

# Oseltamivir: Não funciona

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# O que é “funcionar”

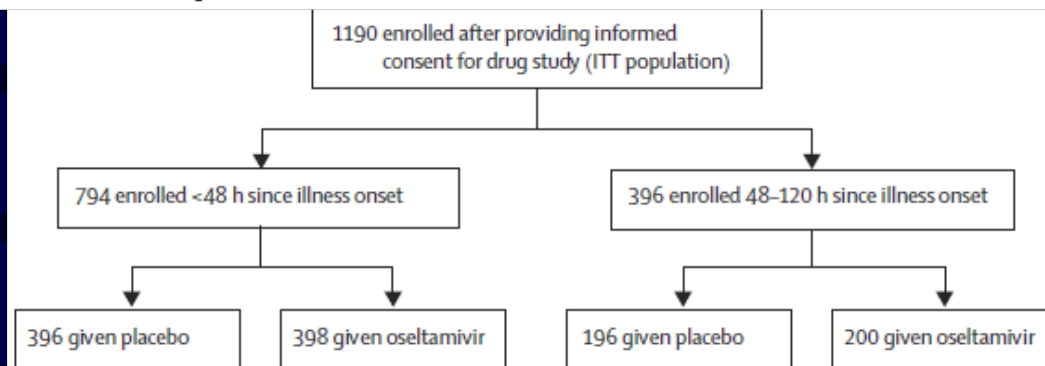
- Lasix “funciona” na IRA?
- Dipirona “funciona” na pneumonia?
- Resfenol “funciona” na gripe?

# O que é “funcionar”?

- Reduzir excreção viral?
- Reduzir tempo de sintomas?
- Reduzir complicações?
- Reduzir hospitalização?
- Reduzir mortalidade?

# Efficacy of oseltamivir treatment started within 5 days of symptom onset to reduce influenza illness duration and virus shedding in an urban setting in Bangladesh: a randomised placebo-controlled trial

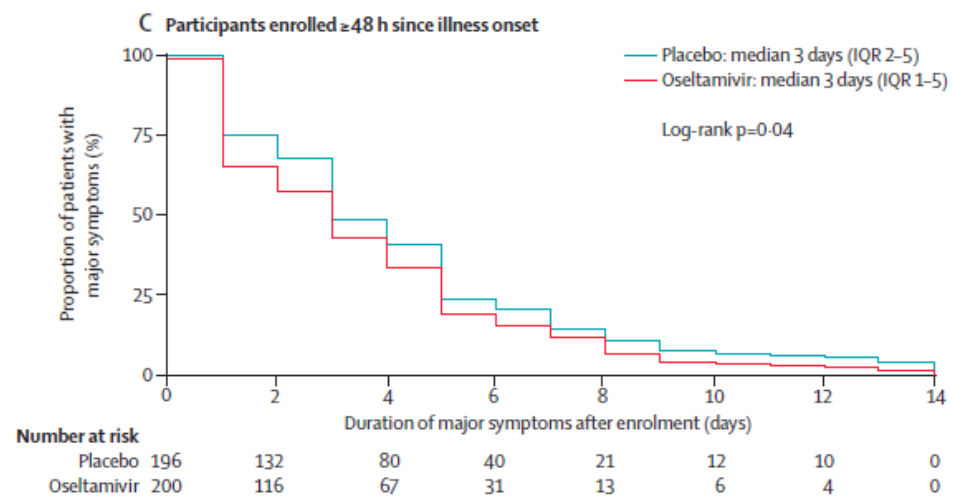
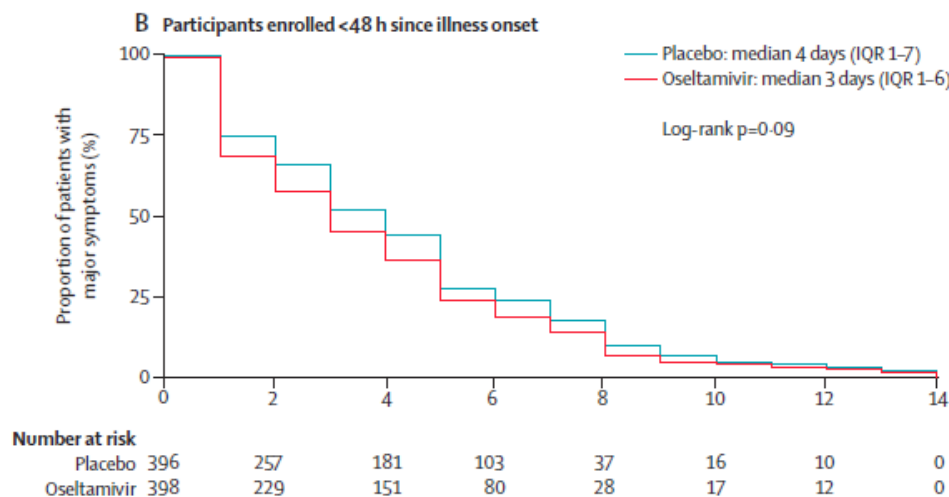
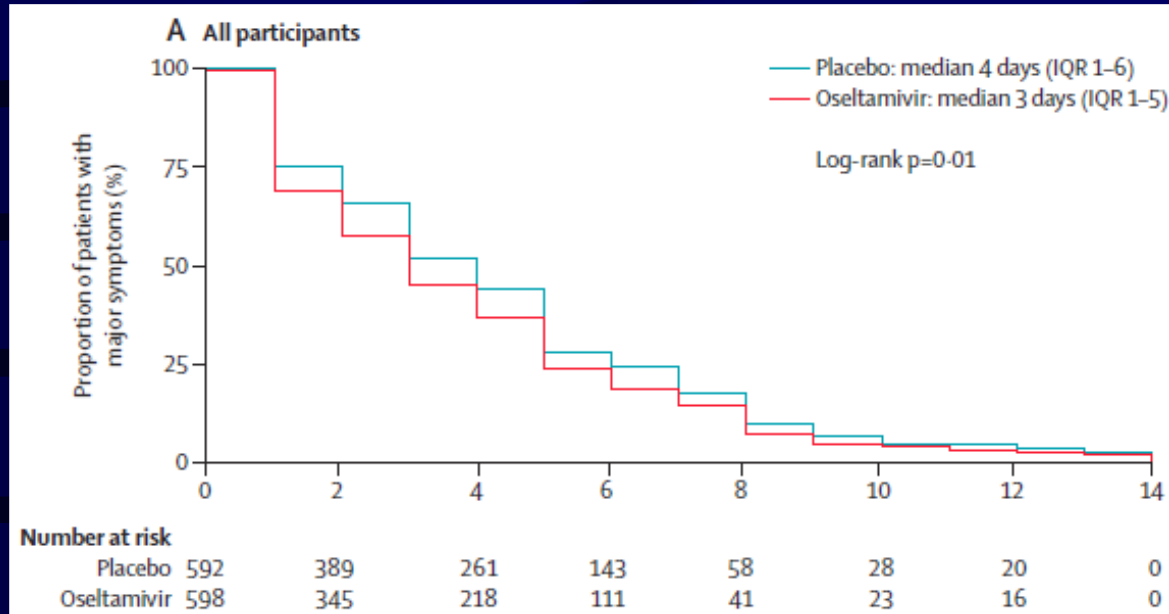
**Lancet Infect Dis 2014;  
14: 109-18**



