patients aged ≥18 years exposed to laboratory-confirmed influenza for up to 24 hours, where immediate separation from index cases was not feasible	222 randomized; 298 exposed patients received oseltamivir prophylaxis, of whom 222 were included in the study	53.6% male	median age 75 years	22/222 (9.9%)	Post-exposure prophylaxis in hospital-exposed adult patients	75 mg once daily, or renal-adjusted equivalent	5 days post-exposure prophylaxis	10-day oseltamivir prophylaxis	Open-label design may introduce reporting bias; exact duration of influenza symptoms in index cases was not recorded; virus sequencing was not performed; transmission from visitors or healthcare personnel could not be excluded in breakthrough cases
van der Sande 2014 [29]	Netherlands	Cluster RCT	Nursing home residents in units where an influenza outbreak was virologically confirmed	By outbreak/unit: 17 outbreaks recruited, 15 randomized according to protocol. By participant: 99 non-ill residents received	Female: 26/36 (72.2%) in oseltamivir group and 39/63 (61.9%) in placebo group	Mean age 83.7 years in oseltamivir group and 79.1 years in placebo group.	36/36 (100%) in oseltamivir group and 51/63 (81.0%) in placebo group	Both treatment of influenza cases and post-exposure prophylaxis in exposed nursing home residents	75 mg once daily for PEP. All of the index patients received therapeutic oseltamivir 75 mg twice daily	PEP: 10 days; therapeutics: 5 days	Placebo	Underpowered because far fewer outbreaks occurred than expected after the 2009 pandemic; logistical delays made timely PEP difficult; some baseline imbalance in age and vaccination; cluster sizes were small; real-world delays in consent

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
				PEP in the 15 protocol-adherent units: 36 in oseltamivir units and 63 in placebo units								and diagnosis may have diluted any effect.
Welliver 2001 [30]	North America and Europe	Cluster RCT	Households with a minimum of 2 and maximum of 8 contacts, recruited within 48 hours of symptom onset in the index case. Contacts were aged ≥12 years. Children <12 years could be index cases but not enrolled as contacts.	377 index cases and 955 eligible household contacts in 371 households; among index cases, 163 had laboratory-confirmed influenza, corresponding to 415 contacts of influenza-positive index cases.	Female: 51% in both placebo and oseltamivir groups among contacts of all index cases; 52% in both groups among contacts of influenza-positive index cases.	Contacts of all index cases: mean age 33.7 years (placebo) and 33.2 years (oseltamivir). Contacts of influenza-positive index cases: 36.1 and 34.3 years, respectively. Mean age of influenza-infected index cases was 27 years.	Contacts of all index cases: 64/462 (13.9%) placebo and 56/493 (11.4%) oseltamivir. Contacts of influenza-positive index cases: 28/206 (14%) placebo and 33/209 (16%) oseltamivir.	Post-exposure prophylaxis in household contacts; index cases were not treated with antivirals.	75 mg once daily	7 days	Placebo	Contacts younger than 12 years were excluded, limiting generalizability to younger children. Some contact cases likely represented infection acquired outside the household; five contacts of influenza-positive index cases developed influenza due to a virus type different from that in the index case. A few participants were already shedding virus at baseline.
RCTs - Oseltamivir vs other antivirals (n=1)												

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
Carrat 2012 [31]	France	Secondary household transmission analysis from a blinded RCT	Adults ≥18 years with influenza confirmed by rapid test presenting within 36 h of symptom onset and their household contacts	267 index patients; 543 household contacts	~48–53% male across treatment arms	Majority 18–44 years	Oseltamivir: 8%, Zanamivir: 5%, Oseltamivir + Zanamivir: 7%	Treatment	Oseltamivir 75 mg orally twice daily; Zanamivir 10 mg inhaled daily	5 days	Oseltamivir monotherapy or Zanamivir monotherapy	Secondary illness not virologically confirmed; possible infections acquired out side household; subgroup analysis for early treatment; loss to follow-up (~14%); no untreated control arm
RCTs - Baloxavir (n=2)												
Ikematsu 2020 [32]	Japan	Placebo-controlled RCT	Laboratory-confirmed influenza index cases and their household contacts	545 index patients, 752 household contacts randomized	Household contacts: male sex 20.6% in baloxavir group and 22.7% in placebo group. Index patients: male sex 53.2%	Household contacts: mean age 33.5 years (baloxavir) and 33.6 years (placebo). Index patients: mean age 11.3 years.	Vaccinated within previous 6 months: 35.0% in baloxavir group and 33.1% in placebo group among household contacts; 31.2% among index patients.	Post-exposure prophylaxis in household contacts	Single, weight-based oral dose of baloxavir or matching placebo.	Single dose	Placebo	follow-up samples were not obtained from index patients, so emergence of resistant variants in index patients could not be determined; PA sequence data were unavailable for several baloxavir-group participants with illness despite prophylaxis; prophylactic efficacy for influenza B could not be assessed because circulation was limited in this single-season trial; time from illness onset in index patients to initiation of prophylaxis in household contacts was not captured
Monto 2025 [33]	Multi-country (15 countries)	Placebo-controlled RCT	Influenza-positive index patients aged 5–64 years enrolled within 48 hours after symptom onset and living with at	1457 index patients randomized; 2681 household contacts enrolled. Primary analysis set included 1092 index patients and	index patients male 45.3% in baloxavir group and 48.9% in placebo group; household contacts male 47.0	mean age of index patients 30.8±15.2 years in baloxavir group and 31.8±15.9 years	Most members of households were mainly unvaccinated; primary analysis of household contacts was restricted to unvaccinate	Treatment of the index case	Single oral dose given within 2 hours after randomization. For patients aged ≥12 years: 40 mg if <80 kg, 80 mg if ≥80 kg. For patients	Single dose	placebo	Authors noted that the first secondary end point was not significant, likely in part because symptomatic transmission incidence in placebo was lower than anticipated, possibly related to Covid-19-era behavioral changes. They also noted that most

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
			least one eligible household contact. Household contacts had to be screened within 24 hours after index-patient randomization, test negative for influenza and SARS-CoV-2 at baseline, and at least one contact in the household had to be unvaccinated within 6 months.	2216 household contacts	% and 44.3%	in placebo group; mean age of household contacts 35.4±18.6 and 35.1±18.3 years, respectively	d, RT-PCR-negative contacts. Exact vaccination percentages were not reported		<12 years: oral suspension 2 mg/kg if <20 kg or 40 mg if ≥20 kg			household members were mainly unvaccinated, so the effect in more vaccinated households remains unclear.
RCTs- Zanamivir (n=3)												
Hayden 2000 [34]	USA, Canada, UK, Finland	Placebo-controlled RCT	Households with an index influenza case and their contacts	337 families randomized, 1158 participants, 321 index cases, 837 contacts	53-57% female	Household contacts, placebo: 26.5 yrs; Zanamivir: 25.9%	14-18%	treatment of index case + prophylaxis for household contacts	Treatment: 10mg twice daily; prophylaxis: 10mg once daily	Treatment: 5 days; Prophylaxis: 10 days	placebo	exclusion of very young children
Kaiser 2000 [35]	Europe and North America	Placebo-controlled RCT	Asymptomatic subjects aged 13–65 years with close contact with index cases of influenza-like illness of no longer	575	39-43% across different groups	Mean age 34 years	Participants with influenza vaccination were excluded.	Post-exposure prophylaxis	Intranasal: 2 sprays of zanamivir 16 mg/mL per nostril (0.1 mL per spray) plus 2 placebo inhalations; inhaled: 2	5 days	placebo	The study did not reach its planned sample size of 840. The placebo event rate was lower than expected at 6%, so the study was underpowered for confirmatory efficacy claims. Authors also suggested that 5 days of

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
			than 4 days' duration						zanamivir inhalations of 5 mg per inhalation plus 2 placebo sprays per nostril; combined arm received both intranasal and inhaled zanamivir.			prophylaxis may not be long enough when influenza is circulating in the community.
Monto 2002 [36]	11 countries across North America, Europe, Australia, New Zealand, and South Africa	Placebo-controlled RCT	Households with 2–5 members, including at least 1 adult and 1 child aged 5–17 years. Once a household member developed influenza-like illness and local influenza activity was confirmed, all other household contacts aged ≥5 years were randomized within 36 hours of symptom onset in the index patient. Index patients were not	487 households randomized; 1291 household contacts randomized. Intent-to-treat: 242 placebo households/ 630 contacts and 245 zanamivir households/ 661 contacts	Contacts: female 53% placebo, 55% zanamivir. Index patients: female 57% placebo-households, 51% zanamivir-households.	Contacts: mean age 27.4 years placebo and 27.2 years zanamivir. Index patients: mean age 19.0 and 18.5 years	Vaccinated prior to randomization: contacts 10% placebo, 11% zanamivir; index patients 5% placebo, 8% zanamivir	Post-exposure prophylaxis in household contacts	10 mg inhaled once daily	10 days	placebo	The paper notes that some infections in contacts may have represented new introductions from the community, not only intra-familial spread. Virus types in index patients and contacts did not match in 16% of placebo-treated and 25% of zanamivir-treated contact households with symptomatic laboratory-confirmed influenza. This means not all apparent household infections can be assumed to be secondary transmission from the index case

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
			treated with influenza antivirals									
Observational studies- Oseltamivir (n=7)												
Dronavalli 2020 [37]	Australia	Cohort study using outbreak surveillance data	Residents of aged care facilities (ACFs) experiencing influenza outbreaks	10,064 residents across 86 outbreaks in 49 ACFs	Not reported	Elderly population (>65 years)	residents: 88 ± 0.18%; staff: 37 ± 24%	Prophylaxis during influenza outbreaks	Not reported	Not reported	Residents not receiving prophylaxis	Observational cohort; confounding by outbreak severity; variation in prescribing practice; facility-level data aggregation
Fujita 2020 [38]	Japan	Retrospective cohort	Inpatients and staff in a long-term care hospital for patients with neurological disabilities	40 inpatients + 41 staff (outbreak cohort)	Not reported	Not reported	0%	Prophylaxis during influenza outbreaks	staff: 75 mg once daily	5 days	Staff without prophylaxis	Small sample, no comparator group for inpatients
Goldstein 2010 [39]	USA	Observational household transmission study	Households with laboratory-confirmed pandemic influenza A(H1N1) index cases and their contacts	362 households initially; 135 households included in primary analysis with full data	Not reported	Not reported	Not reported	Treatment of index cases; some household (n=2) had chemoprophylaxis	Not reported	Not reported	Later (Day ≥3)/no treatment households	Observational design; incomplete case capture; possible selection bias; small number of early treatment households; wide confidence intervals
Gorisek Miksic 2015 [40]	Slovenia	Observational cohort study	Three Slovenian nursing homes	539 residents	57.6% - 80.2% female	79 - 84 years	36% - 56%	1) Oseltamivir for all resident, 2) Oseltamivir for directly exposed residents	75mg PO daily	10 days	No prophylaxis	Observational, did not control for differences between groups, single season, staff info not available for all sites
Shah 2019 [41]	UK	Retrospective cohort study	All residents in CQC (Care Quality Commission)-registered care homes that had a	3498 residents	Not reported	Not reported	Not reported	Oseltamivir prophylaxis during outbreaks. Should be given within 36 or 48h of exposure	Not reported	10 days	No prophylaxis	Observational, no attempt to control for confounding variables, higher ILI-rate with oseltamivir, not confirmed influenza

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
			confirmed influenza outbreak in the Cheshire & Merseyside and Cumbria & Lancashire areas									
Shapiro 2025 [42]	United states	Retrospective cohort	Residential youth summer camp participants, including campers aged about 7–16 years and staff aged 17–57 years, living in communal housing across four camp cohorts over two summers	Cohort 1: 440; Cohort 2: 515; Cohort 3: 488; Cohort 4: 533	Not reported	7-57 yrs	Not reported	Both treatment of influenza cases and post-exposure prophylaxis of exposed close contacts in a camp outbreak setting	Not reported	2022 prophylaxis: 10 days; treatment duration not reported. 2023 prophylaxis: duration not clearly reported	No prophylaxis / delayed protocol / not on prophylaxis, depending on cohort and time period	Authors note they could not determine which prevention strategies were responsible for benefit, since multiple measures were used together; Cohort 3 data were descriptive and limited; rapid antigen testing may have missed early cases; findings may not generalize to other camp settings
Teh 2012 [43]	Australia	Retrospective cohort study	PCR-confirmed influenza A cases (pandemic H1N1 and seasonal influenza A), influenza-negative ILI controls, and their household contacts in metropolitan Melbourne	456 index cases + 1331 household contacts	pH1N1: 50.2% male, 49.8% female; non-H1N1: 62.3% male	Median age: pH1N1 19.7 y ; non-H1N1 19.5 y ; controls 30.3 y	Not reported	Treatment of index cases; prophylaxis of contacts; quarantine measures	Not reported	Not reported	Untreated index cases	No lab confirmation of secondary cases; recall bias; timing of antiviral initiation not assessed; confounding from quarantine and policy changes

