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Pneumònia vírica en l'àmbit de la Medicina Intensiva

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# Epidemiologia i impacte de la Grip A (H1N1)pdm09 a les UCIs espanyoles; període 2009-2014

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[1] Coordinador Nacional Registro GRIPE A SEMICYUC /GTEI

[2] Project Manager Base Datos GETGAG/SEMICYUC

# Financial Disclosure












# Resumen

- Introducción
- Población afectada e importancia
- ¿Qué aprendimos?
- Conclusiones

VIEWPOINT

# Critically Ill Patients With Influenza A(H1N1)pdm09 Virus Infection in 2014

**Corresponding Author:** Lena M. Napolitano, MD, University of Michigan, Department of Surgery, 1500 E Medical Center Dr, 1C340A-UH, Ann Arbor, MI 48109-5033 (lenan@umich.edu).

JAMA Published online February 24, 2014

The NEW ENGLAND JOURNAL of MEDICINE

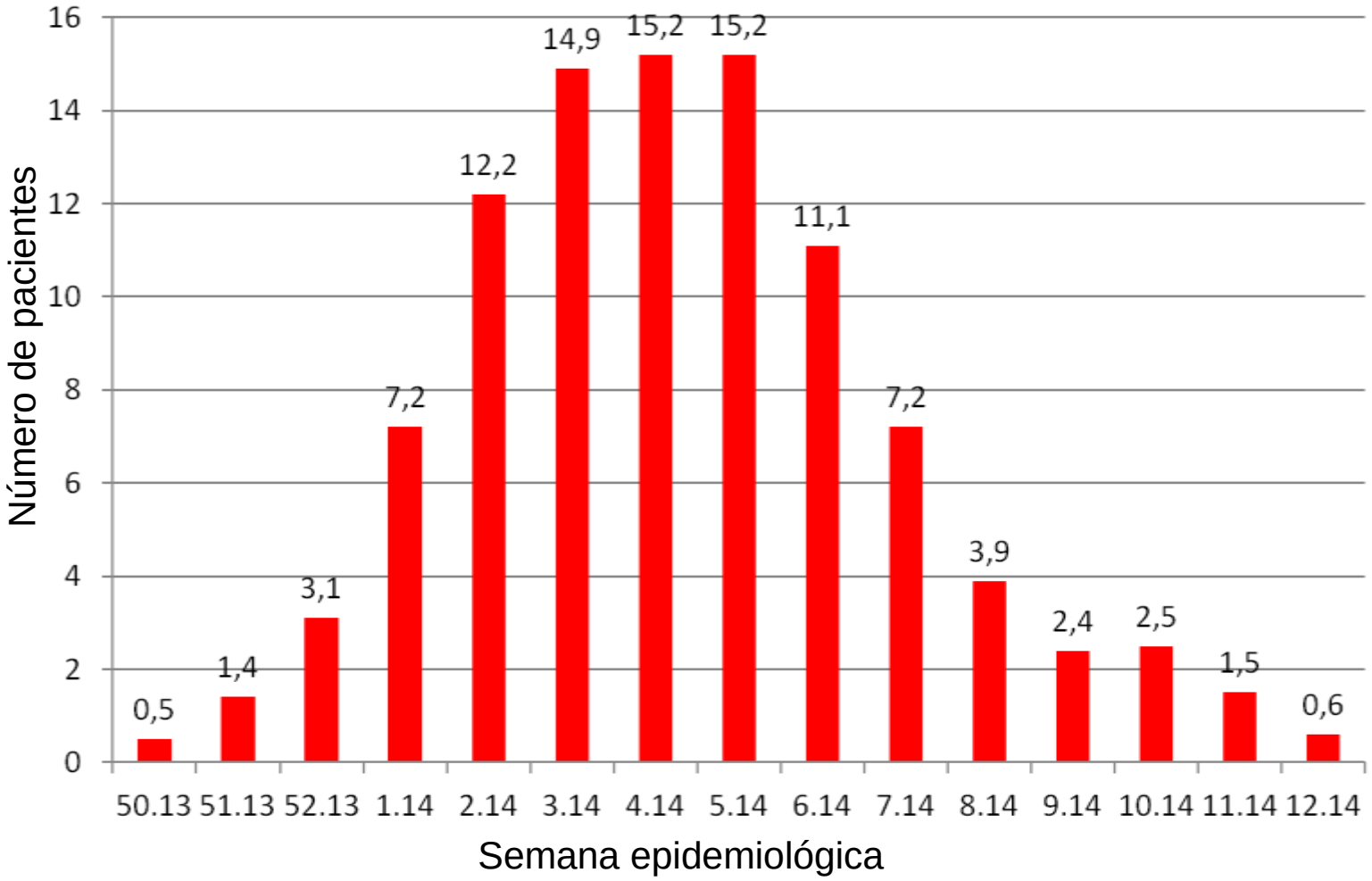
## Preventing and Controlling Influenza with Available Interventions

Timothy M. Uyeki, M.D., M.P.H., M.P.P.

Perspective

FEBRUARY 27, 2014

# 1083 pacientes ingresados en UCI durante 2014



# Tipo de virus diagnosticado

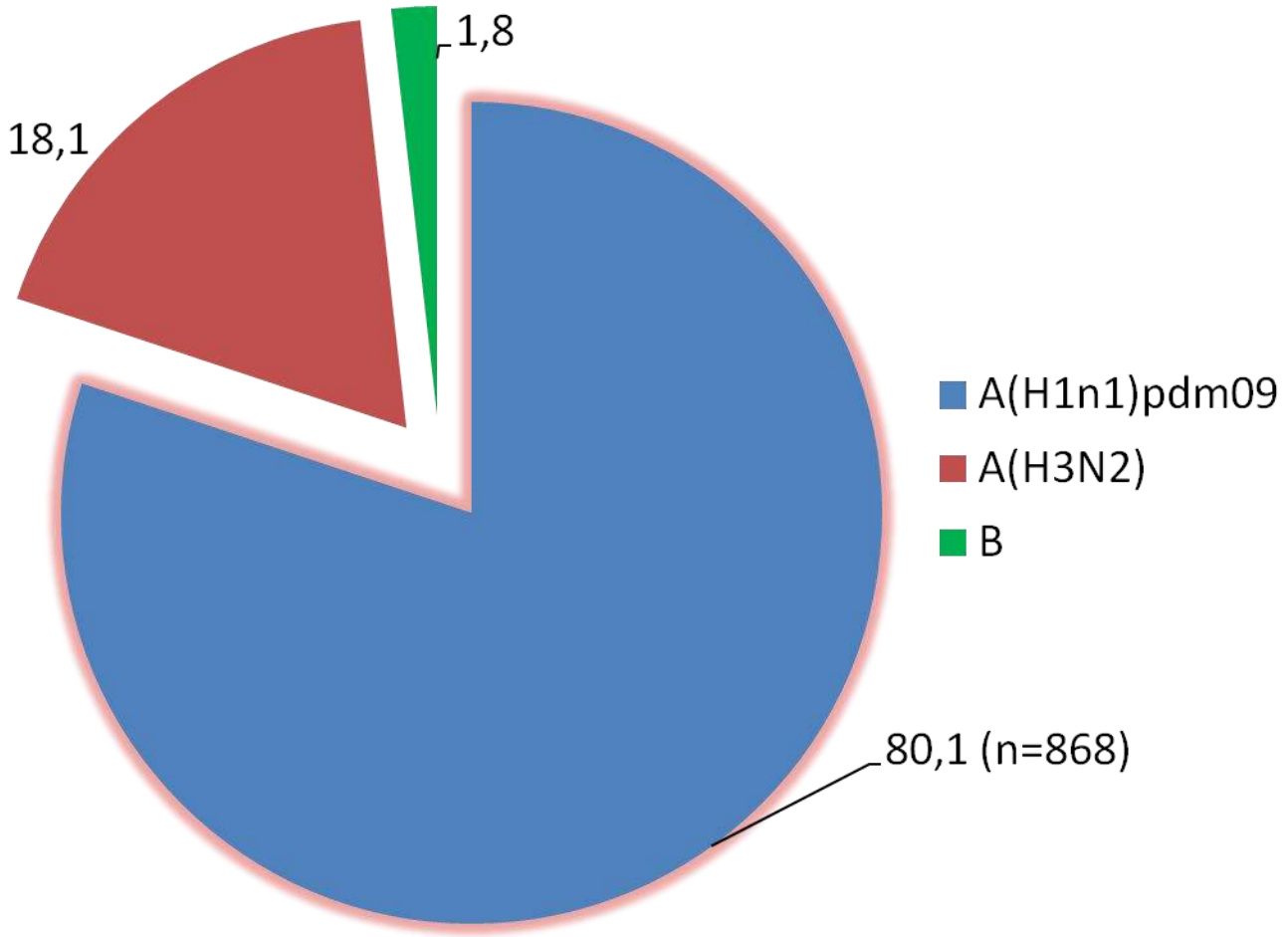
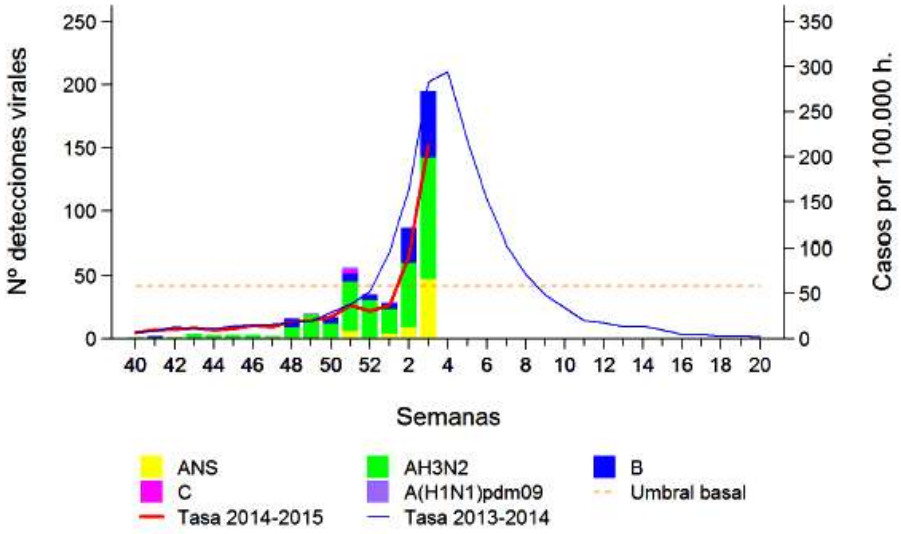
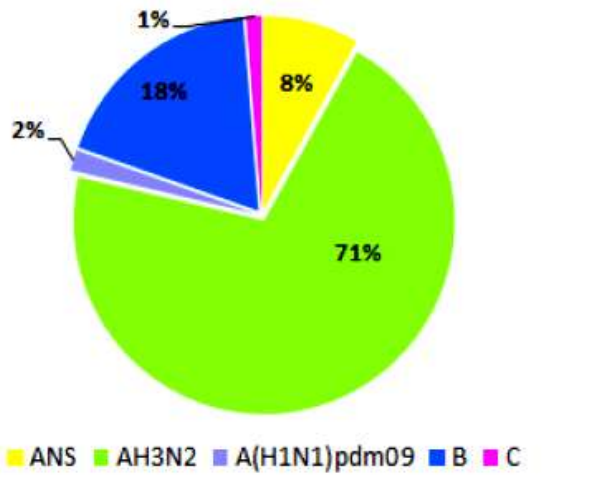


**Figura 1. Tasa de incidencia semanal de gripe y número de detecciones virales. Temporada 2014-2015. Sistemas centinela. España**