	All participants		Enrolled <48 h since illness onset		Enrolled ≥48 h since illness onset	
	Placebo (n=592)	Oseltamivir (n=598)	Placebo (n=396)	Oseltamivir (n=398)	Placebo (n=196)	Oseltamivir (n=200)
<b>Age group (years)</b>						
1-4	309 (52%)	292 (49%)	197 (50%)	177 (44%)	111 (57%)	105 (53%)
5-10	167 (28%)	178 (30%)	115 (29%)	127 (32%)	52 (27%)	51 (26%)
11-17	58 (10%)	66 (11%)	36 (9%)	42 (11%)	16 (8%)	20 (10%)
≥18	58 (10%)	72 (12%)	48 (12%)	52 (13%)	16 (8%)	24 (12%)
Male sex	309 (52%)	318 (53%)	208 (53%)	218 (55%)	101 (52%)	100 (50%)
Z score for weight*	-2.2 (-2.7 to -1.5)	-2.1 (-2.8 to -1.4)	-2.1 (-2.7 to -1.5)	-2.2 (-2.8 to -1.6)	-2.3 (-3.0 to -1.5)	-2.0 (-2.8 to -1.2)
<b>Influenza viruses</b>						
A H3N2	206 (35%)	212 (35%)	144 (36%)	144 (36%)	62 (32%)	68 (34%)
Seasonal A H1N1	70 (12%)	61 (10%)	55 (14%)	52 (13%)	15 (8%)	9 (5%)
A H1N1 pdm09	103 (17%)	110 (18%)	66 (17%)	73 (18%)	37 (19%)	37 (19%)
B	193 (33%)	204 (34%)	116 (29%)	121 (30%)	77 (39%)	83 (42%)
Mixed	4 (1%)	0	4 (1%)	0	0	0
Negative PCR at enrolment	16 (3%)	11 (2%)	11 (3%)	8 (2%)	5 (3%)	3 (2%)
Body temperature at enrolment (°C)	38.6 (38.2 to 39.0)	38.6 (38.3 to 39.0)	38.6 (38.2 to 39.0)	38.6 (38.3 to 39.4)	38.6 (38.2 to 39.0)	38.5 (38.2 to 38.9)
Tachypnoea† at enrolment	473 (80%)	473 (79%)	323 (82%)	309 (78%)	150 (77%)	164 (82%)
Days from onset of illness to enrolment	2 (1 to 3)	2 (1 to 3)	1 (1 to 2)	1 (1 to 2)	3 (2 to 4)	3 (2 to 3)
Antibiotics given with study drug	229 (39%)	205 (34%)	91 (23%)	73 (18%)	138 (70%)	132 (66%)
Paracetamol given before enrolment	155 (26%)	142 (24%)	67 (17%)	69 (17%)	88 (45%)	73 (37%)
Paracetamol given with study drug	592 (100%)	598 (100%)	396 (100%)	398 (100%)	196 (100%)	200 (100%)

Data are n (%) or median (IQR). \* Children only. † Age specific.