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
Observational studies- Oseltamivir vs other antivirals (n=8)												
Best 2024 [44]	USA	Prospective cohort study	Participants >= 18 yrs and filled prescription for baloxavir or oseltamivir at CVS within 2 days of symptom onset	286 index cases	187 (65.6%) females	45.5 +/- 15.3	Not reported	Baloxavir or oseltamivir (Treatment of index cases to reduce household transmission)	Not reported	Not reported	Oseltamivir	Observational, flu diagnosed via self-reported survey, voluntary participation
Higa 2012 [45]	Japan	Retrospective cohort	Hospitalized patients and healthcare workers with close contact to influenza index cases in an acute care university hospital	202 index cases; 762 close contacts	Not reported	Not reported	HCW : 93.6%–94.8%; inpatients: not ascertained	oseltamivir or zanamivir (Post-exposure chemoprophylaxis after close contact with index cases)	Adults with normal renal function: oseltamivir 75 mg/day; hemodialysis patients: oseltamivir 75 mg single dose; pediatric patients: oseltamivir 2 mg/kg/day; some patients received zanamivir 10 mg once daily	Oseltamivir 5–7 days; zanamivir 10 days	No chemoprophylaxis	Retrospective design; possible selection bias; case identification partly based on self-report; some diagnoses based on clinical presentation rather than lab confirmation; could not compare oseltamivir vs zanamivir because zanamivir numbers were small
Hirotsu 2019 [46]	Japan	Prospective observational-single center	index patients with confirmed influenza and their household members who were treated with an NAI	1807 index patients;~ 3400 total index + secondary infection patients from about 1200 families	28.6-50.6% across different groups	mean age ranges from 6.7- 20.4 yrs across the groups	index pts: 40%–59% vaccinated in the same season	Oseltamivir, zanamivir, laninamivir, peramivir (Treatment of index patients; no prophylactic NAI treatment of family members)	Per package insert for each product; exact doses not reported	Per package insert; exact treatment duration not reported	Comparisons among the four NAIs and against untreated patients	Observational, non-randomized design; single clinic; asymptomatic infections not captured; no adherence analysis; smaller numbers for some subtypes/groups

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
Ikematsu 2024 [47]	Japan	Post hoc analysis of the BLOCKSTONE trial; non-randomized comparison within a randomized prophylaxis trial.	Laboratory-confirmed influenza index cases and their household contacts from the BLOCKSTONE trial who received placebo or no antiviral prophylaxis, plus additional household members captured by questionnaire	185 index cases and 410 household contacts included in this analysis	Index cases: male 54.3%; household contact sex incompletely reported	Not reported as a single mean; index cases categorized by age: <12, 12–64, ≥65	Index cases vaccinated within previous 6 months: 34.1% overall; BXM 32.8%, OTV 36.2%; Household contacts - BXM: 17.1% vaccinated (51.4% missing). OTV 17.6% (50.3% missing)	Treatment of index cases to assess effect on household secondary transmission; no BXM prophylaxis allowed in analyzed households	Not reported	Not reported	Oseltamivir-treated index cases	Index treatment not randomized; age imbalance between BXM and OTV groups; possible residual confounding; demographic data for questionnaire-only contacts incomplete; asymptomatic infections not determined; some contacts may already have been infected at enrollment because RT-PCR was not done at enrollment
Komiya 2010 [48]	Japan	Observational household transmission study based on active surveillance during an outbreak	Households of confirmed pandemic influenza A(H1N1) cases in Osaka; index case defined as first person in household to develop symptoms; household contact defined as anyone staying overnight at least 1 night within 1 day before or 7 days after symptom	124 eligible households; 379 household contacts; 124 index cases	Index cases: male 68%; household contacts: male 46%	Median age: index cases 16 years (range 9–53); household contacts 43 years (range 0–82; no data for 4)	Not reported	Oseltamivir or zanamivir or both (post-exposure prophylaxis in household contacts; almost all index cases also treated with antivirals)	PEP: oseltamivir 75 mg/day for adults or 2 mg/kg/day for children, or zanamivir 10 mg/day	7-10 days	No PEP	Authors note that nearly half of household contacts received PEP after 48 hours from onset in the index case, which may have overestimated protective efficacy; reasons for not taking medication were unclear; one infected contact on PEP had an oseltamivir-resistant strain

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
			onset in the index case									
Nakano 2014 [49]	Japan	Retrospective cohort / health-insurance claims database study using JMDC data	Families in the JMDC database in which an index case was prescribed laninamivir, oseltamivir, or zanamivir; the date when the index case was first prescribed one of these drugs was defined as Day 1; household secondary infection was assumed if another family member was prescribed laninamivir, oseltamivir, zanamivir, or peramivir during Days 3–8. Hospitalized patients and families with missing dispensing dates, no other family members, index cases prescribed	24,726 families total: 6,362 laninamivir, 12,142 oseltamivir, 6,222 zanamivir.	Index cases: female 45.0% / 44.7% / 48.6%; male 55.0% / 55.3% / 51.4% in laninamivir / oseltamivir / zanamivir groups. Family members overall were about 50% women in each drug group.	ndex cases: mean age 19.8 ± 14.37 years (laninamivir), 14.5 ± 15.44 (oseltamivir), 14.4 ± 9.79 (zanamivir). Average age of family members: 27.9, 25.7, and 29.4 years, respectively.	Not reported	Laninamivir, oseltamivir, zanamivir, Treatment of the index case; household secondary infection then assessed in family members	Not reported directly as mg dose-oseltamivir twice daily, zanamivir twice daily, laninamivir as a single inhalation.	oseltamivir 5 days, zanamivir 5 days, laninamivir single dose.	Oseltamivir and zanamivir active comparators	Authors noted several limitations: if both husband and wife were working, they could be counted as two households, likely underestimating household infection; some families sharing a family ID may not have lived together, which could overestimate household infection; some antiviral prescriptions may have been for prevention rather than treatment; and the JMDC database underrepresents elderly retired people, limiting generalizability

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
			≥2 antivirals, or ≥2 initially infected patients in the same household were excluded.									
Nishiura 2011 [50]	Japan	Retrospective household survey	1547 eligible households with 1547 index cases and 4609 household contacts; households had at least one symptomatic H1N1-2009 case, contacts had to share the household with the index case for at least 1 of the 7 days after illness onset, and both index cases and contacts were unvaccinated or vaccinated within 14 days of illness onset in the index case	1547 households; 1547 index cases; 4609 household contacts.	Male: 798/1547 (51.6%) index cases; 2196/4609 (47.6%) contacts.	Mean age: index cases 16.3 ± 12.3 years; household contacts 33.6 ± 18.8 years	By design, index cases and household contacts were unvaccinated or vaccinated within 14 days of illness onset in the index case	Oseltamivir; zanamivir (Both treatment of index cases and post-exposure prophylaxis of household contacts)	Not reported	Not reported	>48 h/no treatment or no prophylaxis	Non-random sample; case definition relied on symptoms and alleged medical diagnosis; confounding likely because antiviral use was age patterned (Zanamivir was almost exclusively used for teenagers (100% and 96.5% among the total of cases with zanamivir prophylaxis and treatment, respectively); no adjustment for co-primary cases; prophylaxis analyses were underpowered; no significant prophylaxis effect was shown.
Shinjoh 2012 [51]	Japan	Retrospective cohort of	Pediatric ward contacts exposed to	81 contacts overall; 80 with known follow-up for	Not reported for contacts	mean age of non-PEP contacts	Only partially collected- Among 22	Oseltamivir; zanamivir (Post-exposure prop	Oseltamivir 2 mg/kg/dose once daily	7-10 days	No PEP	Non-randomized design; vaccination status incompletely known;

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
		nosocomial influenza exposures in pediatric wards	index influenza cases in hospital; contacts were defined as patients with direct or close contact from 1 day before the index case developed fever >38°C. Secondary infection was defined as influenza developing within 4 days after exposure to the index case or affected contact.	PEP comparison because 1 contact was lost to follow-up. There were 20 nosocomial introductions of influenza.		104 ± 91 months and of PEP contacts 110 ± 79 months	contacts with known vaccine history, none had received influenza vaccine: 4/17 in non-PEP and 18/63 in PEP.	hylaxis in hospital-exposed pediatric contacts)	(max 75 mg) or zanamivir 10 mg once daily.			diagnoses were based mainly on rapid diagnostic testing rather than routine PCR or culture; some no-PEP contacts did not receive prophylaxis because PEP was not routine in early seasons, they were already discharged, or contact was judged minimal.
Observational studies- Baloxavir marboxil vs no active treatment or vs other antivirals (n=3)												
Kojima 2025 [52]	United states	Outbreak investigation/ brief report	College sports team student-athletes exposed during an influenza A(H3) outbreak; 116 student-athletes attended in-person team meetings and sporting events; 72 were asymptomat	116 student-athletes total; 38 influenza cases; 72 asymptomatic contacts	Among influenza cases, all 38 were male	Median age among influenza cases: 20 years (IQR 19–22); age for contacts not separately reported	Among influenza cases, 1/38 (3%) had received 2024 influenza vaccine; among asymptomatic contacts, 9/72 (13%) had been vaccinated prior to the outbreak; among those who	Post-exposure prophylaxis in asymptomatic contacts during an outbreak	Not reported	Single dose	No baloxavir PEP	Observational outbreak report with no randomization; small sample; comparator was self-selected non-PEP group; exact dose and follow-up duration not reported; PEP was introduced together with nonpharmaceutical interventions, so the independent effect of baloxavir cannot be isolated

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
			ic contacts eligible for post-exposure prophylaxis				received PEP, 6/40 (15%) had been vaccinated					
Komeda 2021 [53]	Japan	Retrospective cohort study with active comparators using the JMDC Claims Database	Families in which the first family member with an outpatient influenza diagnosis during the 2018–2019 season was identified as the index patient (IP); families were grouped according to the anti-influenza drug dispensed to the IP on day 1	208,225 families in the primary analysis population	Index patient sex reported only: male 56%	Index patient sex reported only: common age group: 1-64 yrs (37.8%)	Not reported	Treatment of the index patient; household transmission then assessed among non-index family members	Not reported	Not reported	Oseltamivir (primary control); also zanamivir and laninamivir as active comparators	Family membership was inferred from shared insurance and may not reflect true co-residence; residual confounding likely; important factors such as symptom severity, body temperature, and time from onset to visit were unavailable; pre-existing infection in non-index family members could not be excluded; some prescriptions may have been for prophylaxis rather than treatment; results are based on a single influenza season
Umemura 2020 [54]	Japan	Retrospective, single-center cohort	Index patients with confirmed influenza A treated with baloxavir or oseltamivir, and their household members; household members who had already received prophylactic influenza	169 index patients and 418 household members total.	Index patients: 92/169 male (54.4%)-sex of household members not reported	Median age of index patients: 27.0 years; householder members: most common age grp: 20-64 yrs (~58%)	Index patients vaccinated in same season: 12/49 (24.5%) in baloxavir group and 46/120 (38.3%) in oseltamivir group. Household members vaccinated in same season:	Treatment of the index case; household transmission then assessed among household members	Adults: baloxavir 40 mg once, or 80 mg once if >80 kg; children: 20 mg once if 20–40 kg or 40 mg once if >40 kg.	Baloxavir: single dose	Oseltamivir: adults 75 mg twice daily; children 2 mg/kg twice daily for 5 days	Retrospective design; single-center; one-season study; data partly obtained by telephone; influenza A subtypes, antiviral susceptibility, and viral load were not confirmed.