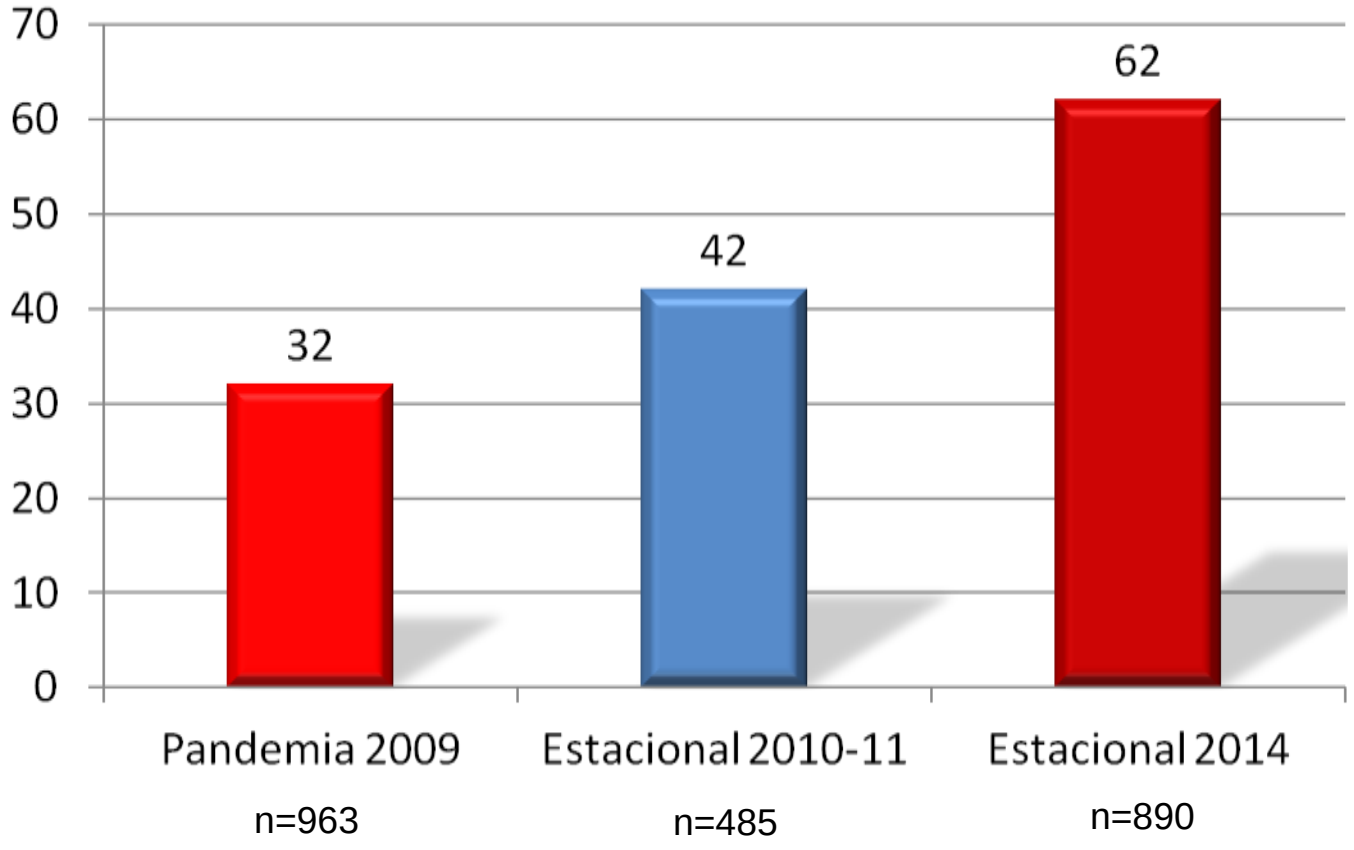

Fuente: CNE. Sistema centinela de Vigilancia de Gripe en España

**Figura 5. Detecciones centinela de virus de la gripe por tipo/subtipo de virus. Temporada 2014-2015. España**




Fuente: CNE. Sistema centinela de Vigilancia de Gripe en España

## Media de Ingresos en UCI / semana



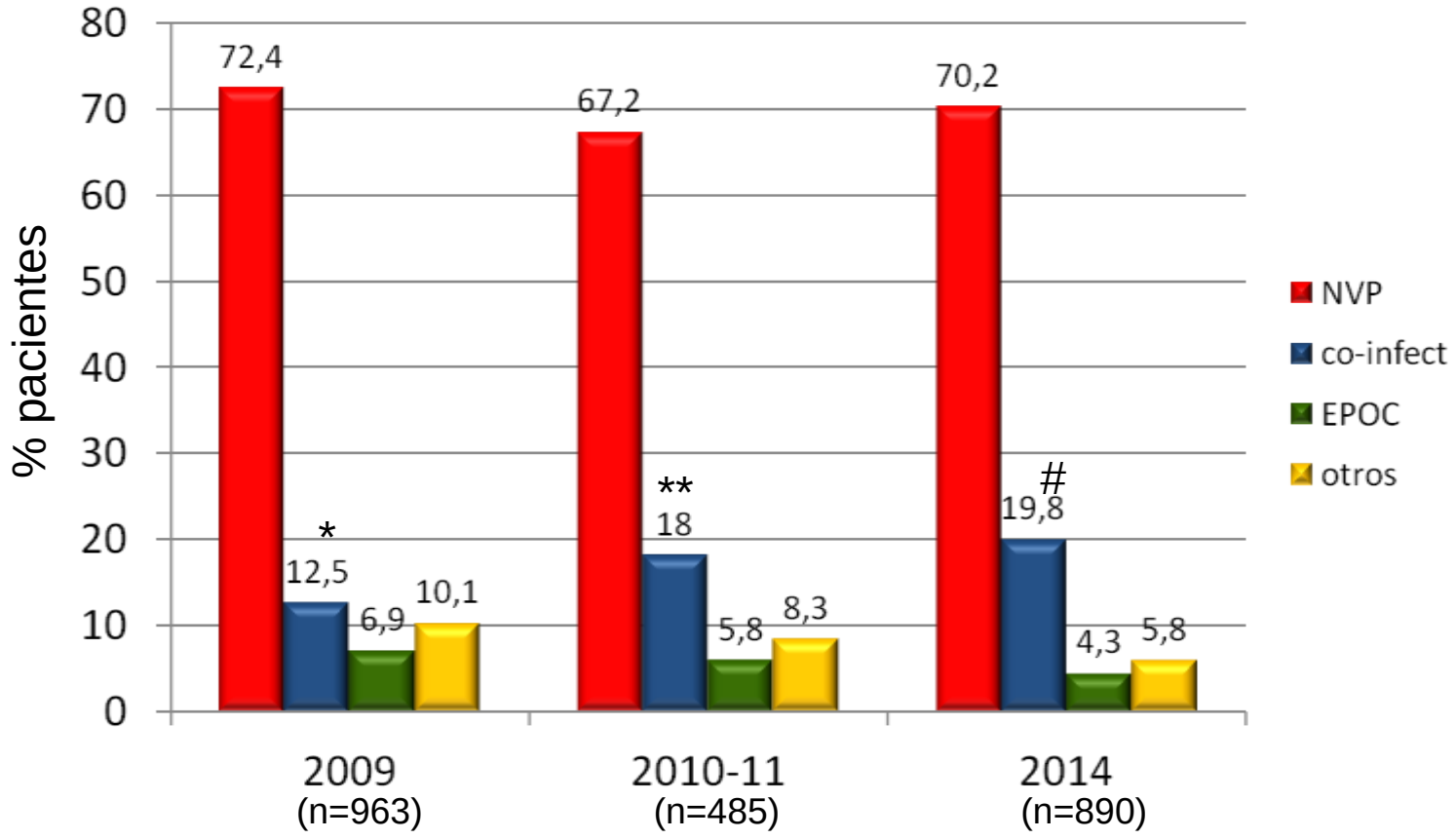
# ¿Qué tipo de pacientes ingresamos?

# Características demográficas de los 2338 pacientes ingresados en 148 UCIs españolas por Gripe A(H1N1)pdm09 desde 2009 al 2014.

| Variables | Gripe A 2009 (n=963) | Gripe A 2010-11 (n=485) | Gripe A 2014 (n=890) |
|---|---|---|---|
| **Edad en años** | | | |
| **Media (DE)** | 44,7 (14,9) | 50,1 (14,4)* | 55,1(14,6)* |
| **Mediana (25%-75%)** | 44 (34-54) | 51 (40-60)# | 56 (44-66)## |
| **Sexo masculino, n(%)** | 532 (55,0) | 316 (65,2)*# | 521 (58,5)## |
| **APACHE II , media (DE)** | 13,9 (7,2) | 16,3 (7,5)* | 16,7 (7,6)* |
| **SOFA , media (DE)** | 5,5 (3,5) | 6,3 (3,8)* | 6,4 (3,5)* |

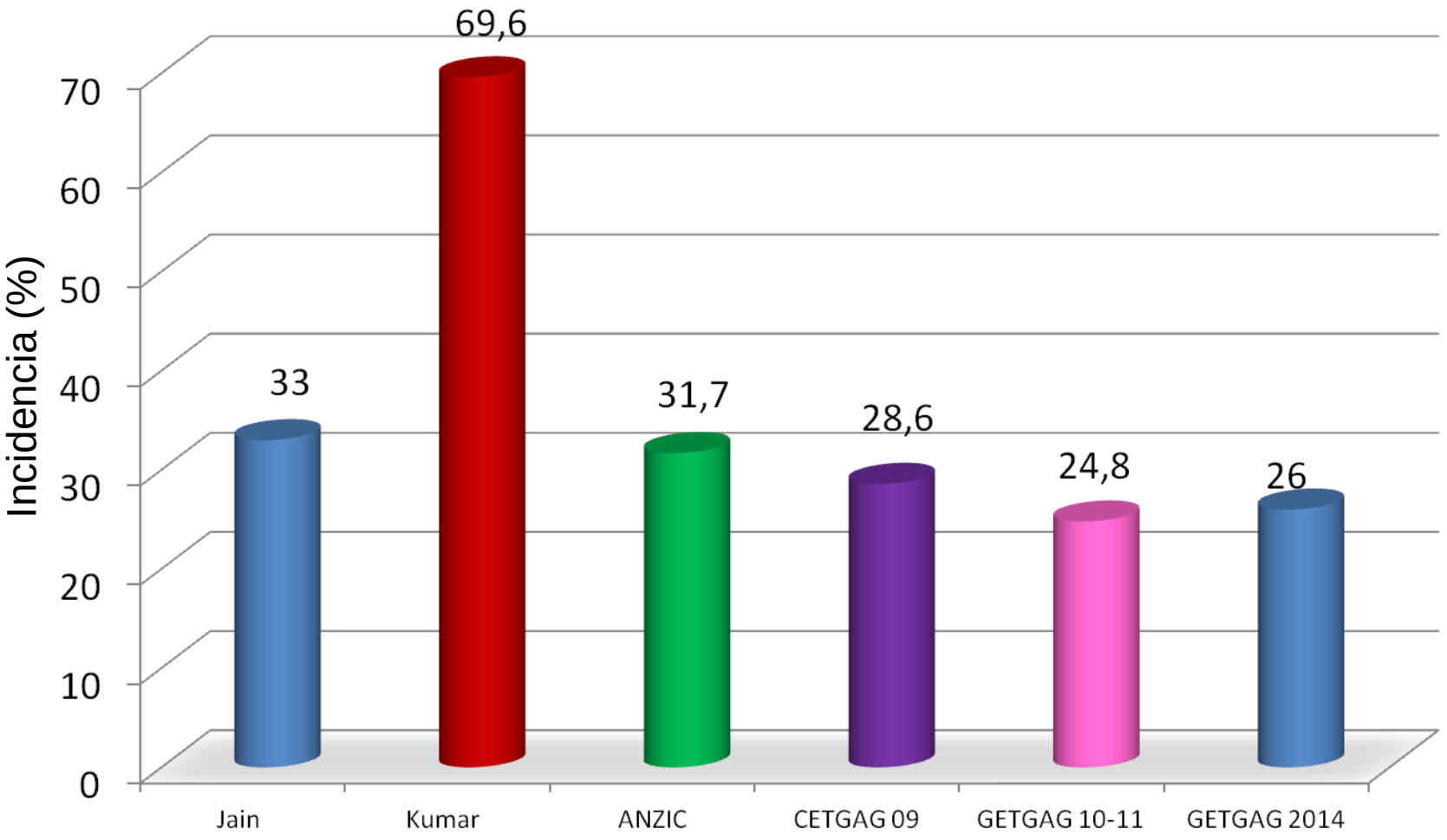
* p<0.01 para todas las comparaciones respecto de gripe A 2009; # vs. ## p<0.01