**Table 1: Baseline characteristics**



	All participants				Enrolled <48 h since illness onset				Enrolled ≥48 h since illness onset			
	Placebo (n=563)	Oseltamivir (n=571)	% reduction (95% CI)	p value	Placebo (n=377)	Oseltamivir (n=378)	% reduction (95% CI)	p value	Placebo (n=186)	Oseltamivir (n=193)	% reduction (95% CI)	p value
<b>Baseline</b>												
PCR positive	563 (100%)	571 (100%)	0	1.00	377 (100%)	378 (100%)	0	1.00	186 (100%)	193 (100%)	0	1.00
Influenza virus isolated from tissue culture	452 (80%)	470 (82%)	-2.5% (-6.9 to 2.0)	0.40	297 (79%)	310 (82%)	-3.0% (-9.4 to 1.9)	0.27	155 (83%)	161 (83%)	0	1.00
Titration*	2.9 (0-8.2) (n=438)	2.7 (0-8.2) (n=438)	..	0.74	2.42 (0-8.2) (n=286)	2.37 (0-8.2) (n=287)	..	0.375	3 (0-8.2) (n=151)	3 (0-7.4) (n=151)	..	0.505
<b>Day 2</b>												
PCR positive	539 (96%)	521 (91%)	5.2% (2.4 to 8.1)	0.003	363 (96%)	344 (91%)	5.0% (1.7 to 8.7)	0.004	176 (95%)	177 (92%)	3.2% (-1.8 to 8.1)	0.31
Influenza virus isolated from tissue culture	374 (66%)	321 (56%)	15.2% (9.5 to 20.8)	0.0004	249 (66%)	217 (57%)	13.6% (6.7 to 20.5)	0.017	125 (67%)	104 (54%)	19.4% (9.7 to 29.2)	0.0087
Titration*	0 (0-8.1)	0 (0-8.1)	..	0.005	0 (0-8.2)	0 (0-7.7)	..	0.010	0 (0-8.2)	0 (0-8.1)	..	0.217
<b>Day 4</b>												
PCR positive	467 (83%)	427 (75%)	9.6% (4.9 to 14.4)	0.0008	321 (85%)	285 (75%)	11.8% (6.1 to 17.4)	0.0009	146 (78%)	142 (74%)	5.1% (-3.4 to 13.7)	0.28
Influenza virus isolated from tissue culture	241 (43%)	174 (30%)	30.2% (24.6 to 35.8)	<0.0001	171 (45%)	126 (33%)	23.2% (16.4 to 30.1)	0.0007	70 (38%)	48 (25%)	34.2% (24.9 to 43.5)	0.0079
Titration*	0 (0-8.2)	0 (0-7.4)	..	0.0012	0 (0-8.2)	0 (0-7.0)	..	0.010	0 (0-7.7)	0 (0-7.4)	..	0.048
<b>Day 7</b>												
PCR positive	332 (59%)	251 (44%)	25.4% (19.7 to 31.2)	<0.0001	225 (60%)	160 (42%)	30.0% (23.0 to 37.0)	<0.0001	107 (58%)	91 (47%)	19.0% (9.0 to 29.0)	0.05
Influenza virus isolated from tissue culture	68 (12%)	36 (6%)	47.5% (44.2 to 50.8)	0.0009	48 (13%)	23 (6%)	50.8% (46.6 to 55.0)	0.0018	20 (11%)	13 (7%)	39.1% (33.4 to 44.8)	0.202
Titration*	0 (0-6.2)	0 (0-7.7)	..	<0.0001	0 (0-6.2)	0 (0-7.7)	..	0.001	0 (0-4.7)	0 (0-6.2)	..	0.0278

Data are n (%) or median (range), unless otherwise indicated. \*Viral titration was measured as log<sub>10</sub> tissue culture infective dose 50 (TCID<sub>50</sub>). Median titrations do not include influenza A H3N2 viruses. If PCR was negative or no virus was isolated, then TCID<sub>50</sub>=0.

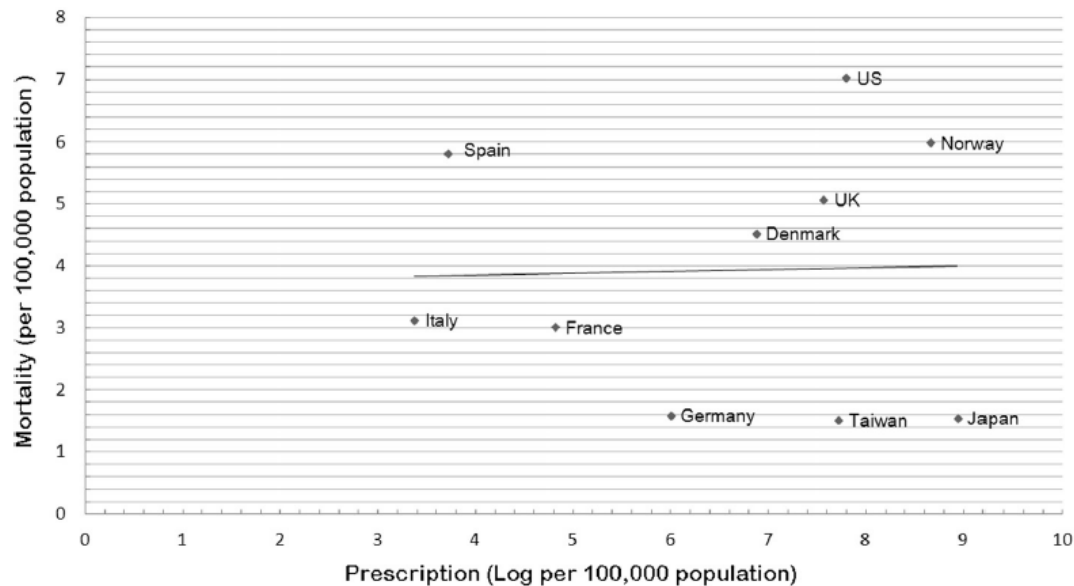
**Table 2: Comparison of virological outcomes in participants with all serial swabs and PCR-confirmed influenza infection**