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
			treatment were excluded. Household transmission was defined as the same influenza type diagnosed in household members 1–7 days after symptom onset in the index case				30/122 (24.6%) and 99/296 (33.4%), respectively					
Mathematical Modelling Studies (n=5)												
Asher 2023 [24]	N/A- model parameterization focused on a simulated Caucasian population and comparisons to BLOCKSTONE data from Japan	Modeling study using a within-host PK–VK model plus three epidemiological transmission models (natural-scale, log-scale, dose–response)	1000 simulated individuals per treatment group for viral titer/infectiousness simulations; additionally, 10,000 simulated household transmission trials with about 480 patients per arm including drop-out for secondary-case-rate analyses	N/A- model informed by prior phase II/III baloxavir trials and compared against BLOCKSTONE	1000 simulated individuals per arm for transmission-mitigation modeling; ~480 per arm in simulated household trials; 10,000 trial simulations total	Not reported	Not reported	Baloxavir marboxil; oseltamivir (Treatment of the index case)	Simulated baloxavir dose based on body weight: 40 mg if <80 kg, 80 mg if ≥80 kg; Oseltamivit: 75mg twice a day	Baloxavir: single dose; Oseltamivir: 5 days	Placebo / no antiviral; and oseltamivir served as comparator to baloxavir in some analyses	The model assumes a functional relationship between nasal viral shedding and infectiousness, which remains uncertain; simulated patients were Caucasian whereas BLOCKSTONE participants were Japanese; the model needs further validation across age groups, influenza B, and Asian populations; oseltamivir PK data were unavailable so its effect was modeled using an inhibition factor.
Doyle 2006 [22]	France	Monto Carlo simulation model of	Simulated population of France métropole (59.6	Population size based on 1 January 2003 estimates.	Simulated national population of 59.6 million	Not reported	Not reported	Oseltamivir (Therapeutic treatment, post-exposure prophylaxis in	Treatment: 10 doses/person. Post-exposure	Therapeutic treatment: 5 days. Post-exposure prophylaxis:	No intervention; influenza vaccination (2 doses per	strong assumptions about attack rate, hospitalizations, deaths, effectiveness, adherence, coverage,

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
		pandemic influenza interventions	million), stratified into 3 age groups (0–19, 20–64, ≥65 years) and by high-risk vs average risk status; separate priority population of essential workers also modeled	Pandemic assumed to have 2 waves of 10 weeks each				high-risk groups, and seasonal prophylaxis in priority workers)	prophylaxis: 7 doses/person per exposure episode. Seasonal prophylaxis: 1 dose/day. Cost assumed €1 per oseltamivir dose	7 days per episode; high-risk population assumed exposed 3 times per wave. Seasonal prophylaxis: throughout the pandemic, i.e., 20 weeks	person); alternative antiviral strategies	and exposure frequency; effectiveness parameters were based on interpandemic data and expert opinion; impact of non-pharmaceutical interventions and changing pandemic dynamics not modeled
Du 2020 [26]	USA	hierarchical mathematical modelling study linking within-host viral load dynamics from clinical trial data to between-host influenza transmission	The stochastic simulations assumed a population of 10,000 individuals. The within-host component was fitted to clinical trial data from 1014 influenza virus-infected patients treated with baloxavir, oseltamivir, or placebo.	Influenza seasons 2016–2017, 2017–2018, and 2018–2019 were used for model fitting; the main population-level projections emphasized the 2017–2018 US influenza epidemic season.	10,000 individuals per stochastic simulation for the transmission model; 1014 influenza virus-infected patients in the clinical trial data used to fit the within-host model.	Not reported	Not reported	Baloxavir and oseltamivir (Antiviral treatment of infected cases; scenarios examined scaling up the proportion of cases treated and changing timing of treatment initiation after symptom onset. Treatment was generally initiated within 48 h of symptom onset, with additional analyses for 0–24 h and 24–48 h windows.)	Baloxavir: single dose mentioned in background/ discussion. Oseltamivir: multiple treatments over 5 consecutive days mentioned in background. Exact dose was not reported	Baloxavir: single-dose treatment. Oseltamivir: 5 consecutive days.	No drug / placebo / untreated baseline scenario	treatment efficacy and timing were assumed from clinical trial data and applied to the general population; possible bias by disease severity or timing of treatment was not modelled; no age- or risk-group heterogeneity in viral kinetics/treatment efficacy; no modelling of baloxavir-resistant viruses; infectiousness assumed to be logarithmically related to viral load; contact pattern changes during illness were not considered
Kelso 2010 [25]	Australia	Simulation using census, state	Simulated epidemic in a community	Community of approximate	Not Reported	Not Reported	Not Reported	1) Treatment only; 2) Treatment + household	Treatment: two doses daily; prophylaxis:	Treatment 5 days; prophylaxis 10 days	No intervention / baseline epidemic;	Did not model antiviral resistance; did not model reduction/prevention of

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
		and local government data to model the impact of 3 antiviral intervention strategies (treatment only; treatment + household prophylaxis; and treatment + household prophylaxis + workplace or school class contacts prophylaxis) with delayed diagnosis (ranging from immediate [<6 hours] to 48 hours after symptoms	of 30,000 individuals based on the chararcteristics of the 2009 A/H1N1 pandemic	ly 30,000 individuals				prophylaxis; 3) Treatment + household prophylaxis + extended prophylaxis of school/work contacts; each also simulated with and without school closure	one dose daily		also comparisons across alternative antiviral strategies	serious adverse clinical outcomes from antivirals; simulated population reflects an industrialized-country setting and may not generalize elsewhere; assumed pandemic strain susceptible to neuraminidase inhibitors; infectiousness not modelled as age-dependent; antiviral effectiveness in reducing infectivity initially assumed constant regardless of treatment timing

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
		appeared) and the ratio of diagnosed to undiagnosed symptomatic cases (diagnosis coverage ranging from 10% to 100%); simulated all antiviral interventions with and without school closure										
Kommandantvold 2024 [21]	UK	Modeling study: linked susceptible-exposed-infected-recovered (SEIR) transmission model and cost-effectiveness model (CEM)	Simulated UK population, including otherwise healthy and high-risk individuals; results reported at the population level per 10,000 individuals at risk of infection	One influenza season; no specific year considered for the SEIR model	Not an empirical sample; model population of 10,000 individuals, with one initially infected at time zero	Not reported	Not reported	Baloxavir marboxil (Treatment of symptomatic influenza in modeled populations; comparisons with oseltamivir treatment and no antiviral treatment)	Baloxavir described as an oral, single-dose agent, but no study-specific administered dose because this is a model	Not applicable as an administered intervention; model used infectious period assumptions of 2.3 days for baloxavir-treated, 3.7 days for oseltamivir-treated, and 4.5 days for untreated individuals	Oseltamivir; no antiviral treatment	attack rates were predicted from clinical-trial viral shedding data and literature rather than direct household transmission data; the model did not account for timing of infectiousness at the population level or time-varying infectiousness at the individual level; extreme R0 values affected model behavior; public health interventions such as

Study	Country	Study design	Study population	Total sample size	Sex	Mean age	Vaccinated (%)	Intervention type	Dose	Duration	Comparator	Study limitations
												masking/lockdowns were not included; treatment-emergent resistance assumptions were uncertain; the CEM assumed that only 49.5% of antiviral-treated symptomatic individuals had true influenza, effectively doubling antiviral treatment costs; decision tree structure allowed only one complication at a time
Miyazawa 2022 [23]	Japan	Retrospective cohort study with simulation modeling using a health insurance claims database and intra-familial transmission model	Families in the JMDC Claims Database during the 2018–2019 influenza season; the first family member diagnosed with influenza was defined as the index case (IC); families were grouped according to whether the IC received baloxavir marboxil (BXM) or oseltamivir (OTV) on day 1	Data retrieved 1 October 2018 to 30 April 2019; IC day 1 had to occur between 1 October 2018 and 23 April 2019	146,676 families in primary analysis population	Index cases only: male 57.2% in BXM group and 55.2% in OTV group	Index patient sex reported only: common age group: 19-64 yrs (38.4%)	Baloxavir marboxil (Treatment of the index case)	Not reported	Not reported	Oseltamivir	Family code may not reflect true co-residence; external exposure could still occur; pre-existing infection in non-index family members and prophylaxis among non-index family members could not be excluded; only one season was studied; type B cases were limited; viral subtype and resistance information were unavailable; model assumptions included asymptomatic shedding period b = 0

Abbreviations: ACFs = Aged Care Facilities; BXM = Baloxavir Marboxil; CEM = Cost-Effectiveness Model; CQC = Care Quality Commission; F:M = Female-to-Male Ratio; HCW = Healthcare Worker; IC = Index Case; ILI = Influenza-Like Illness; IQR = Interquartile Range; JMDC = Japan Medical Data Center; N/A = Not Applicable / Not Available; NAI = Neuraminidase Inhibitor; NRS = Non-Randomized Studies; OTV = Oseltamivir; PA = Polymerase Acidic (protein/gene); PCR = Polymerase Chain Reaction; PEP = Post-Exposure Prophylaxis; pH1N1 = Pandemic H1N1 Influenza; PK = Pharmacokinetic; PO = By Mouth (per os); R0 = Basic Reproduction Number; RCT = Randomized Controlled Trial; RT-PCR = Reverse Transcription Polymerase Chain Reaction; SARS-CoV-2 = Severe Acute Respiratory Syndrome Coronavirus 2; SEIR = Susceptible-Exposed-Infected-Recovered; T = Treatment; T&P = Treatment and Prophylaxis; UK = United Kingdom; USA = United States of America; VK = Viral Kinetic / Viral Kinetics; yrs = Years

Table 2: Systematic Review Characteristics (n=17)

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
Beck 2012 [55]	UK	Rapid systematic review	Seasonal and pandemic influenza studies evaluating neuraminidase inhibitors for treatment and prophylaxis, including household post-exposure prophylaxis and long-term prophylaxis	Evidence published up to June 2010	Not clearly reported as a single total	Systematic reviews, randomized controlled trials, and observational studies	Oseltamivir, zanamivir	Treatment, long-term prophylaxis, household post-exposure prophylaxis	Placebo, no prophylaxis, or no treatment, depending on the included studies	Zanamivir household PEP: 81% protective efficacy, RR 0.19 (95% CI 0.11–0.33). Oseltamivir household PEP: 81% protective efficacy in contacts of all index cases, RR 0.19 (95% CI 0.08–0.45), and 79% protective efficacy in contacts of influenza-positive index cases, RR 0.21 (95% CI 0.08–0.58).	Rapid review methods, not all pooled estimates were based on the same level of evidence; raw trial-level data were not fully presented, Pandemic-period data were limited and did not substantially expand the prophylaxis evidence base.
Boikos 2017 [56]	Canada	Systematic review	Studies of pandemic and/or novel/variant influenza evaluating neuraminidase inhibitor safety and effectiveness for treatment, prophylaxis, or outbreak control in patients of all ages and multiple settings/populations	Searches covered studies published from 1 April 2009 to 31 October 2015	165 studies	Observational studies (94%) and RCTs	Oseltamivir, zanamivir, peramivir, lanina mivir	Treatment, prophylaxis, and outbreak control	Another antiviral regimen/class, standard of care, placebo, or no treatment/no prophylaxis	NI prophylaxis or outbreak control was judged likely effective in reducing secondary transmission. The review concluded that NI pre- or post-exposure prophylaxis is likely effective in reducing secondary transmission in general populations, but the evidence base was largely observational and heterogeneous	Most included studies were observational, statistically underpowered, and at high risk of bias/confounding; lack of adjustment for confounding was a major problem. The authors did not meta-analyze results. Study quality was generally low.
Doll 2017 [57]	Canada	Systematic review of systematic reviews and/or meta-analyses	Systematic reviews/meta-analyses of randomized and/or observational studies examining neuraminidase inhibitor effectiveness or safety for influenza treatment or prophylaxis across any population or	Databases searched from 1 January 1995 to 10 November 2015	27 SR/MAs	Among 27 included SR/MAs, 2 were SR only, 9 MA only, and 16 SR/MA; among 25 MAs, 19 examined RCTs only, 5 examined RCTs plus	Oseltamivir, zanamivir, peramivir, lanina mivir were eligible, but the authors state they were unable to find pooled effect measures for peramivir or laninamivir; the review findings mainly reflect	Treatment, prophylaxis, and outbreak control	Another antiviral regimen/class, standard of care, placebo, or no treatment/no prophylaxis	For prophylaxis, oseltamivir and zanamivir consistently lowered the odds/risk of symptomatic secondary transmission, with OR /RR ranges of about 0.1–0.5. The review concluded that oseltamivir or zanamivir prophylaxis are likely effective at	Major overlap across reviews: of 492 primary studies, only 312 were unique, and on average 74.8% of primary studies in each SR/MA overlapped with at least one other SR/MA. About 37% of included SR/MAs were judged at serious risk of bias by eOQAQ

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
			setting; primary prophylaxis outcome was secondary transmission of symptomatic and asymptomatic influenza			observational studies, and 1 examined observational studies only	oseltamivir and zanamivir			reducing secondary symptomatic influenza transmission, but not asymptomatic transmission.	
Jackson 2011 [58]	UK	Systematic review with narrative synthesis and random-effects meta-analysis where appropriate	Children, adults, and older people, each subdivided into healthy individuals or those at risk of influenza complications; review covered two prophylactic settings: seasonal prophylaxis and post-exposure prophylaxis	Searches conducted in August 2007 and updated in August 2009; no publication date restrictions	18 RCTs reported in 22 publications: 5 oseltamivir RCTs, 8 zanamivir RCTs, and 5 amantadine RCTs	RCTs; systematic reviews were searched for identification purposes,	Oseltamivir, zanamivir, amantadine	Seasonal prophylaxis, post-exposure prophylaxis, and outbreak control	Placebo, no treatment, expectant treatment after symptom onset, or active comparator depending on trial	Oseltamivir: effective for seasonal prophylaxis in healthy adults and at-risk elderly subjects, and for post-exposure prophylaxis in mixed households. For household post-exposure prophylaxis, pooled RR for symptomatic laboratory-confirmed influenza (SLCI) was 0.19 (95% CI 0.08–0.45). Zanamivir: effective for seasonal prophylaxis in healthy adults and at-risk adults/adolescents, and for post-exposure prophylaxis in mixed households; pooled RR for household post-exposure prophylaxis was 0.21 (95% CI 0.13–0.33).	English-language full text restriction at inclusion stage; no included studies evaluated prophylaxis against pandemic strains; evidence gaps remained for several subgroups and settings, especially elderly subjects in post-exposure settings and some child/adult risk groups; adverse-event reporting varied and limited pooling; some included trials had incomplete reporting of randomization, allocation concealment, or blinding.
Jefferson 2009 [59]	Italy	Clinical Evidence systematic review / evidence synthesis with GRADE assessment	People with influenza or influenza-like illness and no major comorbid conditions; review covered prevention and treatment questions, including antiviral chemoprophylaxis and antiviral treatment for	Searches covered Medline 1966 to June 2008, Embase 1980 to June 2008, and Cochrane databases to 2008 Issue 2;	21 systematic reviews, RCTs, or observational studies	Mixed evidence base: systematic reviews and RCTs in any language were eligible; non-randomized evidence was included only when it was	Oseltamivir, zanamivir, amantadine, rimantadine	Antiviral chemoprophylaxis and antiviral treatment	Placebo, no intervention, or another treatment depending on the included studies	For chemoprophylaxis, the review concluded that oseltamivir is more effective than placebo at preventing symptoms of influenza A and B, but not influenza-like illness, and that post-exposure prophylaxis with oseltamivir may be more effective at	limited evidence for pandemics, lack of direct evidence in some populations/settings, incomplete reporting in some underlying studies, and that routine antiviral use when influenza circulation is unknown is unlikely to be beneficial.