# Principales condiciones clínicas por la que ingresan a UCI con Gripe A(H1N1)pdm09

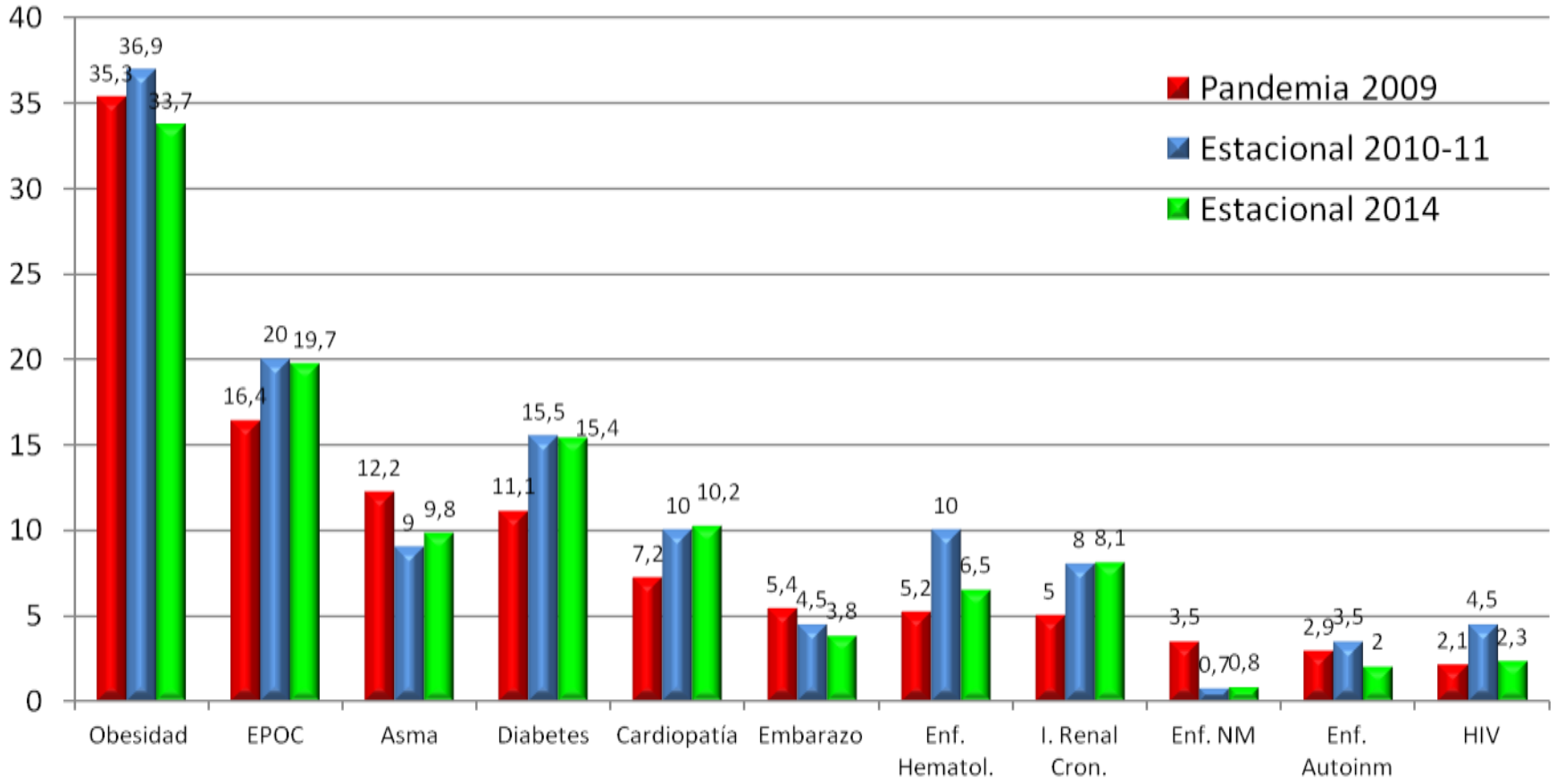



* vs. **: p<0.001 ; * vs. #: p<0.001

## Porcentaje de pacientes con Gripe A(H1N1)pdm09 que no presentan comorbilidades según diferentes autores y el registro GETGAG

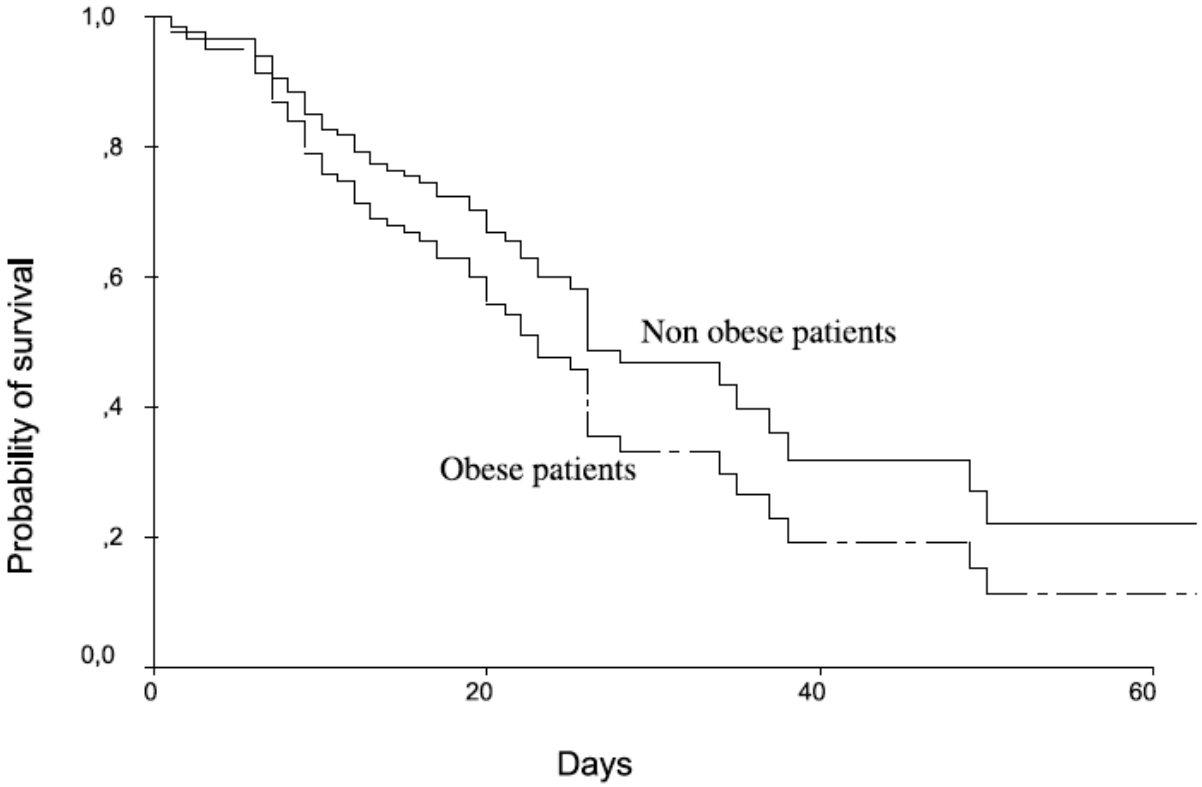


# Porcentaje de comorbilidades/factores de riesgo en los pacientes ingresados en UCI por gripe A(H1N1)pdm09(Base GETGAG)



# Impact of Obesity in Patients Infected With 2009 Influenza A(H1N1)

*Emili Díaz, MD, PhD; Alejandro Rodríguez, MD, PhD; Ignacio Martin-Loeches, MD, PhD; Leonardo Lorente, MD, PhD; María del Mar Martín, MD; Juan Carlos Pozo, MD; Juan Carlos Montejo, MD; Angel Estella, MD; Ángel Arenzana, MD; Jordi Rello, MD, PhD; and H1N1 SEMICYUC Working Group**




(hazard ratio 1.1; 95% CI, 0.69-1.75; $P = .68$)

*CHEST 2011; 139(2):382–386*

# Risk Factors for Severe Outcomes following 2009 Influenza A (H1N1) Infection: A Global Pooled Analysis

Maria D. Van Kerkhove[1,2], Katelijn A. H. Vandemaele[1], Vivek Shinde[1], Giovanna Jaramillo-Gutierrez[1], Artemis Koukounari[2], Christl A. Donnelly[2], Luis O. Carlino[3], Rhonda Owen[4], Beverly Paterson[4], Louise Pelletier[5], Julie Vachon[5], Claudia Gonzalez[6], Yu Hongjie[7], Feng Zijian[7], Shuk Kwan Chuang[8], Albert Au[8], Silke Buda[9], Gerard Krause[9], Walter Haas[9], Isabelle Bonmarin[10], Kiyosu Taniguichi[11], Kensuke Nakajima[12], Tokuaki Shobayashi[12], Yoshihiro Takayama[12], Tomi Sunagawa[11], Jean Michel Heraud[13], Arnaud Orelle[13], Ethel Palacios[14], Marianne A. B. van der Sande[15], C. C. H. Lieke Wielders[15], Darren Hunt[16], Jeffrey Cutter[17], Vernon J. Lee[18,19], Juno Thomas[20], Patricia Santa-Olalla[21], Maria J. Sierra-Moros[21], Wanna Hanshaoworakul[22], Kumnuan Ungchusak[22], Richard Pebody[23], Seema Jain[24], Anthony W. Mounts[1]*, on behalf of the WHO Working Group for Risk Factors for Severe H1N1pdm Infection