# Oseltamivir use and outcomes during the 2009 influenza A H1N1 pandemic in Taiwan

Liu et al. BMC Public Health 2013, 13:646

**Table 3 Oseltamivir prescription and mortality rate in country level during 2009 H1N1 pandemic from literature review**

Country	Reference	Population (millions)	Study period	Oseltamivir per 100,000 population	Mortality rate per million (Ref 8)
Japan	Ref 9	128	Aug 2009- Mar 2010	7625	1.55
Norway	Ref 10	4.8	Jan 2009- Dec 2009	5795.6	6.00
US	Ref 11	307	Apr 2009- Mar 2010	2420.5	7.04
Taiwan	This article	23.1	Aug 2009-Dec 2009	2233.1	1.52
UK	Ref 12	60.6	July 2009- Feb 2010	1933.6	5.08
Denmark	Ref 13	5.5	Jan 2009- Dec 2009	959.6	4.53
Germany	Ref 14	82.6	Oct 2009- Dec 2009	405.3	1.6
France	Ref 14	65	Oct 2009- Dec 2009	122.6	3.02
Spain	Ref 14	46.6	Oct 2009- Dec 2009	40.9	5.82
Italy	Ref 14	60	Oct 2009- Dec 2009	29.3	3.13



**Figure 4 Oseltamivir prescription rates and mortality of influenza patients among different countries.** X axis: prescription (Log per 100,000 population); Y axis :mortality (per 100,000 population).

# Effect of double dose oseltamivir on clinical and virological outcomes in children and adults admitted to hospital with severe influenza: double blind randomised controlled trial

BMJ 2013;346:f3039 doi: 10.1136/bmj.f3039

**Table 1** | Patients' characteristics at enrolment in study of double or standard dose oseltamivir for treatment of severe influenza. Continuous data are shown as mean (SD), categorical data as number (percentage)

Parameter	Total	Children (n=246)		Adults (n=80)	
		Double dose (n=124)	Standard dose (n=122)	Double dose (n=41)	Standard dose (n=39)
Sex (male)	185	79 (63.7)	71 (58.2)	17 (41.5)	18 (46.2)
Age (years)	—	2.8 (2.4)	2.8 (1.9)	37.9 (13.6)	45.9 (18.7)

## Radiology:

Infiltrates on CXR	266	96 (77)	96 (79)	39 (95)	35 (90)
ARDS	25	3 (2.4)	4 (3.3)	8 (19.5)	10 (25.6)
Treatment needed:					
Intensive care	57	6 (4.8)	8 (6.6)	19 (46.3)	24 (61.5)
Supplemental oxygen	93	23 (18.5)	17 (13.9)	25 (61)	28 (71.8)
Mechanical ventilation	34	3 (2.4)	5 (4.1)	11 (26.8)	15 (38.5)

**Table 2** | Subgroup analyses of percentages of patients still positive for viral RNA at day five of treatment in samples taken from nose. Patients grouped according to age, detected virus, and day of illness on enrolment

	Standard dose			Double dose			P value‡
	No* (%)	Copy number (range)†	No with positive quantitative RT-PCR result	No* (%)	Copy number (range)†	No with positive quantitative RT-PCR result	
Age groups							
All	22/143 (15.4)	4.33e+03 (1.00e+03-7.40e+04)	8	22/150 (14.7)	2.94e+03 (1.00e+03-5.62e+04)	9	0.85

**Table 4| Risk factors identified by conditional multiple logistic regression for being viral RNA negative by RT-PCR on day five. Important non-significant factors are also included. Patients with no detected influenza were excluded from analysis**

Factor	No of patients*	No of events*	OR (95% CI)	P value
Nose viral load†	304	213	0.73 (0.62 to 0.86)	<0.01
Karnofsky score <50‡	35	15	0.24 (0.08 to 0.78)	0.02
Child	236	49	0.62 (0.17 to 2.22)	0.46
Double dose oseltamivir	156	112	1.27 (0.73 to 2.20)	0.39

**Table 6| Effect of dose on measures of respiratory compromise, expressed as Kaplan Meier estimates and 95% confidence intervals, in study of double or standard dose oseltamivir for treatment of severe influenza**

	Double dose	Standard dose	P value*
<b>Receipt of oxygen</b>			
Median (IQR) time (days)	3 (2-5)	3.5 (2-7)	0.48†
No of patients	50	48	—
% on oxygen on day 3	55.5 (39.7 to 68.7)	60.5 (44.1 to 73.4)	0.72‡
% on oxygen on day 5	36.3 (21.7 to 51.1)	42.8 (26.8 to 57.8)	
% on oxygen on day 7	22.7 (9.6 to 39.1)	28.5 (14.4 to 44.4)	
% on oxygen on day 10	17.0 (5.4 to 34.1)	28.5 (14.4 to 44.4)	
<b>Time in intensive care unit (ICU)</b>			
Median (IQR) time (days)	4.5 (3-6)	5 (2-11)	0.66†
No of patients	27	34	—
% in ICU on day 3	84.7 (64.0 to 94.0)	77.1 (57.8 to 88.5)	0.57‡
% in ICU on day 5	47.4 (23.0 to 68.4)	60.9 (40.1 to 76.4)	
% in ICU on day 7	37.9 (14.5 to 61.5)	38.8 (18.7 to 58.5)	
% in ICU on day 10	25.3 (5.3 to 52.5)	33.2 (14.5 to 53.3)	
<b>Time on ventilation</b>			
Median (IQR) time (days)	2.5 (1-16)	8 (1-16)	0.58†
No of patients	19	21	—
% on ventilation on day 3	89.5 (64.1 to 97.3)	85.7 (62.0 to 95.2)	0.68‡
% on ventilation on day 5	71.6 (26.1 to 92.0)	75.0 (42.4 to 90.8)	
% on ventilation on day 7	71.6 (26.1 to 92.0)	75.0 (42.4 to 90.8)	
% on ventilation on day 10	71.6 (26.1 to 92.0)	45.0 (11.9 to 74.1)	