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
			seasonal influenza, with some discussion of pandemic relevance			within an included systematic review				reducing symptomatic influenza in households and contacts. It summarized two household RCTs: one found reductions of 59% for households and 68% for individual contacts versus placebo/expectant treatment; the other found 89% reduction in symptomatic influenza in individuals and 84% in households versus placebo. For zanamivir, the review concluded it was more effective than placebo at preventing symptoms and that post-exposure prophylaxis reduced symptomatic influenza in households and contacts; one household RCT showed 81% reduction in households and 82% in individuals, and another showed 79% reduction in contacts.	
Jefferson 2014 a [8]	UK	Cochrane systematic review of clinical study reports and regulatory comments from randomized,	Adults and children with confirmed or suspected exposure to naturally occurring influenza; previously healthy populations, including some with chronic illness such	Trial registries, electronic databases, and regulatory archives searched to 22 July 2013; review also included	53 trials included in Stage 1; 46 trials included in Stage 2 formal analysis, comprising 20 oseltamivir trials and 26 zanamivir trials	RCTs only	Oseltamivir and zanamivir	Treatment, prophylaxis, and post-exposure prophylaxis	Placebo	For prophylaxis, both agents reduced the risk of symptomatic influenza at the individual and household levels. - Oseltamivir reduced symptomatic influenza in	Major limitations included high risk of bias in many trials, incomplete reporting, selective reporting, missing protocols/statistical analysis plans, possible active placebos, poor or

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
		placebo-controlled trials	as asthma/diabetes/hypertension, but excluding major immune-compromising illness; review covered treatment, prophylaxis, and post-exposure prophylaxis	manufacturer clinical study reports and regulatory files						individuals (RR 0.45, 95% CI 0.30–0.67) and households (RR 0.20, 95% CI 0.09–0.44). - Zanamivir showed similar effects, with reductions in individuals (RR 0.39, 95% CI 0.22–0.70) and households (RR 0.33, 95% CI 0.18–0.58). In contrast, neither drug demonstrated a significant effect on asymptomatic influenza: - Oseltamivir: individuals (RR 0.78, 95% CI 0.49–1.24); households (RR 1.14, 95% CI 0.39–3.33). - Zanamivir: individuals (RR 0.97, 95% CI 0.76–1.24); households (RR 0.88, 95% CI 0.65–1.20).	absent definitions for complications, and extensive manufacturer sponsorship. The review deliberately excluded journal articles as primary data sources because of publication/reporting bias and relied instead on clinical study reports and regulatory data.
Jefferson 2014 b [60]	UK	Systematic review of clinical study reports and regulatory information from randomized placebo-controlled trials	Adults and children with confirmed or suspected exposure to naturally occurring influenza; previously healthy populations, including some with chronic illness such as asthma/diabetes/hypertension, but excluding major immune-compromising illness; review covered treatment, prophylaxis, and post-exposure prophylaxis	Trial registries, electronic databases, and regulatory archives searched to 22 July 2013; review also included manufacturer clinical study reports and regulatory files	20 trials in stage 2 formal analysis; 23 trials in stage 1. Of the 20 stage-2 trials, 5 were prophylaxis trials.	RCTs only- all were based on full Roche clinical study reports/regulatory data rather than journal articles.	Oseltamivir only.	Treatment, prophylaxis, and post-exposure prophylaxis	Placebo	In prophylaxis trials, oseltamivir reduced symptomatic influenza in individuals by 55% (RR 0.45, 95% CI 0.30–0.67) and in households by 80% (RR 0.20, 95% CI 0.09–0.44) based on one household study. There was no significant effect on asymptomatic influenza in individuals (RR 0.78, 95% CI 0.49–1.24) or households (RR 1.14, 95% CI 0.39–3.33).	Major limitations included high risk of bias, missing protocols and statistical analysis plans, incomplete reporting, selective reporting, weak outcome definitions, and inability to assess transmission properly because the key household PEP trial left index cases untreated and only measured viral shedding in symptomatic participants. The review also highlighted problems with study design, reporting bias,

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
											and manufacturer sponsorship.
Jefferson 2009 [61] (Update of Jefferson 2006 Cochrane Systematic Review [62])	Italy	Systematic review and meta-analysis	Otherwise healthy adults exposed to naturally occurring influenza; review addressed prophylaxis, post-exposure prophylaxis, treatment, transmission, complications, and adverse effects	Updated searches of Cochrane CENTRAL (2009 issue 2), MEDLINE (1950–Aug 2009), EMBASE (1980–Aug 2009), plus post-marketing pharmacovigilance and comparative safety sources	20 trials included in 19 publications; specifically 4 prophylaxis trials, 12 treatment trials, and 4 post-exposure prophylaxis trials	RCTs only	Oseltamivir and zanamivir	Treatment, prophylaxis, and post-exposure prophylaxis	Placebo	Neuraminidase inhibitors had no effect on influenza-like illness or asymptomatic influenza in prophylaxis trials. For symptomatic laboratory-confirmed influenza, prophylaxis was effective: oseltamivir 75 mg daily RR 0.39 (95% CI 0.18–0.85), oseltamivir 150 mg daily RR 0.27 (95% CI 0.11–0.67), and zanamivir 10 mg daily RR 0.38 (95% CI 0.17–0.85). In post-exposure prophylaxis, oseltamivir showed 58% and 84% efficacy in two household trials, and zanamivir showed similar household protection.	Many trials were at risk of bias because of poor reporting, missing data, and inability to fully scrutinize unpublished material. Eight unpublished studies on complications were excluded as ineligible/inaccessible. Estimates based on hazard ratios were approximate because many hazard ratios were not directly reported.
Law 2025 [63]	Canada	Rapid systematic review	Nonhospitalized individuals exposed to influenza A or B	January 1, 2020 - January 8, 2025	2 SR reviews (21 and 33 RCTs in each)	Systematic reviews of RCTs	Zanamivir, oseltamivir, baloxavir	1st SR: 2 RCTs compared Zanamivir to rimantadine and placebo (3 arms), 1 RCT compared Zanamivir to placebo, 3 RCTs compared Oseltamivir to placebo. 2nd SR: 4 RCTs of Zanamivir, 1 RCT of Oseltamivir, 1 RCT of Baloxavir	Rimantadine, placebo	Lab-confirmed influenza - Oseltamivir vs placebo: 1) OR 0.59 (0.32-1.08), 2) RR 0.58 (0.39-0.86) - zanamivir vs placebo: RR 0.57 (0.43-0.76) - Baloxavir vs placebo: RR 0.50 (0.24-1.05). Lab-confirmed symptomatic influenza - oseltamivir vs placebo: 1) OR 0.39 (0.16-0.94), 2) RR 0.40 (0.26-0.62) - zanamivir vs placebo: 1) OR 0.66	SRs did not focus entirely on PEP. SRs published in 2024 but primary studies were not recent. None contained info on peramavir

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
										(0.33-1.29) 2) RR 0.35 (0.25-0.5) - baloxavir: RR 0.43 (0.23-0.79)	
Okoli 2014 [64]	UK	Systematic review and meta-analysis of RCTs	People of any age with laboratory-confirmed influenza, influenza-like illness, or close contact exposure; focused on seasonal and pandemic influenza transmission in community or household-type settings, including individual and household transmission studies	Searches covered literature in any language up to December 2012	17 studies total: 9 RCTs and 8 observational studies	RCTs, cohort and other observational designs	Oseltamivir, zanamivir, lanina mivir were eligible, but included studies involved oseltamivir and zanamivir only	Prophylaxis (pre- and post-exposure), treatment of index case alone, and rapid containment–style use	Placebo, no therapy, sham antivirals, or no comparator depending on study design	For oseltamivir, pooled individual protection was OR 0.11 (95% CI 0.06–0.20) across 8 studies, and pooled household protection for seasonal influenza was OR 0.23 (95% CI 0.09–0.59). For zanamivir, pooled individual protection was OR 0.23 (95% CI 0.16–0.35) and pooled household protection was OR 0.18 (95% CI 0.10–0.31).	Considerable heterogeneity across studies in population, influenza type, intervention strategy, dose, duration, vaccination status, and setting. Many RCTs were at high or unclear risk of bias in key domains, all RCTs were manufacturer-sponsored, and observational studies were susceptible to confounding and effect modification. Evidence beyond household settings was limited, and no direct population-level community transmission data were identified
Rainwater-Lovett 2014 [65]	USA	Systematic review and meta-analysis	Elderly adults in long-term care facilities (LTCFs) experiencing influenza outbreaks	Up to September 2013	37 articles describing 60 influenza outbreaks	Primarily observational outbreak reports; includes some randomized and non-randomized studies	Adamantanes (amantadine, rimantadine); neuraminidase inhibitors (oseltamivir, zanamivir)	Chemoprophylaxis, vaccination, and non-pharmaceutical interventions (NPIs) such as PPE, cohorting, hand hygiene, staff furlough	Facilities with no interventions or different combinations of interventions	neuraminidase inhibitors did not show a statistically significant effect. Attack rates by antiviral (unadjusted): Zanamivir: 17% (95% CI: 7–34); Oseltamivir: 29% (95% CI: 25–42); P>0.05	Predominantly observational data with heterogeneity in outbreak definitions, interventions, and reporting. Limited ability to isolate individual intervention effects. Lack of standardized reporting and limited high-quality RCT evidence for NPIs

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
Shun-Shin 2009 [66]	UK	Systematic review and meta-analysis of RCTs	Community-based children aged ≤12 years with seasonal influenza for treatment studies, and paediatric household contacts of index cases for post-exposure prophylaxis studies	Medline 1966 to 1 July 2009, Embase 1980 to 28 June 2009, plus trial registries, manufacturers, and authors	7 RCTs total: 4 treatment trials and 3 post-exposure prophylaxis trials	RCTs only	Oseltamivir and zanamivir	Treatment of influenza and household post-exposure prophylaxis	Placebo in treatment and prophylaxis RCTs; in one zanamivir household trial the index case received no study drug, while in the oseltamivir household trial all index cases received active drug	Household PEP with zanamivir or oseltamivir reduced the risk of confirmed symptomatic influenza in paediatric contacts by 8% (risk difference −0.08, 95% CI −0.12 to −0.05), corresponding to a number needed to treat of 13 to prevent one additional child case.	Only 7 trials were included, study quality was generally moderate, reporting was inconsistent, and pooling was limited for several outcomes. Most data were from seasonal influenza, not the then-current pandemic strain. Few data were available for children with comorbidities, none for children under 1 year, and trials were not powered for serious complications such as pneumonia or hospitalization.
Tappenden 2009 [67]	UK	Systematic review and economic evaluation	Seasonal and post-exposure prophylaxis: adults and children exposed to influenza, adults and children for whom seasonal prophylaxis would be appropriate in exceptional circumstances	Up to July 2007	26 published references	22 RCTs, 1 unpublished report	Amantadine (8), oseltamivir (6), zanamivir (9)	Seasonal prophylaxis & post-exposure prophylaxis	Placebo	Symptomatic lab-confirmed influenza (SLCI): Oseltamivir for seasonal prophylaxis in health unvaccinated adults (RR 0.27 [0.09-0.83] p=0.21), oseltamivir for PEP in mixed households (all index cases) (RR 0.19 [0.08-0.45], p=0.15), oseltamivir for PEP in mixed households (influenza-positive index cases) (RR 0.21 [0.08-0.58], p=0.13), zanamivir for PEP in mixed households (all index cases) (RR=0.21 [0.13-0.33], p=0.72), zanamivir for PEP in mixed households (influenza-positive index cases) (RR 0.19 [0.11-0.33], p=0.93)	Variable study quality, low attack rates during seasons under study