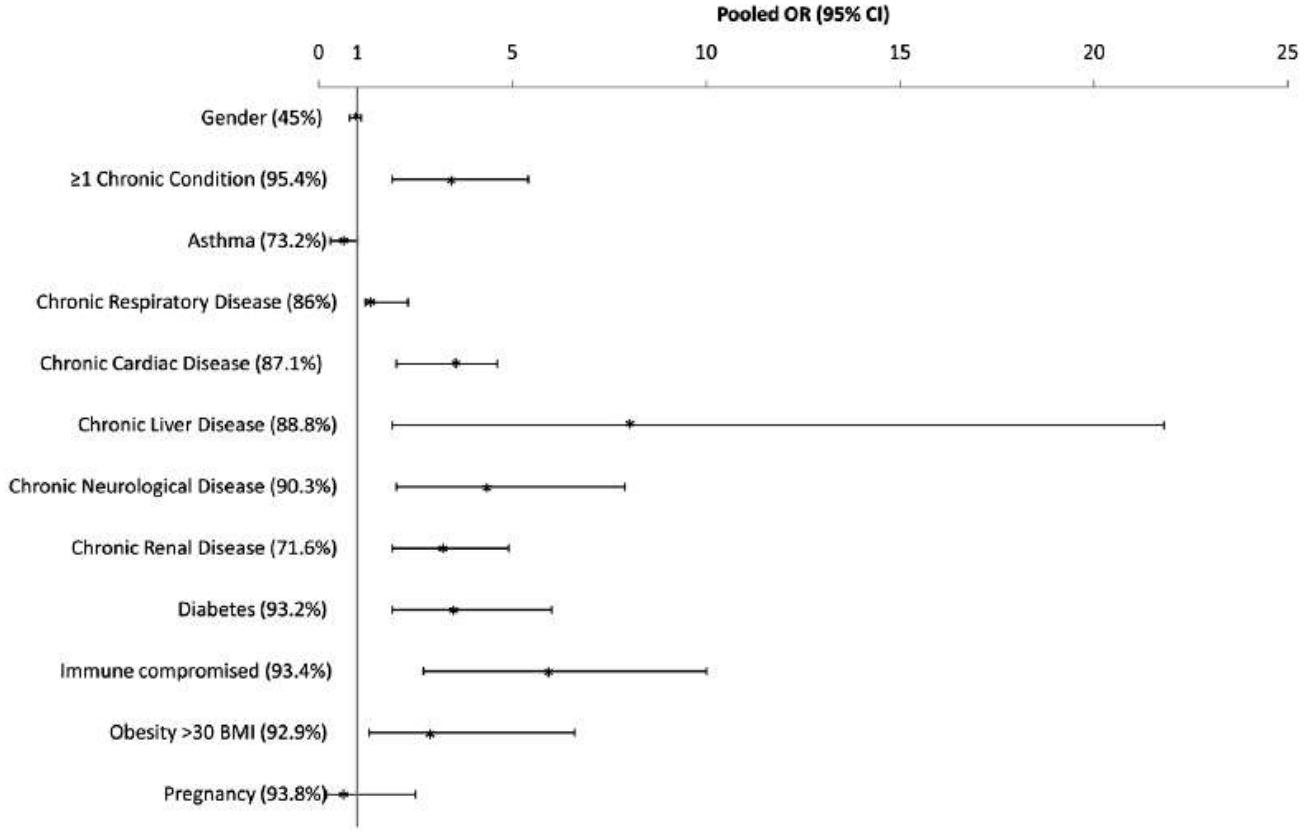



**Figure 3. Pooled odds ratio and 95% CIs of risk of death given hospitalization for selected countries.** See Text S1 for countries included in the pooled risk factor ORs.

# Influenza A H1N1 in HIV-infected adults*

E Martínez,[1] MA Marcos,[2] I Hoyo-Ulloa,[1,3] A Antón,[2] M Sánchez,[4] A Vilella,[5] M Larrousse,[1] I Pérez,[1] A Moreno,[1] A Trilla,[5] T Pumarola[2] and JM Gatell[1]

**Table 3** Prognosis in HIV-positive patients and HIV-negative controls presenting with influenza A H1N1 infection

| | HIV-positive patients ($n = 56$) | HIV-negative patients ($n = 168$) | *P*-value |
|---|---|---|---|
| Duration of hospital stay (days) (mean ± SD) | 1.1 ± 2.3 | 2.0 ± 3.4 | 0.0812 |
| ≥ 1 day at hospital [*n* (%)] | 15 (27) | 70 (42) | 0.0564 |
| Complications after admission [*n* (%)] | 7 (13) | 18 (11) | 0.8066 |
| Anti-influenza therapy (oseltamivir) [*n* (%)] | 53 (95) | 119 (71) | <0.0001 |
| Antibiotic therapy [*n* (%)] | 29 (52) | 82 (49) | 0.6997 |
| Clinical recovery <1 week [*n* (%)] | 43 (77) | 94 (56) | 0.0068 |
| Evolution to death [*n* (%)] | 0 (0) | 3 (2) | 0.5750 |

# HIV-Infected Hospitalized Patients with 2009 Pandemic Influenza A (pH1N1)—United States, Spring and Summer 2009

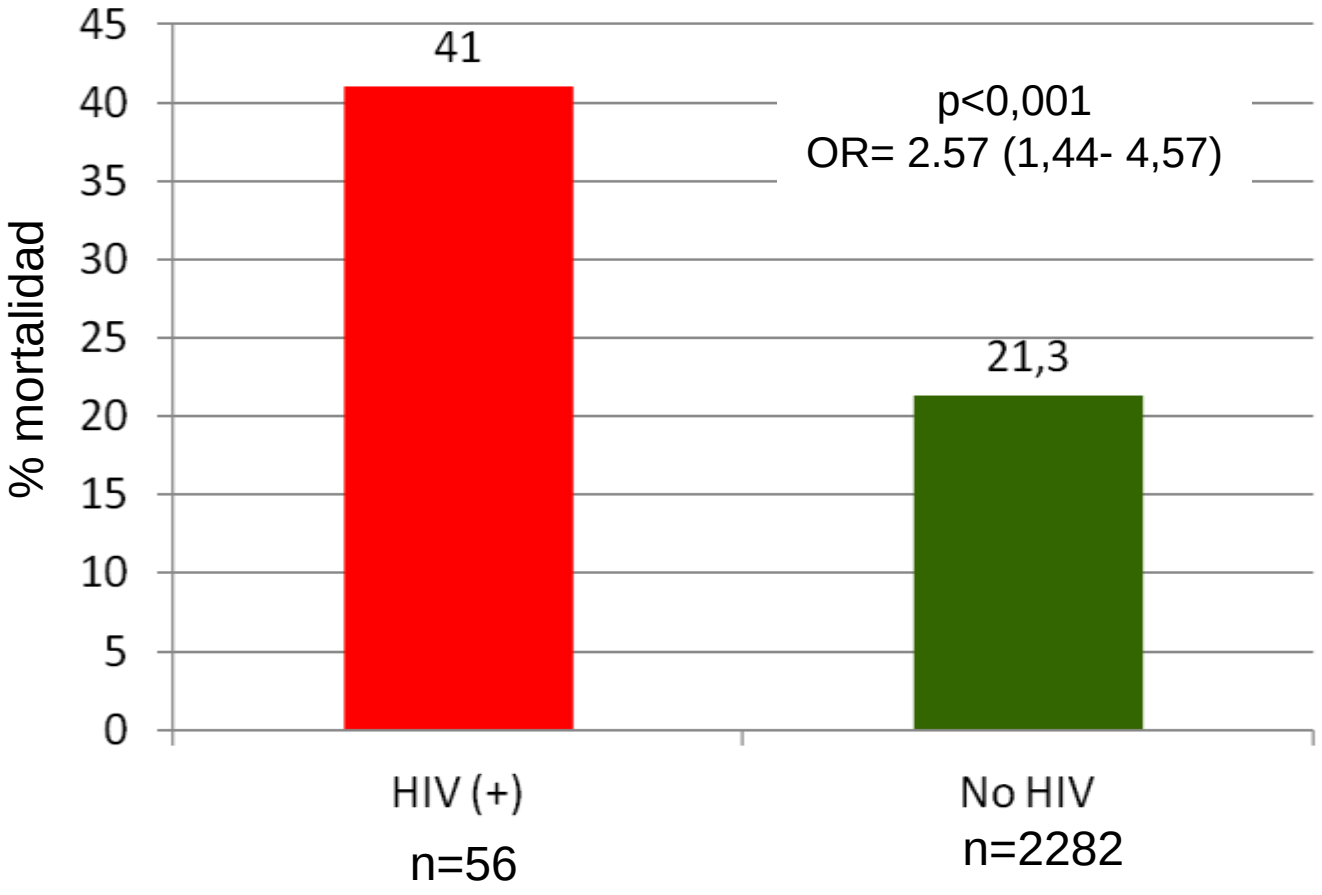
Philip J. Peters,[1] Jacek Skarbinski,[1] Janice K. Louie,[2] Seema Jain,[1] New York City Department of Health Swine Flu Investigation Team,[3] Michelle Roland,[4] Shilpa G. Jani,[2] Lyn Finelli,[1] and John T. Brooks[1]

**Table 3. Clinical Findings, Hospital Course, and Treatment of HIV-Infected and Non–HIV-Infected Hospitalized Adults with 2009 Pandemic Influenza A (pH1N1) in the United States Reported from 3 Case Series, April–August 2009[a]**

| Medical Conditions | HIV-infected | Non–HIV-infected | *P* value |
|---|---|---|---|
| Clinical Findings | | | |
| Positive influenza rapid test result | 9/19 (47) | 252/490 (51) | .82 |
| Infiltrates present on chest radiograph | 17/30 (57) | 488/789 (62) | .57 |
| Secondary bacterial infection diagnosed | 2/30 (7) | 43/880 (5) | .66 |
| Hospital Course | | | |
| Admitted to intensive care unit | 9/31 (29) | 300/875 (34) | .70 |
| Required mechanical ventilation | 6/29 (21) | 223/806 (28) | .53 |
| Died | 4/31 (13) | 118/879 (13) | 1.00 |
| Influenza Antiviral Treatment | | | |
| Received influenza antiviral treatment | 25/31 (81) | 672/831 (81) | 1.00 |
| Initiated treatment ≤48 h after symptom onset | 8/24 (33) | 221/592 (37) | .83 |

[a] Denominators are based on number of patients with available data.

# HIV y Mortalidad




Base datos GETGAG / No publicados

# Pandemic and post-pandemic Influenza A (H1N1) infection in critically ill patients

Ignacio Martin-Loeches[1,2*], Emili Díaz[2], Loreto Vidaur[3], Antoni Torres[4], Cesar Laborda[5], Rosa Granada[6], Juan Bonastre[7], Mar Martín[8], Josu Insausti[9], Angel Arenzana[10], Jose Eugenio Guerrero[11], Ines Navarrete[12], Jesus Bermejo-Martin[13], David Suarez[14] and Alejandro Rodriguez[2], for the H1N1 SEMICYUC/REIPI/CIBERES Working group

**Table 4 Multivariate analysis for risk factors associated with ICU mortality during the 2009 pandemic and post-pandemic Influenza (H1N1)v infection period.**