# Critically Ill Children During the 2009–2010 Influenza Pandemic in the United States

PEDIATRICS Volume 128, Number 6, December 2011

**TABLE 1** Characteristics of the 838 Children Admitted to a PICU With Confirmed or Probable pH1N1 in the United States (April 15, 2009, to April 15, 2010)

Characteristic	n (%)
Female gender	353 (42.1)
Age group <sup>a</sup>	
<6 mo	71 (8.5)
6–23 mo	113 (13.5)
2–4 y	131 (15.6)
5–12 y	336 (40.1)
13–17 y	157 (18.7)
18–20 y	30 (3.6)
Underlying health conditions	
Previously healthy (none)	251 (30.0)
<u>≥1 underlying conditions</u>	<u>587 (70.0)</u>
Chronic respiratory	356 (42.5)
Asthma	258 (30.8)
Neurologic or neuromuscular	263 (31.4)
Cardiovascular	80 (9.6)
Gastrointestinal or hepatic	80 (9.6)
Metabolic	37 (4.4)
Immune compromise	33 (3.9)
Current/active metastatic solid cancer	6 (0.7)
Current/active hematologic malignancy	9 (1.1)
Other immunosuppression (ie, transplant, HIV)	18 (2.1)
Renal	10 (1.2)
Hemoglobinopathy	22 (2.6)
Other chronic condition	126 (15.0)

**TABLE 2** Selected Laboratory Abnormalities Closest to PICU Admission in Patients With pH1N1 and Their Association With Mortality

Laboratory Abnormality	n/N (%)	RR (95% CI)
Leukocytopenia (white cell count < 5000 per $\mu\text{L}$ )	161/753 (21.4)	1.8 (1.2–2.9) <sup>a</sup>
Leukocytosis (white cell count > 11 000 per $\mu\text{L}$ ) <sup>b</sup>	289/753 (38.4)	0.7 (0.4–1.1)
Lymphocytopenia (<1000 per $\mu\text{L}$ )	365/719 (50.8)	1.3 (0.8–2.1)
Neutropenia (<500 per $\mu\text{L}$ )	33/630 (5.2)	2.8 (1.5–5.5) <sup>c</sup>
Thrombocytopenia (platelet count < 150 000 per $\mu\text{L}$ )	190/748 (25.4)	2.9 (1.8–4.4) <sup>d</sup>
Elevated creatinine level <sup>e</sup>	150/739 (20.3)	1.8 (1.2–2.9) <sup>f</sup>
Elevated total bilirubin level (>1.2 mg/dL [21 $\mu\text{mol/L}$ ]) <sup>b</sup>	44/447 (9.8)	0.5 (0.2–1.5)
Suspected rhabdomyolysis (CPK > 200 U/L) <sup>b</sup>	51/115 (44.4)	1.4 (0.6–3.7)
Severe hypoxia <sup>g</sup>		
$\text{PaO}_2/\text{FiO}_2 < 100$	115/239 (48.1)	3.1 (1.6–5.8) <sup>h</sup>
$\text{PaO}_2/\text{FiO}_2 = 100\text{--}199$	65/239 (27.2)	1.1 (0.4–3.4)

**TABLE 3** Adjunctive and Antiviral Treatments Received in the PICU and Survival (N = 838)

Parameter	n (%)	RR Death (95% CI)	P
Mechanical ventilation			
Via invasive route only	259 (30.9)	4.0 (2.5–6.2)	<.0001
Noninvasive ventilation only	136 (16.2)	0.4 (0.2–0.9)	.02
Both endotracheal and noninvasive ventilation	169 (20.2)	1.6 (1.0–2.6)	.04
High-frequency ventilation	115 (13.7)	8.4 (5.6–12.8)	<.0001
Inhaled nitric oxide	76 (9.1)	7.5 (5.0–11.0)	<.0001
Prone positioning	33 (3.9)	3.8 (2.1–6.6)	<.0001
Vasopressors for shock <sup>a</sup>			
At time of PICU admission	90 (10.7)	4.4 (2.9–6.7)	<.0001
During PICU course	162 (19.3)	7.9 (5.0–12.3)	<.0001
Dialysis	44 (5.3)	4.5 (2.8–7.3)	<.0001
ECMO	33 (3.9)	8.9 (6.1–12.9)	<.0001
High-dose corticosteroids <sup>b</sup>	262 (31.3)	3.5 (2.2–5.4)	<.0001
Fresh-frozen plasma	75 (9.0)	6.8 (4.6–10.1)	<.0001
Intravenous immunoglobulin	26 (3.1)	3.7 (2.0–6.9)	<.0001
Influenza antiviral medications			
Oseltamivir	751 (89.6)	0.8 (0.4–1.4)	NS
Peramivir <sup>c</sup>	21 (2.5)	6.0 (3.6–9.9)	<.0001
Zanamivir	12 (1.4)	0.9 (0.1–6.2)	NS
Amantadine	17 (2.0)	0.7 (0.1–4.4)	NS
Ribavirin	5 (0.6)	2.3 (0.4–13.2)	NS
Rimantadine (none died)	5 (0.6)	—	NS

# Oseltamivir Shortens Hospital Stays of Critically Ill Children Hospitalized with Seasonal Influenza: A Retrospective Cohort Study

*Pediatr Infect Dis J.* 2011 November ; 30(11): 962–966.