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
Turner 2003 [68]	UK	Systematic review and economic evaluation	Children (≤12 years), healthy adults (12–65 years), high-risk individuals (≥65 years and/or with concomitant disease), and for prophylaxis also elderly people in residential homes; review covered both treatment and prevention of influenza A and B	Data available up to 31 December 2001	Zanamivir: 4 RCTs included; Oseltamivir: 4 RCTs included	RCTs only	Oseltamivir and zanamivir	Four prophylaxis strategies: 1- outbreak prophylaxis in elderly LTCFs, 2- seasonal prophylaxis in elderly LTCFs, 3-seasonal prophylaxis in healthy populations, 4-household post-exposure prophylaxis	Placebo, no treatment, or active comparator	Household post-exposure prophylaxis: Zanamivir: OR 0.19 (95% CI 0.09–0.38) (pooled from 2 RCTs) Oseltamivir: OR 0.10 (95% CI 0.04–0.29) (1 RCT) Seasonal prophylaxis (healthy): Zanamivir: OR 0.31 (95% CI 0.14–0.64) Oseltamivir: OR 0.26 (95% CI 0.08–0.84) Elderly LTCF prophylaxis: Oseltamivir: OR 0.08 (95% CI 0.01–0.61)	Heterogeneity across populations, strategies, and vaccination status limited pooling. Very small number of trials per strategy. Some cluster trials did not adjust for clustering. Evidence gaps in children and subgroup-specific analyses. Potential publication bias and reliance on manufacturer data
Wang 2012 [69]	UK	Cochrane systematic review of published trials only	Children aged ≤12 years with influenza or exposed to influenza in household/community settings; treatment and prevention of symptomatic influenza were both assessed	CENTRAL (2011 Issue 1), MEDLINE (1966 to January week 2, 2011), and EMBASE (January 2010 to January 2011)	9 studies total: 6 treatment trials and 3 prophylaxis trials	Primarily double-blind RCTs; one prophylaxis trial (WV16193) was open-label but included because the authors judged the overall data sufficiently reliable	Oseltamivir, zanamivir, laninamivir octanoate; peramivir was eligible but no included pediatric trial contributed data	Treatment of influenza and household post-exposure prophylaxis	Placebo or active antiviral comparator (laninamivir vs oseltamivir in one trial)	For prophylaxis, zanamivir or oseltamivir was associated with an 8% absolute reduction in developing influenza after introduction of a household case (RD −0.08, 95% CI −0.12 to −0.05; P<0.001).	Only published trials were included, so publication bias was a concern. Study quality was generally moderate, sample sizes were small, and pooling was limited for several outcomes. Evidence in children with comorbidities, children <1 year, and pandemic influenza was lacking. Most data were from seasonal influenza, and many studies were manufacturer-sponsored.
Zhao 2024 [9]	Not reported as a single-country review	Systematic review and network meta-analysis of RCTs	Individuals exposed to influenza viruses. Included studies enrolled 19,096 individuals, with reported mean ages ranging from 6.75 to 81.15 years. The review included both	Up to Sept 20, 2023	33 RCTs	RCTs (7 cluster-randomized (household or nursing home as unit) and 26 individually randomized)	Zanamivir, oseltamivir, laninamivir, baloxavir, amantadine, rimantadine	Antiviral post-exposure prophylaxis and also antiviral prophylaxis in some studies with unclear exposure status or pre-exposure prophylaxis during influenza season/outbreaks.	Placebo, standard care, or another antiviral. Most key relative effect estimates came from direct	In individuals at high risk of severe disease, zanamivir (RR 0.35, 95% CI 0.25–0.50), oseltamivir (0.40, 0.26–0.62), laninamivir (0.43, 0.30–0.63), and baloxavir (0.43, 0.23–	Data were unavailable for some outcomes considered important by the WHO panel, including length of hospitalisation, ICU admission, invasive mechanical ventilation, and influenza disease

Study	Country	Study design	Population	Search period	Number of included studies	Design of included studies	Antiviral agents	Intervention type	Comparator	Key findings	Study limitations
			populations with clear post-exposure definitions and populations with unclear exposure status or pre-exposure prophylaxis during influenza season/outbreaks.						comparisons versus placebo or standard care	0.79) probably reduce symptomatic seasonal influenza when given promptly after exposure.	severity. Data were scarce for pregnant people and infants <1 year. Studies varied in route of administration, dose, and duration, but were combined in the network meta-analysis. Three trials included index cases with influenza-like illness rather than confirmed influenza, although sensitivity analyses were unchanged. There were no RCTs for prophylaxis against zoonotic influenza, so indirect evidence from seasonal influenza was used. Mortality assumptions for zoonotic influenza may overestimate some virus contexts. Effects against influenza B remain uncertain for most antivirals other than zanamivir

Abbreviations: CENTRAL = Cochrane Central Register of Controlled Trials; CI = Confidence Interval; eOQAQ = Enhanced Overview Quality Assessment Questionnaire; GRADE = Grading of Recommendations Assessment, Development and Evaluation; ICU = Intensive Care Unit; LTCF = Long-Term Care Facility; MA = Meta-Analysis; NPI = Non-Pharmaceutical Intervention; OR = Odds Ratio; PEP = Post-Exposure Prophylaxis; PPE = Personal Protective Equipment; RCT = Randomized Controlled Trial; RD = Risk Difference; RR = Relative Risk; SLCI = Symptomatic Laboratory-Confirmed Influenza; SR = Systematic Review; SR/MA = Systematic Review and/or Meta-Analysis; UK = United Kingdom; USA = United States of America; WHO = World Health Organization

Appendix 4: Complete Outcome Extractions

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
Booy et al 2012	Residents	T+P (Oseltamivir)	91	397	22.9	
	Residents	T only (Oseltamivir)	93	255	36.5	
	Staff	T + P (Oseltamivir)	47	350	13.4	
	Staff	T only (Oseltamivir)	46	216	21.3	
Carrat et al 2012	Participants	Oseltamivir	23	161	14	household transmission
	Participants	Zanamivir	25	164	15	household transmission
	Participants	Oseltamivir + Zana	10	141	7	household transmission
	Participants	Oseltamivir	14	81	17	(Early Treatment ≤24 h): 232 contacts of 136 index pts
	Participants	Zanamivir	14	95	15	(Early Treatment ≤24 h): 232 contacts of 136 index pts
	Participants	Oseltamivir + Zanamivir	2	56	4	(Early Treatment ≤24 h): 232 contacts of 136 index pts
	Participants	Oseltamivir	9	80		(Early Treatment >24 h)
	Participants	Zanamivir	11	69		(Early Treatment >24 h)
	Participants	Oseltamivir + Zanamivir	8	85		(Early Treatment >24 h)
Dronavalli et al 2020	Residents	Oseltamivir prophylaxis	84	4,392	1.90	Relative Risk (RR): 0.10 (95% CI 0.08–0.12
	Residents	No prophylaxis	1070	5672	18.90	
Fujita et al 2020	Staff	Oseltamivir prophylaxis	5	16	31.30	
	Staff	No prophylaxis	11	25	44.00	
Goldstein et al 2010	Participants	Treatment timing 0 day	1	8	12.50	household transmission
	Participants	Treatment timing 1 day	4	21	19%	household transmission
	Participants	Treatment timing 2 days	3	11	27.3	household transmission

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
	Participants	Treatment timing >= 3 days	19	51	37.3	household transmission
	Participants	No treatment	10	44	22.7	household transmission
Hayden et al 2000	Participants	Placebo	33	215	15	household transmission
	Participants	Zanamivir	6	195	3	household transmission
Higa et al 2012	Participants	Chemoprophylaxis	5	416	1.2	close contact transmission. OR 0.34 (0.12-0.97) p=0.047
	Participants	No chemoprophalxis	12	346	3.5	close contact transmission
Hirotsu et al 2019	Participants	peramivir	60	447	13.4	household transmission
	Participants	Oseltamivir	95	411	23.1	household transmission
	Participants	Zanamivir	84	596	14.1	household transmission
	Participants	Laninamivir	45	252	17.9	household transmission
	Participants	peramivir	74	1214	6.1	household members with secondary infection
	Participants	Oseltamivir	120	1113	10.8	household members with secondary infection
	Participants	Zanamivir	96	1699	5.7	household members with secondary infection
	Participants	Laninamivir	55	744	7.4	household members with secondary infection
Ikematsu et al - main 2020	Participants	Baloxavir	7	374	1.9	household transmission- Lab confirmed clinical influenza
	Participants	Placebo	51	375	13.6	household transmission- Lab confirmed clinical influenza
	Participants	Baloxavir	49	374	13.1	household transmission- Lab confirmed influenza regardless of symptoms
	Participants	Placebo	114	375	30.4	household transmission- Lab confirmed influenza regardless of symptoms

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
Ikematsu et al - 2 2024	RCT participants	Baloxavir	18	125	14.4	household transmission
	RCT participants	Oseltamivir	18	76	23.7	household transmission
	Questionnaire participants	Baloxavir	17	132	12.9	household transmission
	Questionnaire participants	Oseltamivir	19	77	24.7	household transmission
Kaiser et al 2000	Participants	Intranasal zanamivir	8	141	5.67	symptomatic influenza during 5 days of prophylaxis
	Participants	Inhaled zanamivir	3	144	2.08	symptomatic influenza during 5 days of prophylaxis
	Participants	Inhaled + intranasal zanamivir	5	146	3.42	symptomatic influenza during 5 days of prophylaxis
	Participants	Placebo	9	144	6.25	symptomatic influenza during 5 days of prophylaxis
	Participants	Intranasal zanamivir	9	141	6.38	symptomatic influenza during 10 days of prophylaxis
	Participants	Inhaled zanamivir	4	144	2.78	symptomatic influenza during 10 days of prophylaxis
	Participants	Inhaled + intranasal zanamivir	6	146	4.11	symptomatic influenza during 10 days of prophylaxis
	Participants	Placebo	11	144	7.64	symptomatic influenza during 10 days of prophylaxis
	Participants	Intranasal zanamivir	28	141	19.86	Proven influenza during 21 days after initiation
	Participants	Inhaled zanamivir	16	144	11.11	Proven influenza during 21 days after initiation
	Participants	Inhaled + intranasal zanamivir	21	146	14.38	Proven influenza during 21 days after initiation
	Participants	Placebo	27	144	18.75	Proven influenza during 21 days after initiation

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
Kojima et al 2025	Participants	Baloxavir	0	40	0	symptomatic influenza
	Participants	No Baloxavir	3	32	9.38	symptomatic influenza
Komeda et al 2021	Participants	Baloxavir	15226	84672	17.98	household transmission
	Participants	Oseltamivir	14983	62004	24.16	household transmission
	Participants	Zanamivir	2593	14085	18.41	household transmission
	Participants	Laninamivir	8272	47464	17.43	household transmission
Komiya et al 2010	Participants	Oseltamivir or Zanamivir or both	2	331	0.60	household transmission
	Participants	No PEP	12	46	26.09	household transmission
Lepen et al 2020	Participants	Oseltamivir- 5 day	2	110	1.82	hospital transmission of influenza -> incidence of influenza in exposed patients
	Participants	Oseltamivir- 10 day	0	112	0	hospital transmission of influenza -> incidence of influenza in exposed patients
Monto et al 2025	Participants	Baloxavir	94	1118	8.41	transmission to household contacts by day 5
	Participants	Placebo	131	1098	11.93	transmission to household contacts by day 5
	Participants	Baloxavir	56	1118	5.01	transmission by day 5 resulting in symptoms
	Participants	Placebo	72	1098	6.56	transmission by day 5 resulting in symptoms
	Participants	Baloxavir	85	548	15.51	Household-level day-5 transmission
	Participants	Placebo	106	544	19.49	Household-level day-5 transmission
	Participants	Baloxavir	101	1081	9.34	Day-9 transmission at household-contact level

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
	Participants	Placebo	141	1038	13.58	Day-9 transmission at household-contact level
	Participants	Baloxavir	113	1268	8.90	transmission to household contacts by day 5
	Participants	Placebo	164	1255	13.10	transmission to household contacts by day 5
	Participants	Baloxavir	65	1268	5.10	transmission by day 5 resulting in symptoms
	Participants	Placebo	88	1255	7.00	transmission by day 5 resulting in symptoms baseline
Monto et al 2002	Participants	Zanamivir	10	245	4.08	Primary household-level outcome: at least 1 contact with symptomatic, laboratory-confirmed influenza
	Participants	Placebo	46	242	19.01	Primary household-level outcome: at least 1 contact with symptomatic, laboratory-confirmed influenza
	Participants	Zanamivir	12	661	1.82	Primary contact-level outcome: symptomatic, laboratory-confirmed influenza
	Participants	Placebo	55	630	8.73	Primary contact-level outcome: symptomatic, laboratory-confirmed influenza
	Participants	Zanamivir	35	245	14.29	Laboratory-confirmed influenza (symptomatic or asymptomatic), household level
	Participants	Placebo	75	242	30.99	Laboratory-confirmed influenza (symptomatic or asymptomatic), household level