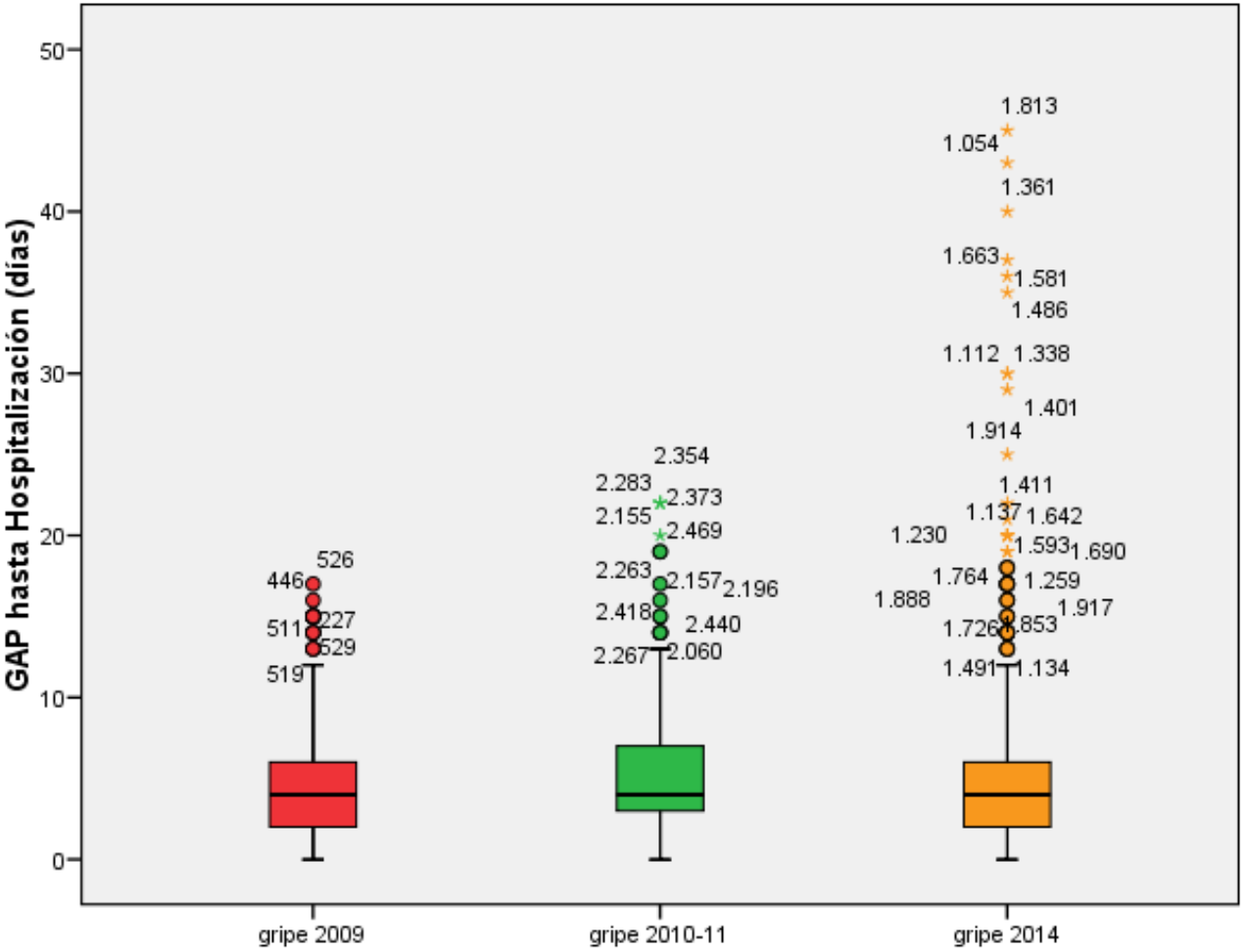
| Variable | OR | 95% CI | *P*-value |
|---|---|---|---|
| APACHE II score | 1.076 | 1.040 to 1.114 | <0.001 |
| Hematologic disease | 3.506 | 1.747 to 7.038 | <0.001 |
| Continuous renal replacement therapy | 5.812 | 3.101 to 10.893 | <0.001 |
| Invasive mechanical ventilation | 6.890 | 3.538 to 13.418 | <0.001 |
| HIV infection in pandemic Influenza (H1N1)v infection period * | 1.362 | 0.279 to 6.648 | 0.702 |
| HIV infection in post-pandemic Influenza (H1N1)v infection period * | 19.835 | 2.236 to 175.954 | 0.007 |

The interaction HIV infection with period was statistically significant (*P*-value = 0.05).

Abbreviations: HIV, human immunodeficiency virus; ICU, intensive care unit

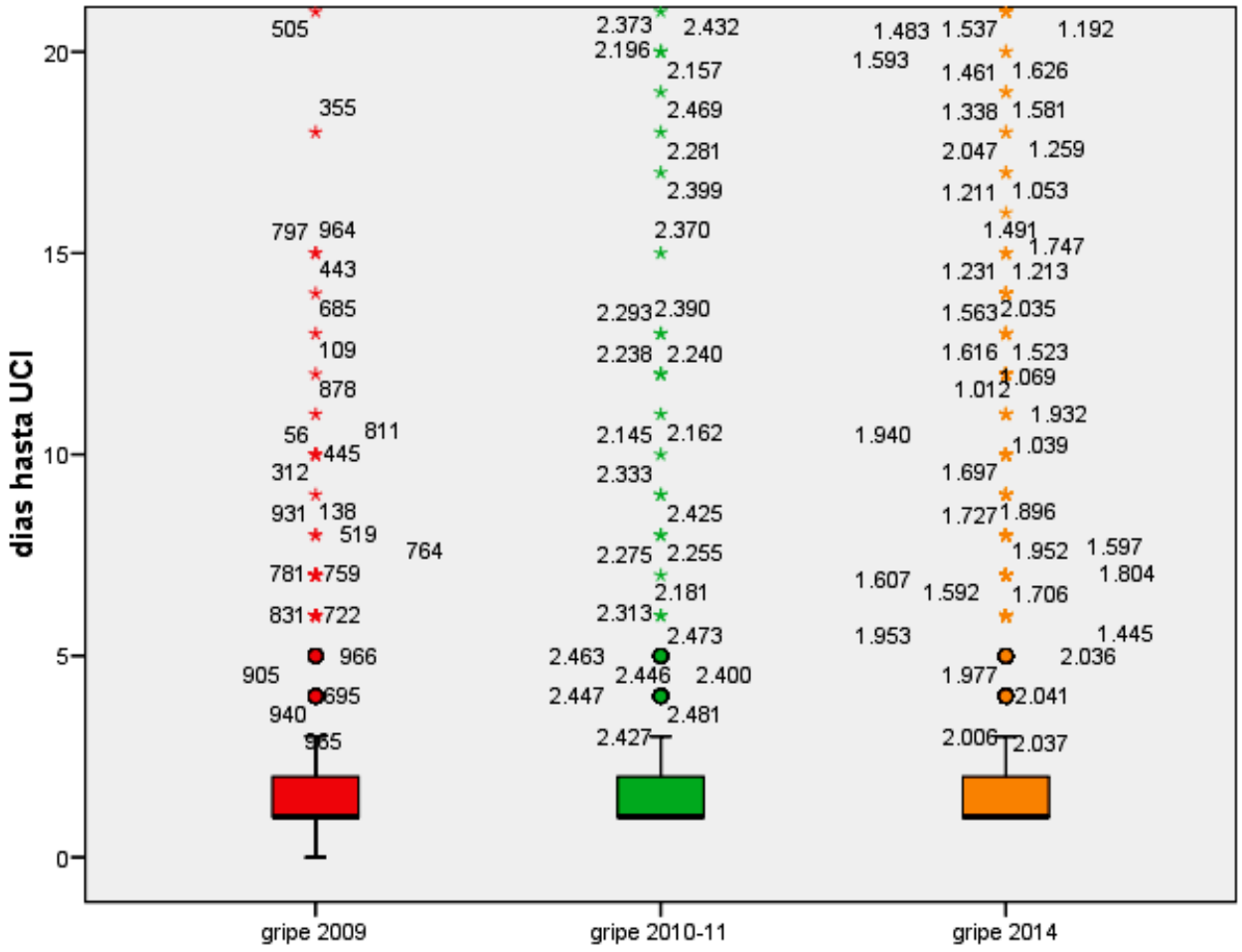
# ¿Qué asistencia sanitaria recibieron?