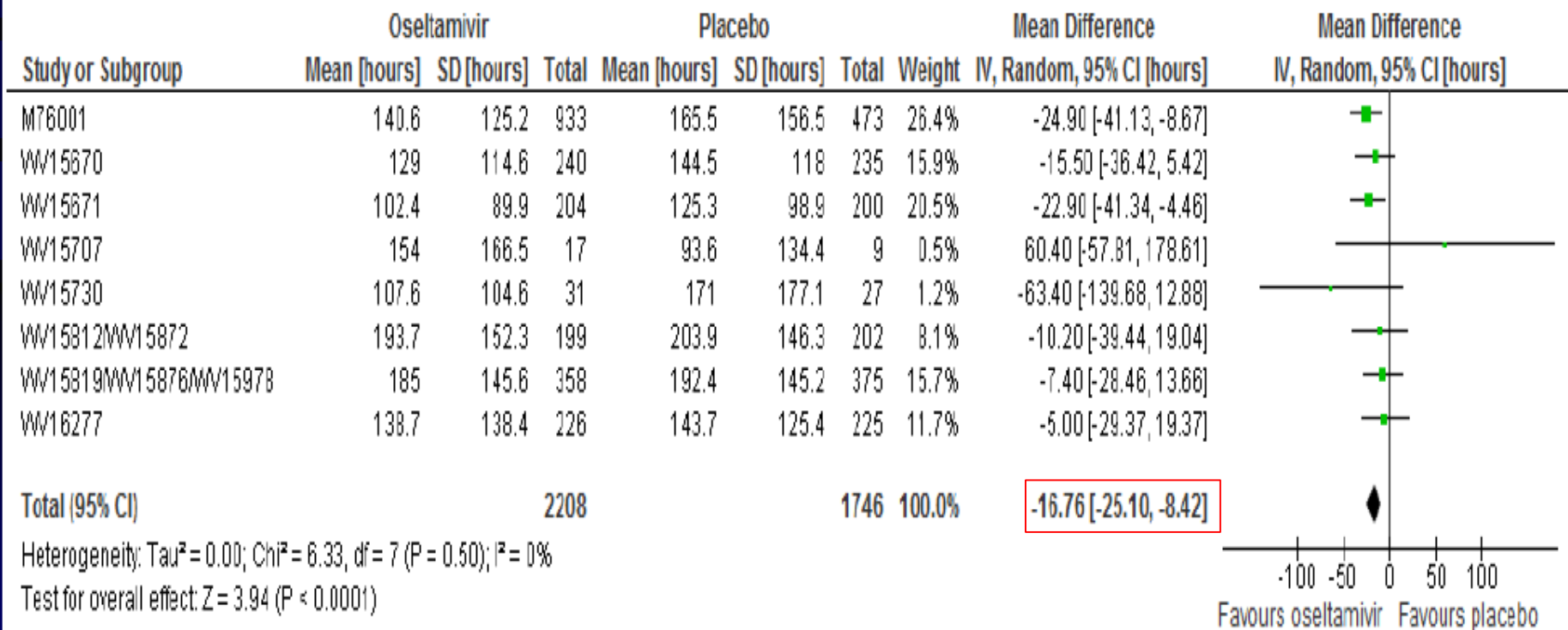
	No Oseltamivir Treatment (N=993)	Oseltamivir Treatment (N=264)	No Oseltamivir Treatment (N=252)	Oseltamivir Treatment (N=252)
Age in years (Median, IQR) <sup>2</sup>	1.33 (0.35, 4.47)	4.59 (1.87, 11.90)	1.68 (0.48, 7.13)	4.45 (1.87, 10.94)
Gender				
Clinical Support at Admission				
Oxygen support	275 (28%)	73 (28%)	76 (30%)	69 (27%)
Mechanical ventilation	54 (5%)	30 (11%)	24 (10%)	29 (12%)
High-frequency ventilation	25 (3%)	13 (5%)	16 (6%)	13 (5%)
Other assisted ventilation	301 (30%)	86 (33%)	82 (33%)	82 (33%)
Use of vasoactive medications	125 (13%)	62 (23%)	48 (19%)	56 (22%)
Nitric oxide	7 (1%)	5 (2%)	3 (1%)	5 (2%)
Severity of Illness Measures				
	Unmatched Analysis		Propensity-Matched Analysis	
	No Oseltamivir Treatment (N=993)	Oseltamivir Treatment (N=264)	No Oseltamivir Treatment (N=252)	Oseltamivir Treatment (N=252)
Total Number of Unique Charges on Hospital Day 1 (Median, IQR)	20 (11, 31)	28.5 (19.0, 46.5)	27 (17, 42)	28 (19, 44)
Risk of Mortality (Median, IQR)	0.0002 (0, 0.031)	0.0043 (0, 0.067)	0.0041 (0, 0.057)	0.0043 (0, 0.058)

Outcome	Oseltamivir-treatment within 24 hrs	Median (IQR)	Time Ratio (95% C.I.)	p-value
Total length of hospital stay	YES vs. NO	6 (3,11)	0.82	0.02
		9 (4, 17)	(0.69, 0.97)	
Total length of intensive care unit stay	YES vs. NO	4 (2, 8)	1.07	0.51
		4 (2, 10)	(0.88, 1.29)	

# Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments

BMJ 2014;348:g2545

**Figure 3:** Oseltamivir versus placebo for treatment. Time to first alleviation of symptoms in adult treatment (ITT population) [hours].