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
	Participants	Zanamivir	48	661	7.26	Laboratory-confirmed influenza (symptomatic or asymptomatic), contact level
	Participants	Placebo	105	630	16.67	Laboratory-confirmed influenza (symptomatic or asymptomatic), contact level
	Participants	Zanamivir	51	398	12.81	Laboratory-confirmed influenza (symptomatic) with lab confirmed Index, contact level
	Participants	Placebo	9	368	2.45	Laboratory-confirmed influenza (symptomatic) with lab confirmed Index, contact level
	Participants	Placebo	93	398	23.37	Laboratory-confirmed influenza, contact level with lab confirmed index
	Participants	Zanamivir	38	368	10.33	Laboratory-confirmed influenza, contact level with lab confirmed index
Nakano et al 2014	Participants	Laninamivir	702	6362	11.03	Rate of household secondary infection
	Participants	Oseltamivir	1735	12142	14.29	Rate of household secondary infection
	Participants	Zanamivir	720	6222	11.57	Rate of household secondary infection
Nishiura et al 2011	Participants	Oseltamivir treatment- Within 24 hours	NA	NA	5.1	Secondary attack ratios
	Participants	Oseltamivir treatment- Within 24-48 hours	NA	NA	12.7	Secondary attack ratios

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
	Participants	Oseltamivir treatment->48hrs/ no antiviral	NA	NA	7.1	Secondary attack ratios
	Participants	Zanamivir treatment-Within 24 hours	NA	NA	17.3	Secondary attack ratios
	Participants	Zanamivir treatment-Within 24-48 hours	NA	NA	17.8	Secondary attack ratios
	Participants	Zanamivir treatment->48hrs/ no antiviral	NA	NA	24.4	Secondary attack ratios
	Participants	Oseltamivir PEP-Within 24 hours	NA	NA	10.3	Secondary attack ratios
	Participants	Oseltamivir PEP-Within 24-48 hours	NA	NA	11.9	Secondary attack ratios
	Participants	Oseltamivir PEP->48hrs/ no antiviral	NA	NA	6.9	Secondary attack ratios
	Participants	Zanamivir PEP-Within 24 hours	NA	NA	18.5	Secondary attack ratios
	Participants	Zanamivir PEP-Within 24-48 hours	NA	NA	20	Secondary attack ratios
	Participants	Zanamivir PEP->48hrs/ no antiviral	NA	NA	21.9	Secondary attack ratios
Shapiro et al 2025	Camp residents	Oseltamivir- cohort 2 delayed mass PEP	1	262	0.38	new influenza cases following outbreak
	Camp residents	No antiviral	5	208	2.4	new influenza cases following outbreak
	Camp residents	Oseltamivir- cohort 3- cabin 1	1	13	7.7	new influenza cases following outbreak
	Camp residents	No antiviral- cohort 3- cabin 1	2	9	22.2	new influenza cases following outbreak
Shinjoh et al 2012	Participants	Oseltamivir	2	48	4.17	Contact level influenza
	Participants	Zanamivir	0	15	0	Contact level influenza

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
	Participants	No antiviral	5	17	29.41	Contact level influenza
	Participants	Oseltamivir	1	31	3.22	Contact level influenza
	Participants	Zanamivir	0	14	0	Contact level influenza (immunocompetent)
	Participants	No antiviral	4	13	30.77	Contact level influenza (immunocompetent)
Umemura et al 2020	Participants	Baloxavir	11	122	9.02	secondary attack rate of household members
	Participants	Oseltamivir	40	296	13.51	secondary attack rate of household members
van der Sande et al 2014	Nursing home units	Oseltamivir	2	6	33.33	Unit level secondary influenza positive ILI cases; 6 units = 36 residents
	Nursing home units	Placebo	2	9	22.22	Unit level secondary influenza positive ILI cases; 9 units = 63 residents
	Nursing home units	Oseltamivir	2	6	33.33	Unit level secondary ILI cases
	Nursing home units	Placebo	5	9	55.56	Unit level secondary ILI cases
	Participants	Oseltamivir	3	32	9.38	Of all PEP participants tested
	Participants	Placebo	10	47	21.28	Of all PEP participants tested
Welliver et al 2001	Participants	Oseltamivir	3	84	3.57	secondary attack rate- household level
	Participants	Placebo	18	79	22.78	secondary attack rate- household level
	Participants	Oseltamivir	3	209	1.44	secondary attack rate- individual level
	Participants	Placebo	26	206	12.62	secondary attack rate- individual level
Teh et al 2012	Participants-pH1N1	Oseltamivir	49	215	22.79	secondary attack rate- household level

Study	Population	Intervention	Event Rate	Denominator	Proportion	Notes
	Participants-pH1N1	No oseltamivir	104	284	36.62	secondary attack rate-household level
	Participants-none H1N1 infleunza	Oseltamivir	5	23	21.74	secondary attack rate-household level
	Participants-none H1N1 infleunza	No oseltamivir	19	74	25.68	secondary attack rate-household level
	Participants-ILI (controls)	Oseltamivir	27	164	16.46	secondary attack rate-household level
	Participants-ILI (controls)	No oseltamivir	109	571	19.08	secondary attack rate-household level
Best et al 2024	Participants/index cases	Baloxavir	16	90	17.8	secondary attack rate-household level. RR = 0.67 (.41-1.11), p=0.11
	Participants/index cases	Oseltamivir	52	196	26.5	secondary attack rate-household level
Gorisek Miksic et al 2014	Nursing home residents	Oseltamivir for all residents	55	208	26	attack rate
	Nursing home residents	Oseltamivir for exposed residents	64	167	38	attack rate
	Nursing home residents	No prophylaxis	31	164	19	attack rate
Shah et al 2019	Care home residents	Oseltamivir prophylaxis	594	2200	27	attack rate
	Care home residents	No prophylaxis	261	1298	20.1	attack rate

Appendix 5: Sensitivity Analysis

Figures 1-4 show sensitivity analyses excluding studies with high risk of bias for pooled analyses that had 3 or more studies.

Figure 1. Antiviral Prophylaxis vs. No Antiviral (NRS) - Secondary Attack Rate

Study or Subgroup	Antiviral prophylaxis Events	Total	No antiviral Events	Total	Weight	Risk ratio IV, Fixed, 95% CI
1.1.1 Longterm care home/ healthcare facility residents						
✖ Shinjoh 2012	2	63	5	17	0.0%	0.11 [0.02 , 0.51]
✖ Higa 2012	5	416	12	346	0.0%	0.35 [0.12 , 0.97]
✖ Gorisek Miksic 2015	119	375	31	164	0.0%	1.68 [1.18 , 2.38]
✔ Shah 2019	594	2200	261	1298	100.0%	1.34 [1.18 , 1.53]
✖ Dronavalli 2020	84	4392	1070	5672	0.0%	0.10 [0.08 , 0.13]
Subtotal		**2200**		**1298**	**100.0%**	**1.34 [1.18 , 1.53]**
Total events:	594		261			
Test for overall effect: Z = 4.50 (P < 0.00001)						
Heterogeneity: Not applicable						
1.1.2 Households/Community						
✖ Komiya 2010	2	331	12	46	0.0%	0.02 [0.01 , 0.10]
✖ Teh 2012	54	238	123	358	0.0%	0.66 [0.50 , 0.87]
✖ Shapiro 2025 cohort 3	1	13	2	9	0.0%	0.35 [0.04 , 3.27]
✖ Shapiro 2025 cohort 2	1	262	5	208	0.0%	0.16 [0.02 , 1.35]
✖ Kojima 2025	0	40	3	32	0.0%	0.11 [0.01 , 2.15]
Subtotal		**0**		**0**		**Not estimable**
Total events:	0		0			
Test for overall effect: Not applicable						
Heterogeneity: Not applicable						
1.1.3 Longterm care home/ healthcare facility Staff						
✖ Fujita 2020	5	16	11	25	0.0%	0.71 [0.30 , 1.66]
Subtotal		**0**		**0**		**Not estimable**
Total events:	0		0			
Test for overall effect: Not applicable						
Heterogeneity: Not applicable						
Total		**2200**		**1298**	**100.0%**	**1.34 [1.18 , 1.53]**
Total events:	594		261			
Test for overall effect: Z = 4.50 (P < 0.00001)						
Test for subgroup differences: Not applicable						
Heterogeneity: Not applicable						

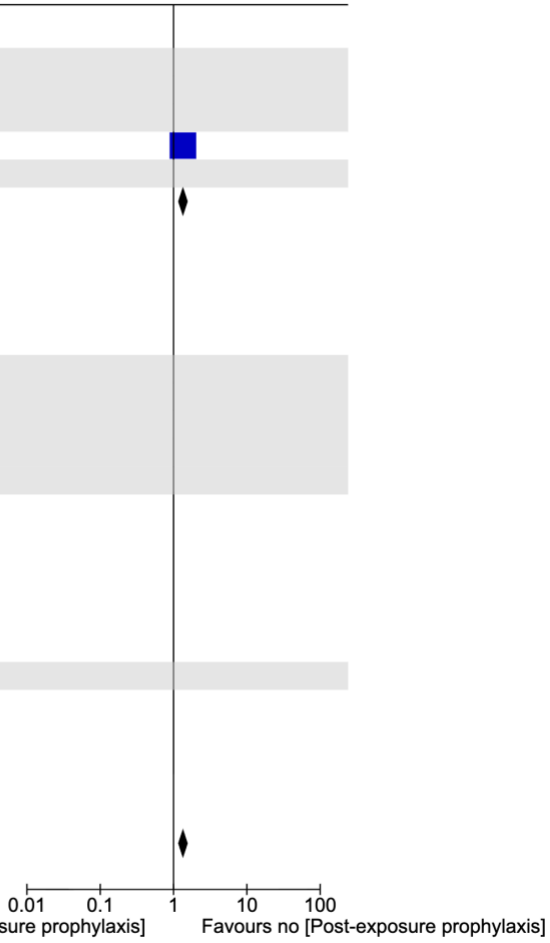
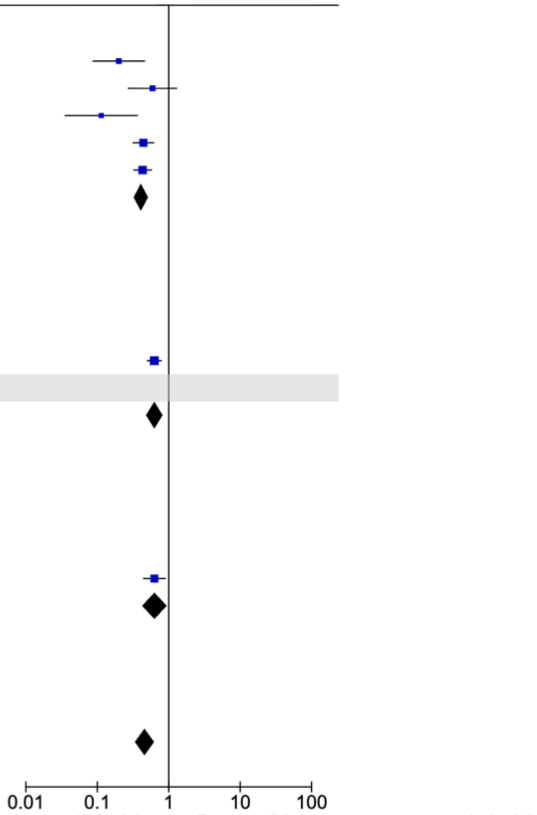