# DIAS HASTA HOSPITALIZACIÓN




4,3 (2,6) 4,8 (3,2) 4,8 ( 4,4) P<0,05

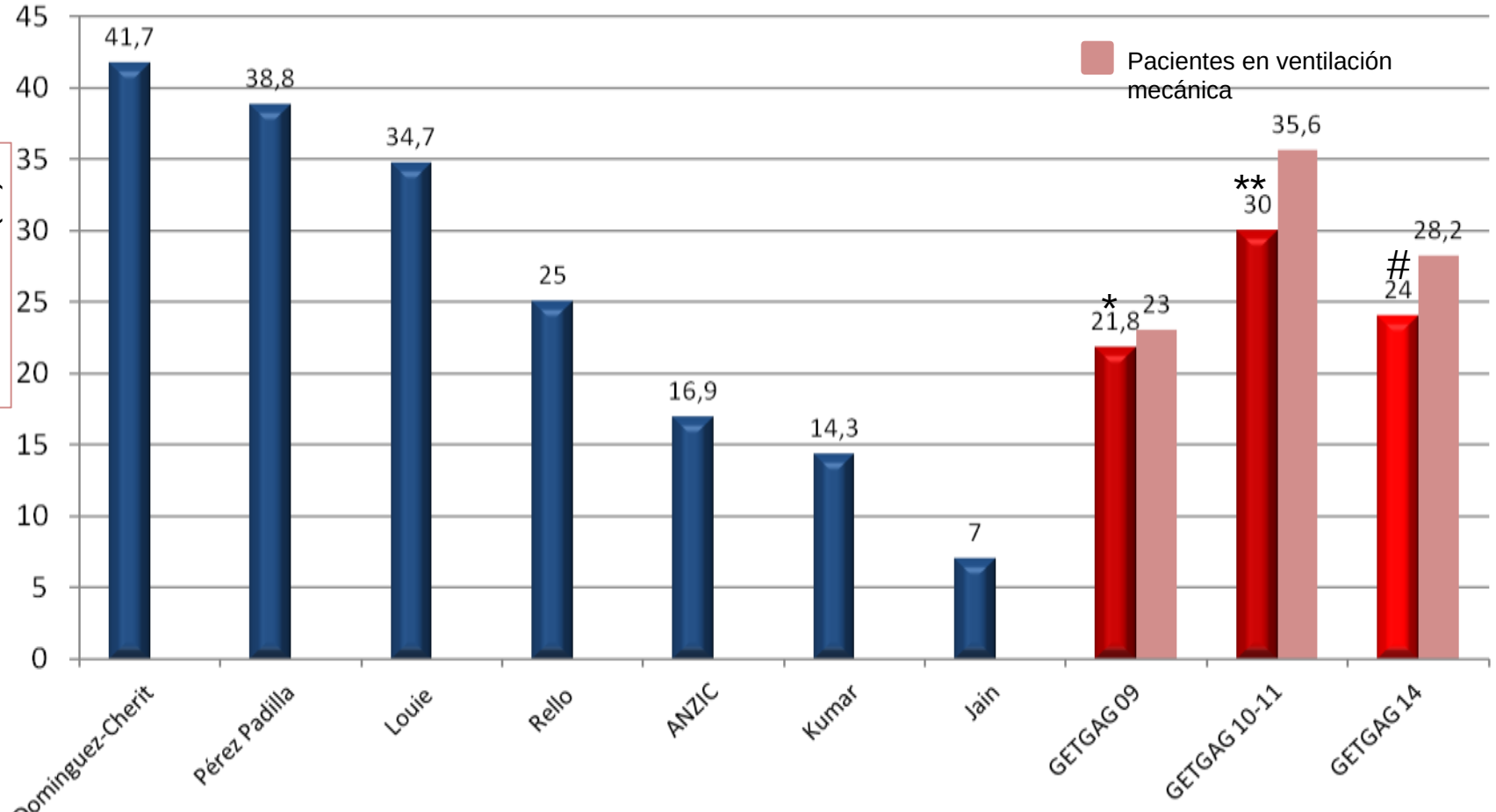
# DIAS HASTA UCI




1,8 (2,0) 2,1 (2,8) 2,6 (3,9) p<0,05

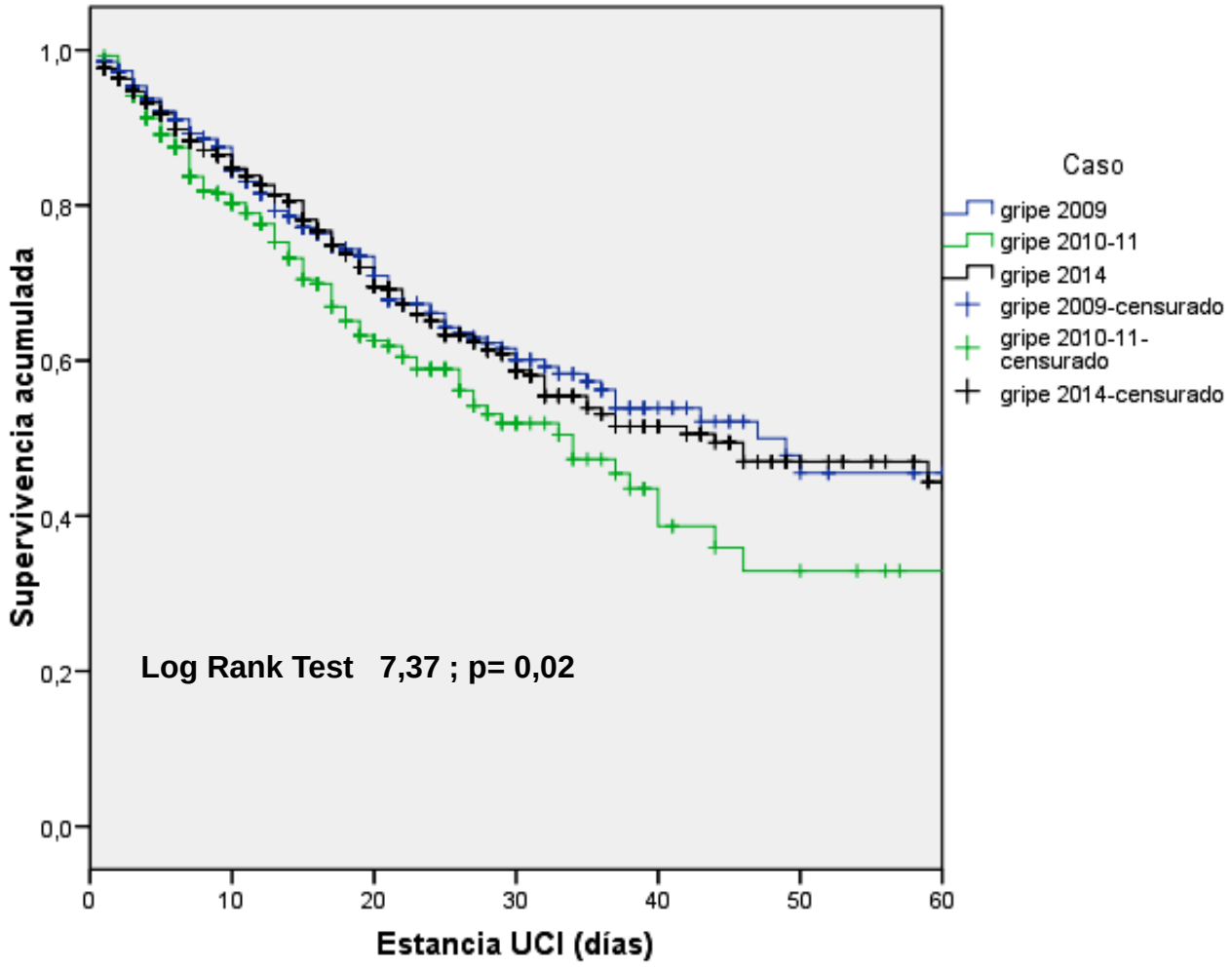
# ¿Qué mortalidad tienen los pacientes?

# Mortalidad cruda (%) de los pacientes hospitalizados por Gripe A(H1N1) según diferentes autores y en la base GETGAG

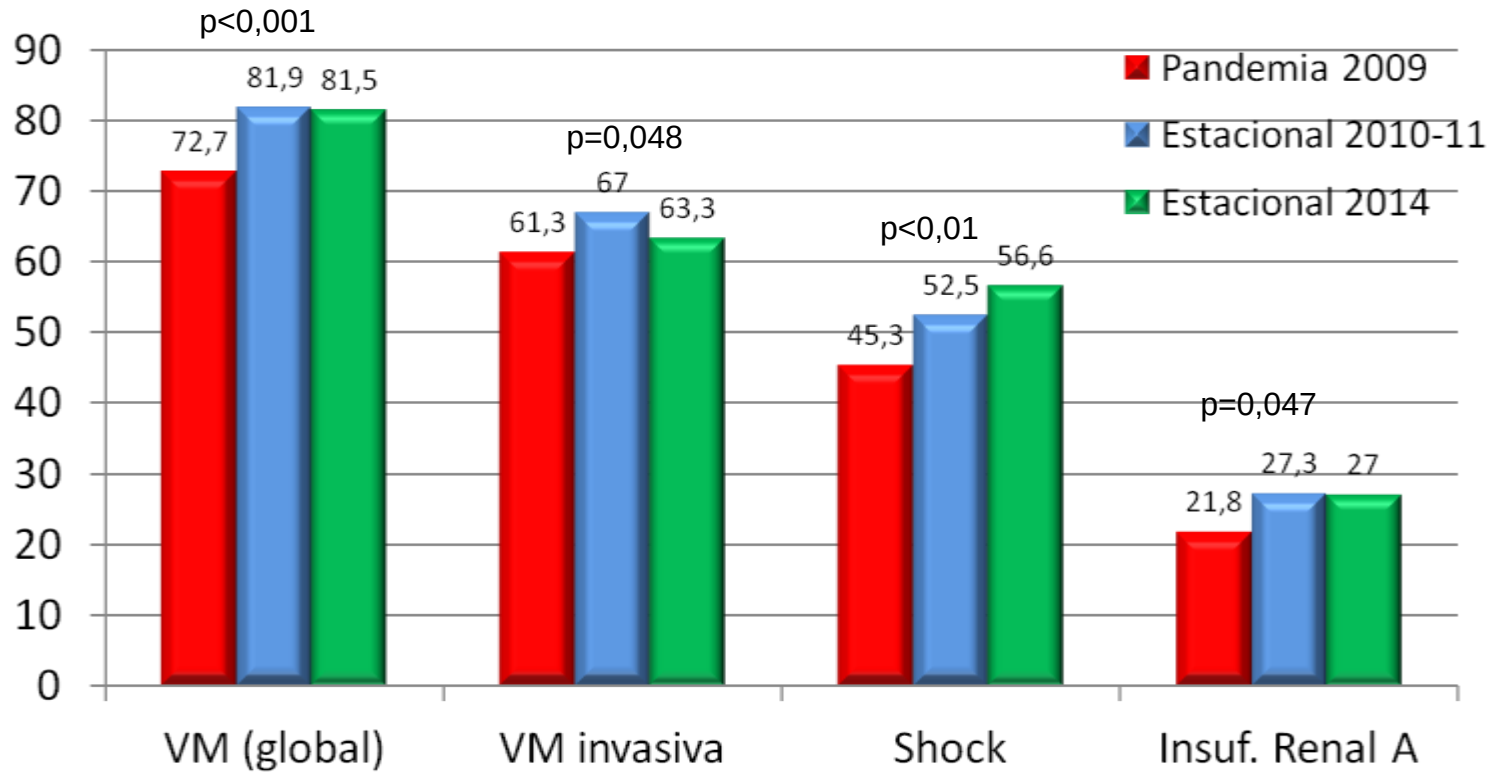



* vs. ** p<0,01 ; * vs. # p=0,04 ; ** vs. # p= 0,02

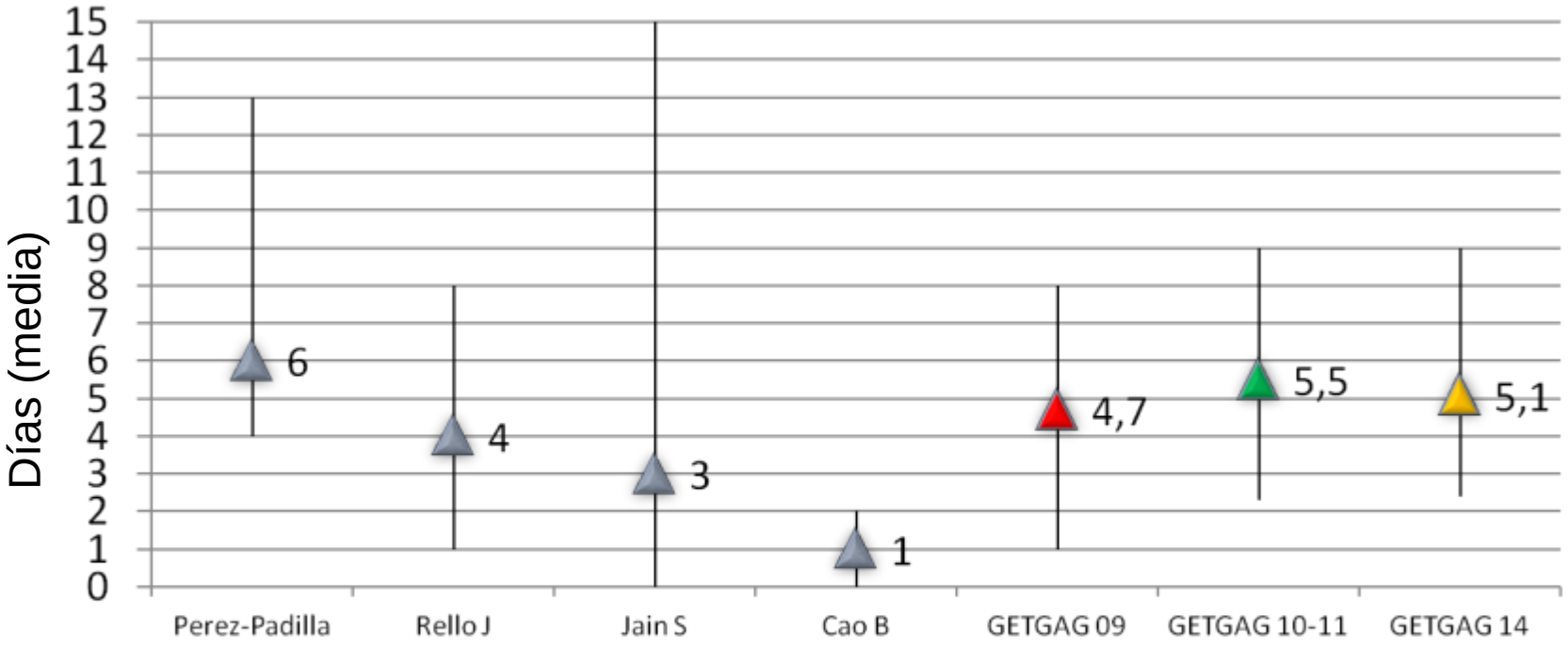
# Mortalidad en el tiempo (K-Meier) de los pacientes incluidos en la base de datos GETGAG según los diferentes periodos considerados



# Complicaciones (%)



**Tiempo medio transcurrido entre el inicio de los síntomas y la administración de la primera dosis del antiviral según diferentes autores y en la base GETGAG**



# Critically Ill Patients With 2009 Influenza A(H1N1) in Mexico

Guillermo Domínguez-Cherit, MD
Stephen E. Lapinsky, MB, BCh, MSc
Alejandro E. Macias, MD
Ruxandra Pinto, PhD(Stat)
Lourdes Espinosa-Perez, MD
Alethse de la Torre, MD
Manuel Poblano-Morales, MD
Jose A. Baltazar-Torres, MD
Edgar Bautista, MD
Abril Martinez, MD
Marco A. Martinez, MD
Eduardo Rivero, MD
Rafael Valdez, MD
Guillermo Ruiz-Palacios, MD
Martín Hernández, MD
Thomas E. Stewart, MD
Robert A. Fowler, MD, MS(Epi)

JAMA. 2009;302(17):(doi:10.1001/jama.2009.1536)

## Hospitalized Patients with 2009 H1N1 Influenza in the United States, April–June 2009

Seema Jain, M.D., Laurie Kamimoto, M.D., M.P.H., Anna M. Bramley, M.P.H., Ann M. Schmitz, D.V.M., Stephen R. Benoit, M.D., M.P.H., Janice Louie, M.D., M.P.H., David E. Sugerman, M.D., M.P.H., Jean K. Druckenmiller, B.S., S.M.(N.R.M.), Kathleen A. Ritger, M.D., M.P.H., Rashmi Chugh, M.D., M.P.H., Supriya Jasuja, M.D., M.P.H., Meredith Deutscher, M.D., Sanny Chen, Ph.D., M.H.S., John D. Walker, M.D., Jeffrey S. Duchin, M.D., Susan Lett, M.D., M.P.H., Susan Soliva, M.P.H., Eden V. Wells, M.D., M.P.H., David Swerdlow, M.D., Timothy M. Uyeki, M.D., M.P.H., Anthony E. Fiore, M.D., M.P.H., Sonja J. Olsen, Ph.D., Alicia M. Fry, M.D., M.P.H., Carolyn B. Bridges, M.D., Lyn Finelli, Dr.P.H., for the 2009 Pandemic Influenza A (H1N1) Virus Hospitalizations Investigation Team*

N Engl J Med 2009;361:1935-44.