# BMJ

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12 December 2009 | bmj.com



## The truth about Tamiflu?

**PLUS** Hypothyroidism after pre-eclampsia  
Managing hepatocellular carcinoma  
Does weight loss improve sleep apnoea?

Jefferson T, Jones MA, Doshi P, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. *Cochrane Database Syst Rev.* 2012;(1):CD008965.

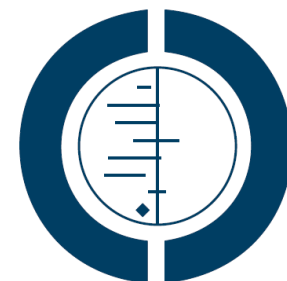
## Oseltamivir vs placebo in nonimmunocompromised adults and children\*

Outcomes	Number of trials (n)	Weighted event rates	Mean difference (95% CI)	
Hours to first symptom relief	5 (3713)		-21 (-30 to -13)	
			RRR (CI)	NNT (CI)
Hospitalization	8 (4696)	1.4% vs 1.5%	5% (-59 to 43)	Not significant
Diarrhea	9 (5651)†	5.2% vs 7.0%	26% (3 to 44)	55 (33 to 477)
			RRI (CI)	NNH (CI)
Nausea	9 (5651)†	8.5% vs 5.5%	55% (15 to 109)	34 (17 to 122)
Vomiting	9 (5651)†	7.9% vs 3.6%	119% (57 to 204)	24 (14 to 49)

\*RRR, RRI, NNT, NNH, and CI calculated from data in article using a random-effects model. All RCTs were done in treatment settings unless otherwise indicated.

†Oseltamivir was used for postexposure prophylaxis in 1 RCT (n = 955).

# Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children (Review)



THE COCHRANE  
COLLABORATION®

107 estudios clínicos!!!

Cochrane Database Syst Rev. 2014 Apr 10;4

Figure 4. Forest plot of comparison: 1 Oseltamivir versus placebo for treatment, outcome: 1.1 Time to first alleviation of symptoms in adult treatment (ITT population) [hours].

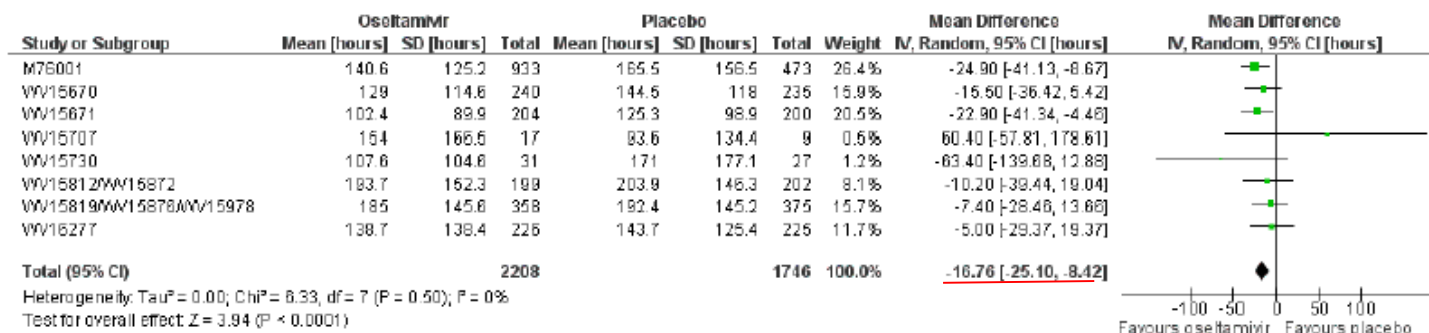
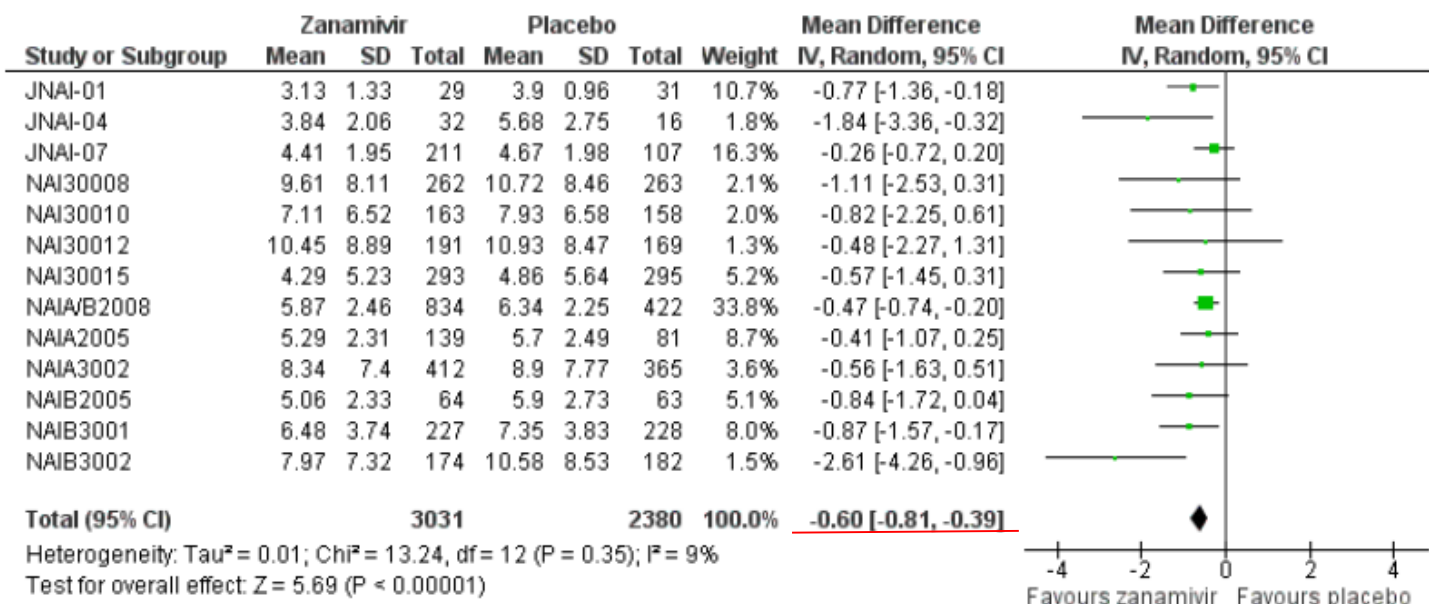