Figure 2. Antiviral Prophylaxis vs. No Antiviral (RCT) - Secondary Attack Rate

Study or Subgroup	Antiviral prophylaxis Events	Total	No antiviral Events	Total	Weight	Risk ratio IV, Random, 95% CI
1.2.1 Household/commmunity						
✔ Hayden 2000	6	195	33	215	7.9%	0.20 [0.09 , 0.47]
✔ Kaiser 2000	16	431	9	144	8.6%	0.59 [0.27 , 1.31]
✔ Welliver 2001	3	209	26	206	4.8%	0.11 [0.03 , 0.37]
✔ Monto 2002	38	368	93	398	18.7%	0.44 [0.31 , 0.63]
✔ Ikematsu 2020	49	374	114	375	20.1%	0.43 [0.32 , 0.58]
Subtotal (Wald[a])		**1577**		**1338**	**60.0%**	**0.41 [0.33 , 0.50]**
Total events:	112		275			
Test for overall effect: Z = 8.41 (P < 0.00001)						
Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 8.39, df = 4 (P = 0.08); I² = 0%						
1.2.2 Longterm care/ healthcare facility - Residents						
✔ Booy 2012- Residents	91	397	93	255	21.9%	0.63 [0.49 , 0.80]
✖ van der Sande 2014	3	32	10	47	0.0%	0.44 [0.13 , 1.48]
Subtotal		**397**		**255**	**21.9%**	**0.63 [0.49 , 0.80]**
Total events:	91		93			
Test for overall effect: Z = 3.75 (P = 0.0002)						
Heterogeneity: Not applicable						
1.2.3 Longterm care/ healthcare facility - Staff						
✔ Booy 2012- Staff	47	350	46	216	18.1%	0.63 [0.44 , 0.91]
Subtotal		**350**		**216**	**18.1%**	**0.63 [0.44 , 0.91]**
Total events:	47		46			
Test for overall effect: Z = 2.45 (P = 0.01)						
Heterogeneity: Not applicable						
Total (Wald[a])		**2324**		**1809**	**100.0%**	**0.46 [0.34 , 0.61]**
Total events:	250		414			
Test for overall effect: Z = 5.38 (P < 0.00001)						
Test for subgroup differences: Chi² = 8.58, df = 2 (P = 0.01), I² = 76.7%						
Heterogeneity: Tau² (REML[b]) = 0.08; Chi² = 16.97, df = 6 (P = 0.009); I² = 65%						



Footnotes

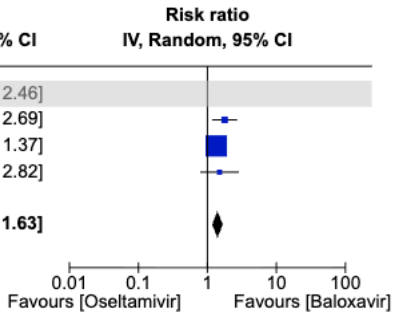
[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 3. Oseltamivir vs. Baloxavir marboxil Treatment of Index Cases (NRS) - Secondary Attack Rate

Study or Subgroup	Events	Total	Events	Total	Weight	Risk ratio IV, Random, 95% CI
✖ Best 2024	52	196	16	90	0.0%	1.49 [0.90 , 2.46]
✔ Ikematsu 2024	37	153	35	257	11.7%	1.78 [1.17 , 2.69]
✔ Komeda 2021	14983	62004	15226	84672	82.8%	1.34 [1.32 , 1.37]
✔ Umemura 2020	40	296	11	122	5.5%	1.50 [0.80 , 2.82]
Total (Wald[a])		**62453**		**85051**	**100.0%**	**1.40 [1.20 , 1.63]**
Total events:	15060		15272			

Test for overall effect: Z = 4.27 (P < 0.0001)



Heterogeneity: Tau² (REML[b]) = 0.01; Chi² = 1.83, df = 2 (P = 0.40); I² = 19%

Footnotes

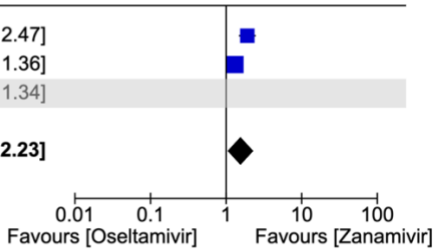
[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Figure 4: Oseltamivir vs. Zanamivir Treatment of Index Case (NRS) - Secondary Attack Rate

Study or Subgroup	Oseltamivir Events	Oseltamivir Total	Zanamivir Events	Zanamivir Total	Weight	Risk ratio IV, Random, 95% CI
✔ Hirotsu 2019	120	1113	96	1699	44.0%	1.91 [1.47 , 2.47]
✔ Komeda 2021	14983	62004	2593	14085	56.0%	1.31 [1.26 , 1.36]
✖ Nakano 2014	1735	12142	720	6222	0.0%	1.23 [1.14 , 1.34]
Total (Wald[a])		**63117**		**15784**	**100.0%**	**1.55 [1.08 , 2.23]**
Total events:	15103		2689			

Test for overall effect: Z = 2.35 (P = 0.02)



Heterogeneity: Tau² (REML[b]) = 0.06; Chi² = 7.94, df = 1 (P = 0.005); I² = 87%

Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Appendix 6: GRADE Evidence Profiles

Question: Influenza antiviral post-exposure prophylaxis or treatment compared to no antivirals for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With no antivirals	With influenza antiviral post-exposure prophylaxis or treatment	Relative effect (95% CI)	Risk with no antivirals	Risk difference with influenza antiviral post-exposure prophylaxis or treatment
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (Observational) - Longterm care/healthcare facility - Residents											
14943 (5 non-randomised studies)[1,2,3,4,5]	serious[a]	very serious[b]	not serious	extremely serious[c]	none	⨁◯◯◯ Very low[a,b,c]	1379/7497 (18.4%)	804/7446 (10.8%)	**RR 0.42** (0.13 to 1.38)	1379/7497 (18.4%)	**107 fewer per 1,000** (from 160 fewer to 70 more)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (Observational) - Longterm care/healthcare facility - Staff											
41 (1 non-randomised study)[6]	serious[a]	not serious	not serious	extremely serious[d]	none	⨁◯◯◯ Very low[a,d]	11/25 (44.0%)	5/16 (31.3%)	**RR 0.71** (0.30 to 1.66)	11/25 (44.0%)	**128 fewer per 1,000** (from 308 fewer to 290 more)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (Observational) - Households/Community											
1537 (5 non-randomised studies)[7,8,9,10,e]	very serious[f]	serious[g]	not serious	serious[h]	none	⨁◯◯◯ Very low[f,g,h]	145/653 (22.2%)	58/884 (6.6%)	**RR 0.17** (0.04 to 0.68)	145/653 (22.2%)	**184 fewer per 1,000** (from 213 fewer to 71 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (Observational) - Total											
16521 (11 non-randomised studies)[1,2,3,4,5,6,7,8,9,10,e]	serious[a]	very serious[b]	not serious	serious[i]	none	⨁◯◯◯ Very low[a,b,i]	1535/8175 (18.8%)	867/8346 (10.4%)	**RR 0.32** (0.14 to 0.72)	1535/8175 (18.8%)	**128 fewer per 1,000** (from 161 fewer to 53 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (RCT) - Household/community											
2915 (5 RCTs)[11,12,13,14,15]	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	275/1338 (20.6%)	112/1577 (7.1%)	**RR 0.41** (0.33 to 0.50)	275/1338 (20.6%)	**121 fewer per 1,000** (from 138 fewer to 103 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (RCT) - Longterm care/healthcare facility - Staff											
566 (1 RCT)[16]	not serious	not serious	not serious	serious[j]	none	⨁⨁⨁◯ Moderate[j]	46/216 (21.3%)	47/350 (13.4%)	**RR 0.63** (0.44 to 0.91)	46/216 (21.3%)	**79 fewer per 1,000** (from 119 fewer to 19 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (RCT) - Longterm care/healthcare facility - Residents											

Certainty assessment							Summary of findings				
731 (2 RCTs)[16,17]	serious[k]	not serious	not serious	serious[h]	none	⊕⊕◯◯ Low[h,k]	103/302 (34.1%)	94/429 (21.9%)	**RR 0.62** (0.49 to 0.79)	103/302 (34.1%)	**130 fewer per 1,000** (from 174 fewer to 72 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Secondary attack rate (RCT) - Total											
4212 (8 RCTs)[11,12,13,14,15,16,17,l]	not serious[m]	serious[n]	not serious	not serious	none	⊕⊕⊕◯ Moderate[m,n]	424/1856 (22.8%)	253/2356 (10.7%)	**RR 0.46** (0.36 to 0.60)	424/1856 (22.8%)	**123 fewer per 1,000** (from 146 fewer to 91 fewer)
Antiviral Treatment vs. Placebo/No Antiviral - Antiviral treatment of index patients vs no treatment (RCT) - Secondary attack rate											
2216 (1 RCT)[18]	not serious	not serious	not serious	serious[h,o]	none	⊕⊕⊕◯ Moderate[h,o]	131/1098 (11.9%)	94/1118 (8.4%)	**RR 0.70** (0.55 to 0.91)	131/1098 (11.9%)	**36 fewer per 1,000** (from 54 fewer to 11 fewer)
Antiviral Prophylaxis vs. Placebo/No Antiviral - Viral Shedding (RCT)											
415 (1 RCT)[11]	not serious	not serious	not serious	serious[o]	none	⊕⊕⊕◯ Moderate[o]	24/206 (11.7%)	4/209 (1.9%)	**RR 0.16** (0.06 to 0.47)	24/206 (11.7%)	**98 fewer per 1,000** (from 110 fewer to 62 fewer)
Household with ≥ 1 Secondary Transmission After Exposure (Observational) - Secondary attack rate											
135 (1 non-randomised study)[19]	serious[a]	not serious	not serious	extremely serious[c]	none	⊕◯◯◯ Very low[a,c]	29/95 (30.5%)	8/40 (20.0%)	**RR 0.66** (0.33 to 1.31)	29/95 (30.5%)	**104 fewer per 1,000** (from 205 fewer to 95 more)
Basic reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Effective reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Serial interval - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Bottleneck analysis - not reported											
-	-	-	-	-	-	-	-	-	-	-	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias was rated down by one level due to failure to match groups or adjust for key confounders in the study's design or analysis.
b. Inconsistency was rate down by two levels due to substantial heterogeneity.
c. Imprecision was rated down by three levels since the 95% CI of the absolute effect included substantial benefit and important harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
d. Imprecision was rated down by three levels since the 95% CI of the absolute effect included substantial benefit and substantial harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
e. Shapiro 2025: cohort 2 and cohort 3 counted as separate studies in the analysis.
f. Risk of bias was rated down by two levels due to failure to match groups or adjust for key confounders in the study's design or analysis.
g. Inconsistency was rated down by one level due to important heterogeneity.
h. Imprecision was rated down by one level since the 95% CI of the absolute effect included important benefit and substantial benefit. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.

i. Imprecision was rated down by one level since the 95% CI of the absolute effect included close to important benefit and substantial benefit. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
j. Imprecision was rated down by one level since the 95% CI of the absolute effect included important benefit and trivial benefit. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel
k. Risk of bias was rated down by one level due to deviations from the intended intervention and missing outcome data.
l. Booy 2012: Residents and staff counted as separate studies in the analysis.
m. 1 RCT had High RoB, 5 RCTs had Some RoB concerns, and 2 RCTs had Low RoB. Sensitivity analysis excluding the RCT with High RoB showed a similar pooled RR of 0.46 (0.34-0.61). Sensitivity analysis only including the 2 RCTs with Low RoB showed a pooled RR of 0.33 (0.16-0.67). Therefore, the certainty of evidence was not rated down for risk of bias.
n. Potentially important inconsistency (I2 = 57%; Chi-square p-value = 0.02; varying point estimates; non-overlapping 95% confidence intervals) that cannot completely be explained based on study characteristics.
o. Imprecision was rated down by one level due to the evidence not meeting the optimal information size.

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Question: 5 days of influenza antiviral post-exposure prophylaxis compared to 10 days of influenza antiviral post-exposure prophylaxis for reducing influenza transmission among exposed (asymptomatic) individuals in community and high-risk settings
Setting: community and high-risk settings

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With 10 days of influenza antiviral post-exposure prophylaxis	With 5 days of influenza antiviral post-exposure prophylaxis	Relative effect (95% CI)	Risk with 10 days of influenza antiviral post-exposure prophylaxis	Risk difference with 5 days of influenza antiviral post-exposure prophylaxis
Duration of Oseltamivir Post- Exposure Prophylaxis - 5 days vs. 10 days (RCT) - Secondary Attack Rate											
222 (1 RCT)[1]	not serious	not serious	not serious	extremely serious[a]	none	⨁◯◯◯ Very low[a]	0/112 (0.0%)	2/110 (1.8%)	**RR 5.09** (0.25 to 104.83)	0/112 (0.0%)	**18 more per 1,000** (from -- to --)
Basic reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Effective reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Serial interval - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Bottleneck analysis - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Viral shedding - not reported											
-	-	-	-	-	-	-	-	-	-	-	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. Imprecision was rated down by three levels due to the very large 95% confident interval of the RR which was calculated based on only 2 events.