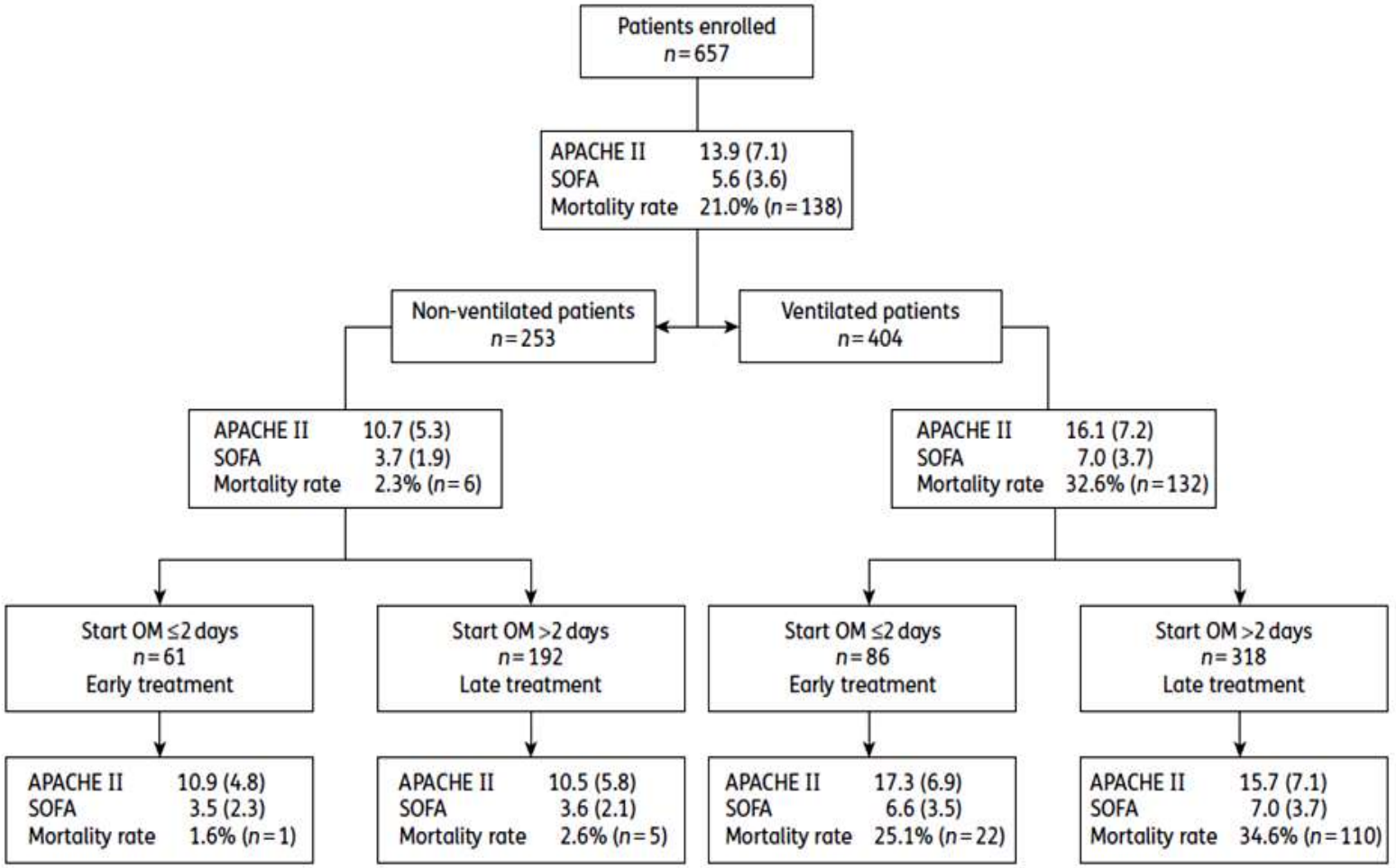
respectively; $P = .52$). After excluding patients dying early (within 72 hours of illness onset), who may have had less opportunity to be exposed to neuraminidase inhibitors, survivors were more likely to have received treatment with neuraminidase inhibitors (odds ratio, 7.4; 95% CI, 1.8-31.0; $P = .006$).

model that included age, admission within 2 days or more than 2 days after the onset of illness, initiation of antiviral therapy within 2 days or more than 2 days after the onset of illness, and influenza-vaccination status, the only variable that was significantly associated with a positive outcome was the receipt of antiviral drugs within 2 days after the onset of illness.

# Impact of early oseltamivir treatment on outcome in critically ill patients with 2009 pandemic influenza A

Alejandro Rodríguez[1*], Emili Díaz[1], Ignacio Martín-Loeches[1], Alberto Sandiumenge[1], Laura Canadell[2], Juan J. Díaz[3], Juan C. Figueira[4], Asunción Marques[5], Francisco Álvarez-Lerma[6], Jordi Vallés[7], Bárbara Baladín[8], Fernando García-López[9], Borja Suberviola[10], Rafael Zaragoza[11], Sandra Trefler[12], Juan Bonastre[13], José Blanquer[14] and Jordi Rello[12] on behalf of the H1N1 SEMICYUC Working Group†

Journal of Antimicrobial Chemotherapy




*J Antimicrob Chemother*
doi:10.1093/jac/dkq511

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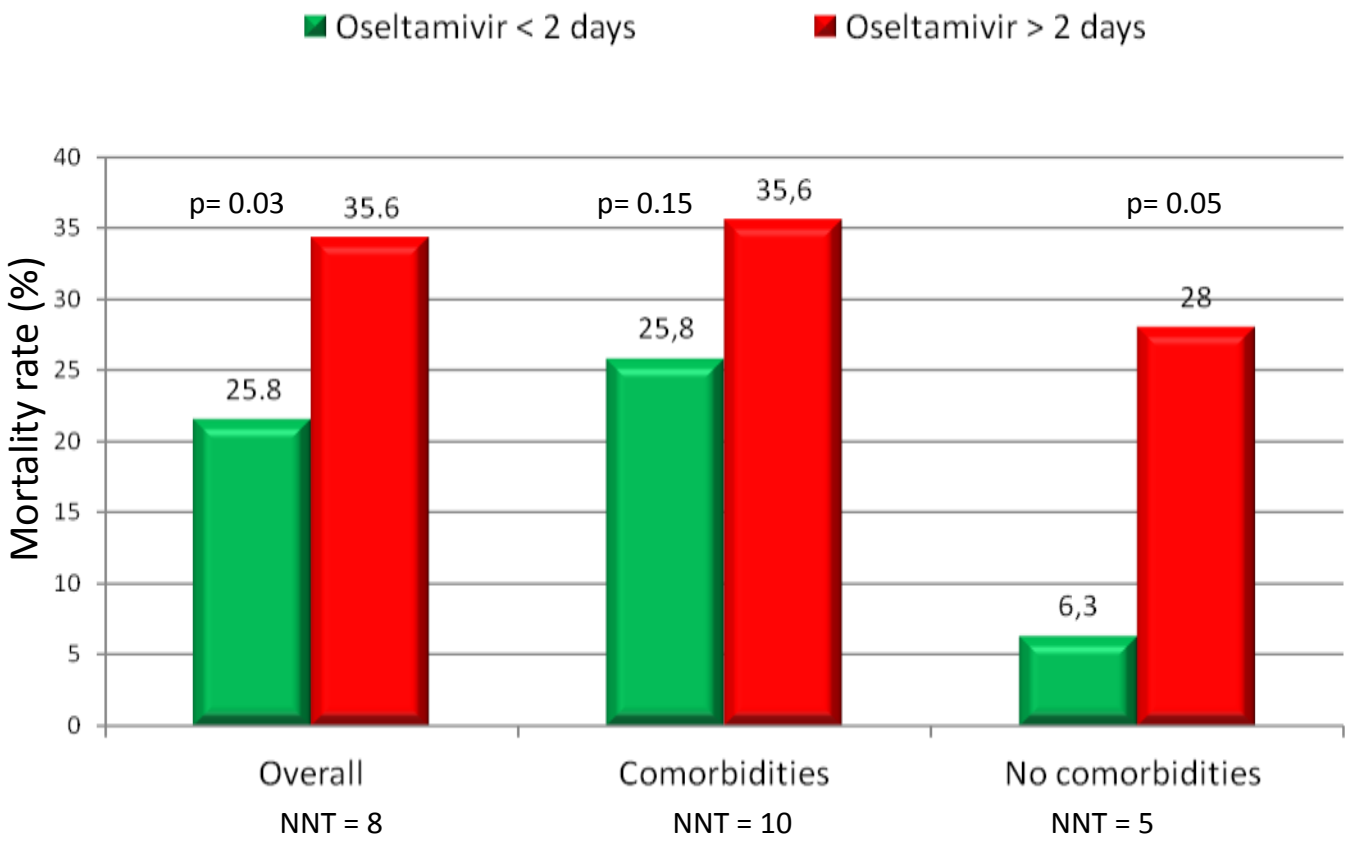
Journal of Antimicrobial Chemotherapy