Figure 5. Forest plot of comparison: 3 Zanamivir versus placebo for treatment, outcome: 3.1 Time to first alleviation of symptoms in adult treatment (days).



**Time to first symptom alleviation.** For the treatment of adults, oseltamivir reduced the time to first alleviation of symptoms by 16.8 hours (95% confidence interval (CI) 8.4 to 25.1 hours,  $P < 0.0001$ ). This represents a reduction in the time to first alleviation of symptoms from 7 to 6.3 days. There was no effect in asthmatic children, but in otherwise healthy children there was (reduction by a mean difference of 29 hours, 95% CI 12 to 47 hours,  $P = 0.001$ ). Zanamivir reduced the time to first alleviation of symptoms in adults by 0.60 days (95% CI 0.39 to 0.81 days,  $P < 0.00001$ ), equating to a reduction in the mean duration of symptoms from 6.6 to 6.0 days. The effect in children was not significant. In subgroup analysis we found no evidence of a difference in treatment effect for zanamivir on time to first alleviation of symptoms in adults in the influenza-infected and non-influenza-infected subgroups ( $P = 0.53$ ).

**Hospitalisations.** Treatment of adults with oseltamivir had no significant effect on hospitalisations: risk difference (RD) 0.15% (95% CI -0.78 to 0.91). There was also no significant effect in children or in prophylaxis. Zanamivir hospitalisation data were unreported.

**Serious influenza complications or those leading to study withdrawal.** In adult treatment trials, oseltamivir did not significantly reduce those complications classified as serious or those which led to study withdrawal (RD 0.07%, 95% CI -0.78 to 0.44), nor in child treatment trials; neither did zanamivir in the treatment of adults or in prophylaxis. There were insufficient events to compare this outcome for oseltamivir in prophylaxis or zanamivir in the treatment of children.

**Pneumonia.** Oseltamivir significantly reduced self reported, investigator-mediated, unverified pneumonia (RD 1.00%, 95% CI 0.22 to 1.49); number needed to treat to benefit (NNTB) = 100 (95% CI 67 to 451) in the treated population. The effect was not significant in the five trials that used a more detailed diagnostic form for pneumonia. There were no definitions of pneumonia (or other complications) in any trial. No oseltamivir treatment studies reported effects on radiologically confirmed pneumonia. There was no significant effect on unverified pneumonia in children. There was no significant effect of zanamivir on either self reported or radiologically confirmed pneumonia. In prophylaxis, zanamivir significantly reduced the risk of self reported, investigator-mediated, unverified pneumonia in adults (RD 0.32%, 95% CI 0.09 to 0.41); NNTB = 311 (95% CI 244 to 1086), but not oseltamivir.

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Committee of Public Accounts

## Access to clinical trial information and the stockpiling of Tamiflu

Thirty-fifth Report of Session 2013–14

The number one risk on the Government's national risk-assessment for civil emergencies, ahead of both coastal flooding and a major terrorist incident, is the risk of pandemic influenza. Between 2006-07 and 2012-13, the Department spent £560 million on stockpiling two antiviral medicines for use in an influenza pandemic—£424 million on Tamiflu and £136 million on Relenza.

**Recommendation:** *Once the Cochrane Collaboration has completed its review of Tamiflu using all clinical study report information, the Department, MHRA and NICE should consider whether it is necessary to revisit previous judgements about the efficacy of Tamiflu.*

**Recommendation:** *Before spending the £49 million to maintain a stockpile at 50% population coverage, scheduled for 2013-14, the Department should review the appropriate level of population coverage; the level of stockpiling in other countries; and take into consideration the fact that the patent for Tamiflu expires in 2016.*

# O que é “funcionar”?

Reduzir excreção viral?

- Parcialmente

Reduzir tempo de sintomas?

- Um pouco

Reduzir complicações?

- Talvez

Reduzir hospitalização?

- Não

Reduzir mortalidade?

- Não

Doubt is not a  
pleasant condition,  
but certainty is  
absurd.

*Voltaire*