References

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Question: Early (<24 h) influenza antiviral post-exposure prophylaxis or treatment compared to late (>48 h) or no antiviral post-exposure prophylaxis or treatment for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings

Setting: community and high-risk settings

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With late (>48 h) or no antiviral post-exposure prophylaxis or treatment	With early (<24 h) influenza antiviral post-exposure prophylaxis or treatment	Relative effect (95% CI)	Risk with late (>48 h) or no antiviral post-exposure prophylaxis or treatment	Risk difference with early (<24 h) influenza antiviral post-exposure prophylaxis or treatment
Early Treatment <24h vs Late >48h/No treatment (Observational) - Secondary Attack Rate											
0 (2 non-randomised studies)[1,a]	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	0/0	0/0	**OR 0.58** (0.46 to 0.73)[b]	0/0	**-- per 1,000** (from -- to --)
Early Treatment + Prophylaxis <24h vs Late >48h/No treatment + Prophylaxis (Observational) - Secondary Attack Rate											
0 (2 non-randomised studies)[1,a]	not serious	not serious	not serious	serious[c]	none	⨁◯◯◯ Very low[c]	0/0	0/0	**OR 1.34** (0.79 to 2.26)[b]	0/0	**-- per 1,000** (from -- to --)
Basic reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Effective reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Serial interval - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Bottleneck analysis - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Viral shedding - not reported											
-	-	-	-	-	-	-	-	-	-	-	-

CI: confidence interval; **OR:** odds ratio

Explanations

a. Nishiura 2011: Oseltamivir cohort and Zanamivir cohort counted as separate studies in the analysis.
b. Pooled adjusted ORs for effect of <24h compared with >48h. Nominator and denominator for event rates were not provided.
c. Imprecision was rated down by one level due to the wide 95% confidence interval of the odds ratio including benefit and harm.

References

1.Nishiura, H., Oshitani, H.. Household transmission of influenza (H1N1-2009) in Japan: age-specificity and reduction of household transmission risk by zanamivir treatment.The Journal of international medical research; 2011.

Question: Oseltamivir treatment compared to baloxavir treatment for reducing influenza transmission among infected individuals in community and high-risk settings
Setting: community and high-risk settings

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With baloxavir treatment	With oseltamivir treatment	Relative effect (95% CI)	Risk with baloxavir treatment	Risk difference with oseltamivir treatment
Oseltamivir vs Baloxavir Treatment of Index Cases (Observational) - Secondary Attack Rate											
147790 (4 non-randomised studies)[1,2,3,4]	not serious	not serious	not serious	serious[a]	none	⨁◯◯◯ Very low[a]	15288/85141 (18.0%)	15112/62649 (24.1%)	**RR 1.38** (1.24 to 1.53)	15288/85141 (18.0%)	**68 more per 1,000** (from 43 more to 95 more)
Basic reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Effective reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Serial interval - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Bottleneck analysis - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Viral shedding - not reported											
-	-	-	-	-	-	-	-	-	-	-	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. Imprecision was rated down by one level since the 95% CI of the absolute effect includes trivial benefit and important benefit. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.

References

1.Umemura, Takumi, Mutoh, Yoshikazu, Kawamura, Takato, Saito, Masayuki, Mizuno, Takahito, Ota, Aiko, Kozaki, Koji, Yamada, Tetsuya, Ikeda, Yoshiaki, Ichihara, Toshihiko. Efficacy of baloxavir marboxil on household transmission of influenza infection.Journal of pharmaceutical health care and sciences; 2020.
2.Komeda, Takuji, Takazono, Takahiro, Hosogaya, Naoki, Ogura, Eriko, Fujiwara, Masakazu, Miyauchi, Hideyuki, Ajisawa, Yoshikazu, Iwata, Shinpei, Watanabe, Hideaki, Honda, Keiichi, Kitanishi, Yoshitake, Hara, Kanae, Mukae, Hiroshi. Comparison of Household Transmission of Influenza Virus From Index Patients Treated With Baloxavir Marboxil or Neuraminidase Inhibitors: A Health Insurance Claims Database Study.Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; 2021.
3.Ikematsu, Hideyuki, Baba, Takamichi, Saito, Masaya M., Kinoshita, Masahiro, Miyazawa, Shogo, Hata, Ayano, Nakano, Saki, Kitanishi, Yoshitake, Hayden, Frederick G.. Comparative Effectiveness of Baloxavir Marboxil and Oseltamivir Treatment in Reducing Household Transmission of Influenza: A Post Hoc Analysis of the BLOCKSTONE Trial.Influenza and other respiratory viruses; 2024.
4.Best, Jennie H., Sadeghi, Mitra, Sun, Xiaowu, Seetasith, Arpamas, Albensi, Lisa, Joshi, Seema, Zervos, Marcus J.. Household Influenza Transmission and Healthcare Resource Utilization Among Patients Treated with Baloxavir vs Oseltamivir: A United States Outpatient Prospective Survey.Infectious diseases and therapy; 2024.

Question: Oseltamivir treatment compared to peramivir treatment for reducing influenza transmission among infected individuals in community and high-risk settings
Setting: community and high-risk settings

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With peramivir treatment	With oseltamivir treatment	Relative effect (95% CI)	Risk with peramivir treatment	Risk difference with oseltamivir treatment
Oseltamivir vs Peramivir Treatment of Index Cases (Observational) - Secondary Attack Rate											
2327 (1 non-randomised study)[1]	not serious	not serious	not serious	serious[a]	none	⨁◯◯◯ Very low[a]	74/1214 (6.1%)	120/1113 (10.8%)	**RR 1.77** (1.34 to 2.34)	74/1214 (6.1%)	**47 more per 1,000** (from 21 more to 82 more)
Basic reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Effective reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Serial interval - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Bottleneck analysis - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Viral shedding - not reported											
-	-	-	-	-	-	-	-	-	-	-	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. Imprecision was rated down by one level since the 95% CI of the absolute effect included trivial harm and important harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.

References

1.Hirotsu, Nobuo, Saisho, Yutaka, Hasegawa, Takahiro. The effect of neuraminidase inhibitors on household transmission in Jap anese patients with influenza A and B infection: A prospective, observational study.Influenza and other respiratory viruses; 2019.

Question: Oseltamivir post-exposure prophylaxis or treatment compared to zanamivir post-exposure prophylaxis or treatment for reducing influenza transmission among exposed (asymptomatic) or infected individuals in community and high-risk settings
Setting: community and high-risk settings

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With zanamivir post-exposure prophylaxis or treatment	With oseltamivir post-exposure prophylaxis or treatment	Relative effect (95% CI)	Risk with zanamivir post-exposure prophylaxis or treatment	Risk difference with oseltamivir post-exposure prophylaxis or treatment
Oseltamivir vs Zanamivir Treatment of Index Cases (RCT) - Secondary Attack Rate											
325 (1 RCT)[1]	serious[a]	not serious	not serious	very serious[b]	none	⊕◯◯◯ Very low[a,b]	25/164 (15.2%)	23/161 (14.3%)	**RR 0.94** (0.56 to 1.58)	25/164 (15.2%)	**9 fewer per 1,000** (from 67 fewer to 88 more)
Oseltamivir vs Zanamivir Treatment of Index Cases (Observational) - Secondary Attack Rate											
97265 (3 non-randomised studies)[2,3,4]	not serious	very serious[c]	not serious	serious[d]	none	⊕◯◯◯ Very low[c,d]	3409/22006 (15.5%)	16838/75259 (22.4%)	**RR 1.41** (1.12 to 1.79)	3409/22006 (15.5%)	**64 more per 1,000** (from 19 more to 122 more)
Oseltamivir vs Zanamivir Post-Exposure Prophylaxis (Observational) - Secondary Attack Rate											
63 (1 non-randomised study)[5]	serious[e]	not serious	not serious	very serious[f]	none	⊕◯◯◯ Very low[e,f]	0/15 (0.0%)	2/48 (4.2%)	**RR 1.63** (0.08 to 32.25)	0/15 (0.0%)	**42 more per 1,000** (from 0 fewer to 0 fewer)
Basic reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Effective reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Serial interval - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Bottleneck analysis - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Viral shedding - not reported											
-	-	-	-	-	-	-	-	-	-	-	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias was downgraded by one level due to missing outcome data.
b. Imprecision was rated down by two levels since the 95% CI of the absolute effect includes important benefit and important harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
c. Inconsistency was downgraded by two levels due to substantial heterogeneity.
d. Imprecision was rated down by one level since the 95% CI of the absolute effect includes trivial harm and important harm. For judgments regarding Imprecision, the suggested minimally important difference (MID) of 5.5% for antiviral prophylaxis of laboratory-confirmed symptomatic seasonal influenza in low-risk populations from Zhao et al. 2024 was used, which was determined based on input from a WHO guideline panel.
e. Risk of bias was rated down by one level due to failure to match groups or adjust for key confounders in the study's design or analysis.
f. Imprecision was rated down by two levels due to the evidence not meeting the optimal information size.

References

1.Carrat, Fabrice, Duval, Xavier, Tubach, Florence, Mosnier, Anne, Van der Werf, Sylvie, Tibi, Annick, Blanchon, Thierry, Leport, Catherine, Flahault, Antoine, Mentre, France. Effect of oseltamivir, zanamivir or oseltamivir-zanamivir combination treatments on transmission of influenza in households.Antiviral therapy; 2012.
2.Nakano, Takashi, Shiosakai, Kazuhito. Spread of viral infection to family members from influenza patients treated with a neuraminidase inhibitor.Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy; 2014.
3.Komeda, Takuji, Takazono, Takahiro, Hosogaya, Naoki, Ogura, Eriko, Fujiwara, Masakazu, Miyauchi, Hideyuki, Ajisawa, Yoshikazu, Iwata, Shinpei, Watanabe, Hideaki, Honda, Keiichi, Kitanishi, Yoshitake, Hara, Kanae, Mukae, Hiroshi. Comparison of Household Transmission of Influenza Virus From Index Patients Treated With Baloxavir Marboxil or Neuraminidase Inhibitors: A Health Insurance Claims Database Study.Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; 2021.
4.Hirotsu, Nobuo, Saisho, Yutaka, Hasegawa, Takahiro. The effect of neuraminidase inhibitors on household transmission in Japanese patients with influenza A and B infection: A prospective, observational study.Influenza and other respiratory viruses; 2019.
5.Shinjoh, Masayoshi, Takano, Yaoko, Takahashi, Takao, Hasegawa, Naoki, Iwata, Satoshi, Sugaya, Norio. Postexposure prophylaxis for influenza in pediatric wards oseltamivir or zanamivir after rapid antigen detection.The Pediatric infectious disease journal; 2012.

Question: Zanamivir treatment compared to baloxavir treatment for reducing influenza transmission among infected individuals in community and high-risk settings
Setting: community and high-risk settings

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With baloxavir treatment	With zanamivir treatment	Relative effect (95% CI)	Risk with baloxavir treatment	Risk difference with zanamivir treatment
Zanamivir vs Baloxavir Treatment of Index Cases (Observational) - Secondary Attack Rate											
98757 (1 non-randomised study)[1]	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	15226/84672 (18.0%)	2593/14085 (18.4%)	**RR 1.02** (0.99 to 1.06)	15226/84672 (18.0%)	**4 more per 1,000** (from 2 fewer to 11 more)
Basic reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Effective reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Serial interval - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Bottleneck analysis - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Viral shedding - not reported											
-	-	-	-	-	-	-	-	-	-	-	-

CI: confidence interval; **RR:** risk ratio

References

1.Komeda, Takuji, Takazono, Takahiro, Hosogaya, Naoki, Ogura, Eriko, Fujiwara, Masakazu, Miyauchi, Hideyuki, Ajisawa, Yoshikazu, Iwata, Shinpei, Watanabe, Hideaki, Honda, Keiichi, Kitanishi, Yoshitake, Hara, Kanae, Mukae, Hiroshi. Comparison of Household Transmission of Influenza Virus From Index Patients Treated With Baloxavir Marboxil or Neuraminidase Inhibitors: A Health Insurance Claims Database Study.Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; 2021.

Question: Zanamivir treatment compared to peramivir treatment for reducing influenza transmission among infected individuals in community and high-risk settings
Setting: community and high-risk settings

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With peramivir treatment	With zanamivir treatment	Relative effect (95% CI)	Risk with peramivir treatment	Risk difference with zanamivir treatment
Zanamivir vs Peramivir Treatment of Index Cases (Observational) - Secondary Attack Rate											
2913 (1 non-randomised study)[1]	not serious	not serious	not serious	serious[a]	none	⨁◯◯◯ Very low[a]	74/1214 (6.1%)	96/1699 (5.7%)	**RR 0.93** (0.69 to 1.24)	74/1214 (6.1%)	**4 fewer per 1,000** (from 19 fewer to 15 more)
Basic reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Effective reproduction number - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Serial interval - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Bottleneck analysis - not reported											
-	-	-	-	-	-	-	-	-	-	-	-
Viral Shedding - not reported											
-	-	-	-	-	-	-	-	-	-	-	-

CI: confidence interval; **RR:** risk ratio

Explanations

a. Imprecision was rated down by one level due to the evidence not meeting the optimal information size.

References

1.Hirotsu, Nobuo, Saisho, Yutaka, Hasegawa, Takahiro. The effect of neuraminidase inhibitors on household transmission in Japanese patients with influenza A and B infection: A prospective, observational study.Influenza and other respiratory viruses; 2019.