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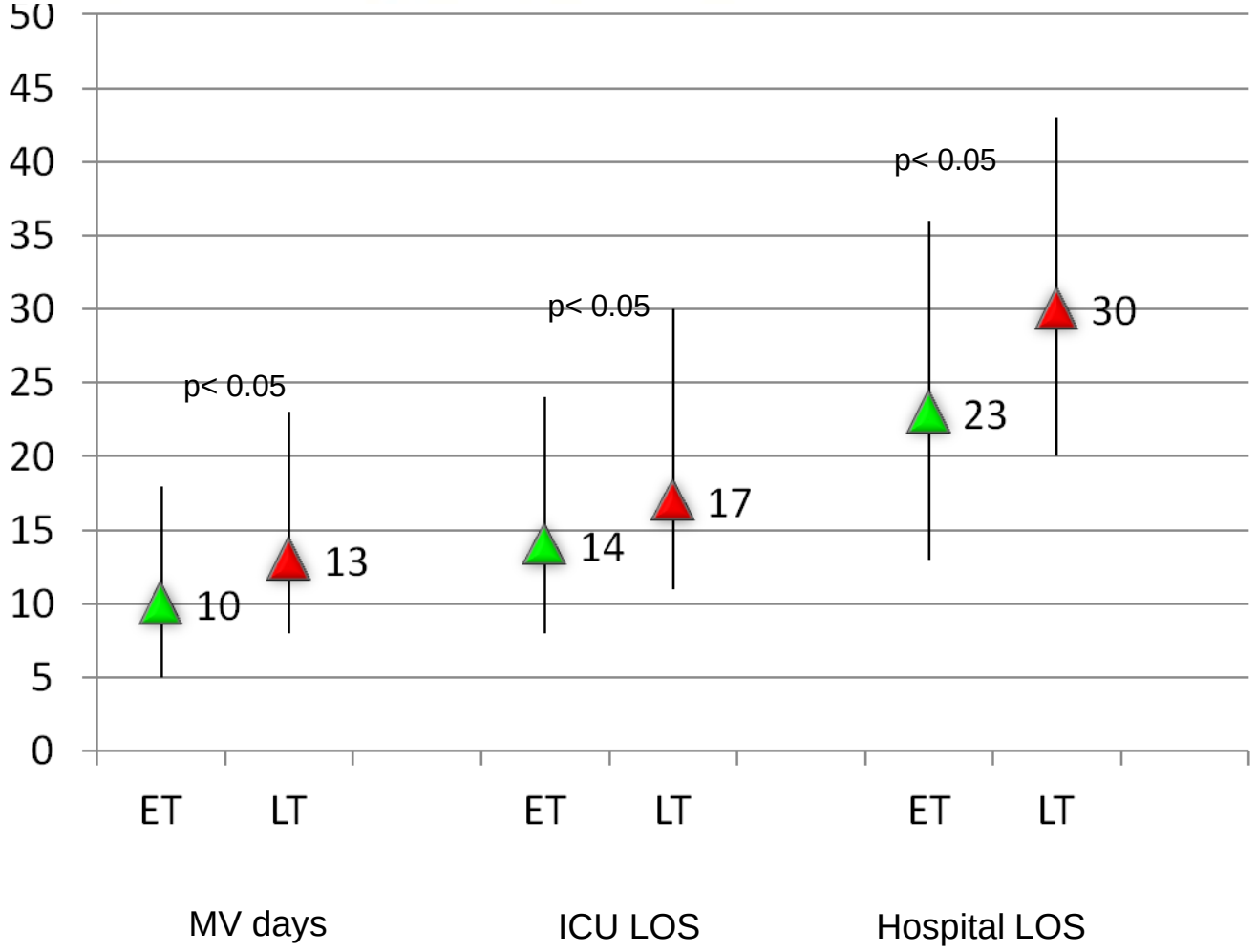
Journal of Antimicrobial Chemotherapy

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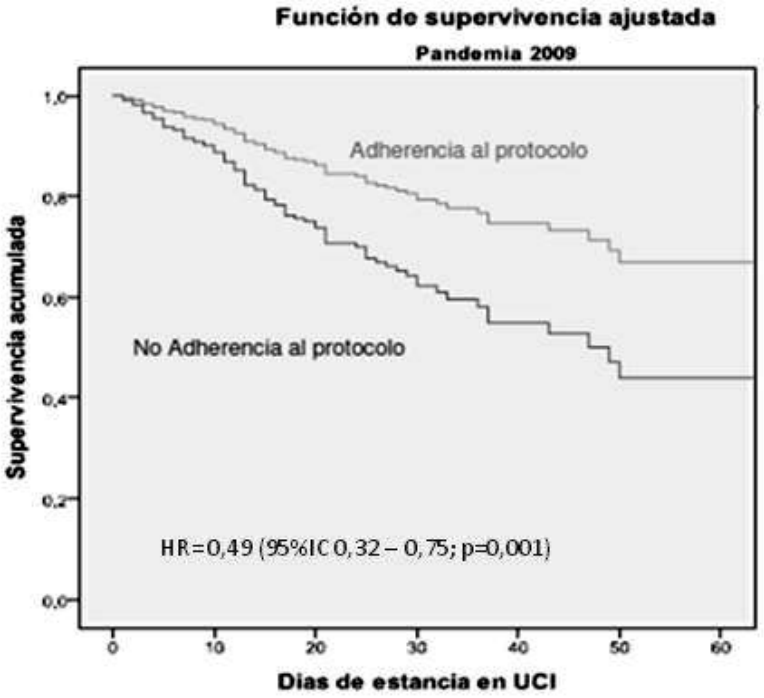
Journal of Antimicrobial Chemotherapy

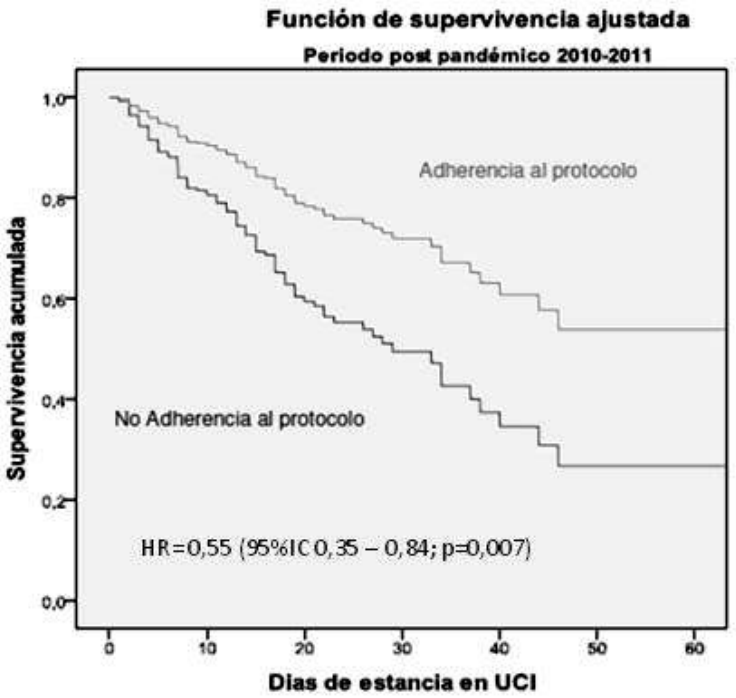
Impact of Early Oseltamivir Treatment on mortality (Multivariate analysis)

| Variable | OR 95% CI | p-value |
|---|---|---|
| Prone ventilation | 2.75 (1.45 – 5.23) | 0.001 |
| Quadrants infiltrates in chest x-ray | 1.70 (1.28 – 2.25) | 0.001 |
| APACHE II (by point) | 1.10 (1.05 – 1.14) | 0.001 |
| **Early OM treatment** | **0.44 (0.21 – 0.87)** | **0.02** |

*J Antimicrob Chemother*
doi:10.1093/jac/dkq511

# Adherencia a las recomendaciones de tratamiento antiviral y mortalidad




Canadell L et al. Med Intensiva 2014

REVIEW | Annals of Internal Medicine

# Antivirals for Treatment of Influenza

## A Systematic Review and Meta-analysis of Observational Studies

*Ann Intern Med.* 2012;156:512-524.

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**Conclusion:** Therapy with oral oseltamivir and inhaled zanamivir may provide a net benefit over no treatment of influenza. However, as with the randomized trials, the confidence in the estimates of the effects for decision making is low to very low.

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MAJOR ARTICLE

# Impact of Neuraminidase Inhibitor Treatment on Outcomes of Public Health Importance During the 2009–2010 Influenza A(H1N1) Pandemic: A Systematic Review and Meta-Analysis in Hospitalized Patients

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***Conclusions.*** During the 2009–2010 influenza A(H1N1) pandemic, early initiation of NAI treatment reduced the likelihood of severe outcomes compared with late or no treatment.

***PROSPERO Registration.*** CRD42011001273.

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PLOS ONE

# The Value of Neuraminidase Inhibitors for the Prevention and Treatment of Seasonal Influenza: A Systematic Review of Systematic Reviews

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## Abstract

Controversy has arisen regarding the effectiveness of neuraminidase inhibitors (NIs), especially against influenza-related complications. A literature search was performed to critically assess the evidence collected by the available systematic reviews (SRs) regarding the benefits and disadvantages of NIs (oseltamivir, zanamivir) compared to placebos in healthy and at-risk individuals of all ages for prophylaxis and treatment of seasonal influenza. A SR was done using the Cochrane Database of Systematic Reviews, Health Technology Assessment Database, Database of Abstracts of Reviews of Effects, and Medline (January 2006–July 2012). Two reviewers selected SRs based on randomized clinical trials, which were restricted to intention-to-treat results, and they assessed review (AMSTAR) and study quality indicators (GRADE). The SRs included (N = 9) were of high quality. The efficacy of NIs in prophylaxis ranged from 64% (16–85) to 92% (37–99); the absolute risk reduction ranged from 1.2% to 12.1% (GRADE moderate to low). Clinically relevant treatment benefits of NIs were small in healthy adults and children suffering from influenza-like illness (GRADE high to moderate). Oseltamivir reduced antibiotic usage in healthy adults according to one SR, but this was not confirmed by other reviews (GRADE low). Zanamivir showed a preventive effect on antibiotic usage in children (95% (77–99);GRADE moderate) and on the occurrence of bronchitis in at-risk individuals (59% (30–76);GRADE moderate). No evidence was available on the treatment benefits of NIs in elderly and at-risk groups and their effects on hospitalization and mortality. In oseltamivir trials, nausea, vomiting and diarrhea were significant side-effects. For zanamivir trials, no adverse effects have been reported. The combination of diagnostic uncertainty, the risk for virus strain resistance, possible side effects and financial cost outweigh the small benefits of oseltamivir or zanamivir for the prophylaxis and treatment of healthy individuals. No relevant benefits of these NIs on complications in at-risk individuals have been established.

# Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data

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**Findings** We included data for 29 234 patients from 78 studies of patients admitted to hospital between Jan 2, 2009, and March 14, 2011. Compared with no treatment, neuraminidase inhibitor treatment (irrespective of timing) was associated with a reduction in mortality risk (adjusted odds ratio [OR] 0·81; 95% CI 0·70–0·93; p=0·0024). Compared with later treatment, early treatment (within 2 days of symptom onset) was associated with a reduction in mortality risk (adjusted OR 0·48; 95% CI 0·41–0·56; p<0·0001). Early treatment versus no treatment was also associated with a reduction in mortality (adjusted OR 0·50; 95% CI 0·37–0·67; p<0·0001). These associations with reduced mortality risk were less pronounced and not significant in children. There was an increase in the mortality hazard rate with each day's delay in initiation of treatment up to day 5 as compared with treatment initiated within 2 days of symptom onset (adjusted hazard ratio [HR 1·23] [95% CI 1·18–1·28]; p<0·0001 for the increasing HR with each day's delay).

**Interpretation** We advocate early instigation of neuraminidase inhibitor treatment in adults admitted to hospital with suspected or proven influenza infection.

**Funding** F Hoffmann-La Roche.

RESEARCH NEWS

# Study claiming Tamiflu saved lives was based on "flawed" analysis

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RESEARCH NEWS

# Study claiming Tamiflu saved lives was based on "flawed" analysis

Zosia Kmietowicz

## Have You Heard?"

# CDC Recommendations for Influenza Antiviral Medications Remain Unchanged

**April 10, 2014** – CDC continues to recommend the use of the neuraminidase inhibitor antiviral drugs (oral oseltamivir and inhaled zanamivir) as an important adjunct to influenza vaccination in the treatment of influenza. CDC's current influenza antiviral recommendations are available on the CDC website and are based on all available data, including the most recent Cochrane report, about the benefits of antiviral drugs in treating influenza.

# CONCLUSIONES

✓ Gripe A (H1N1)pdm09 es una entidad que se mantiene con escaso reconocimiento social

✓ Afecta a una población relativamente joven y condiciona frecuentemente insuficiencia respiratoria grave

✓ 3/10 pacientes no tienen comorbilidades graves y 2/10 fallecen

✓ La asistencia sanitaria es tardía así como el inicio del tratamiento AV

✓ La adherencia a las recomendaciones de tratamiento antiviral es baja y parece estar en relación con la mortalidad

✓ La vacunación y la administración de tratamiento antiviral precoz deberían ser medidas recomendadas en cada periodo invernal

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# GRACIAS

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