# Ιογενής πνευμονία

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# Η αιτιολογία της πνευμονίας της κοινότητας σύμφωνα με την μελέτη CAPITA

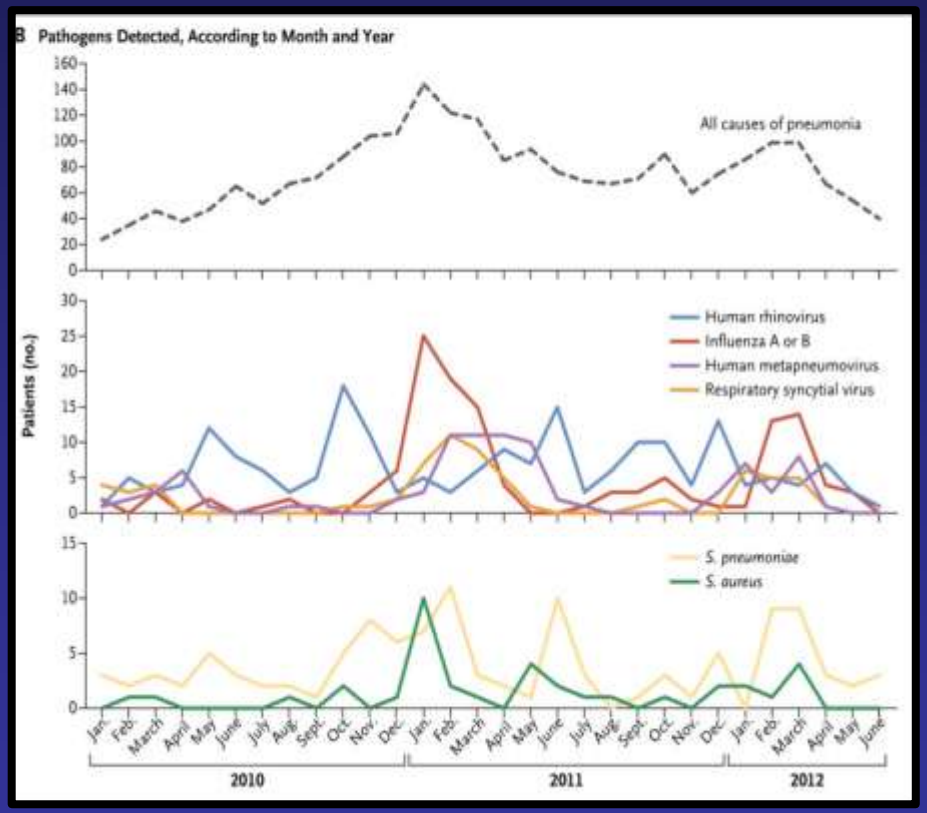
Huijts SM, et al. Clin Microbiol Infect 2018

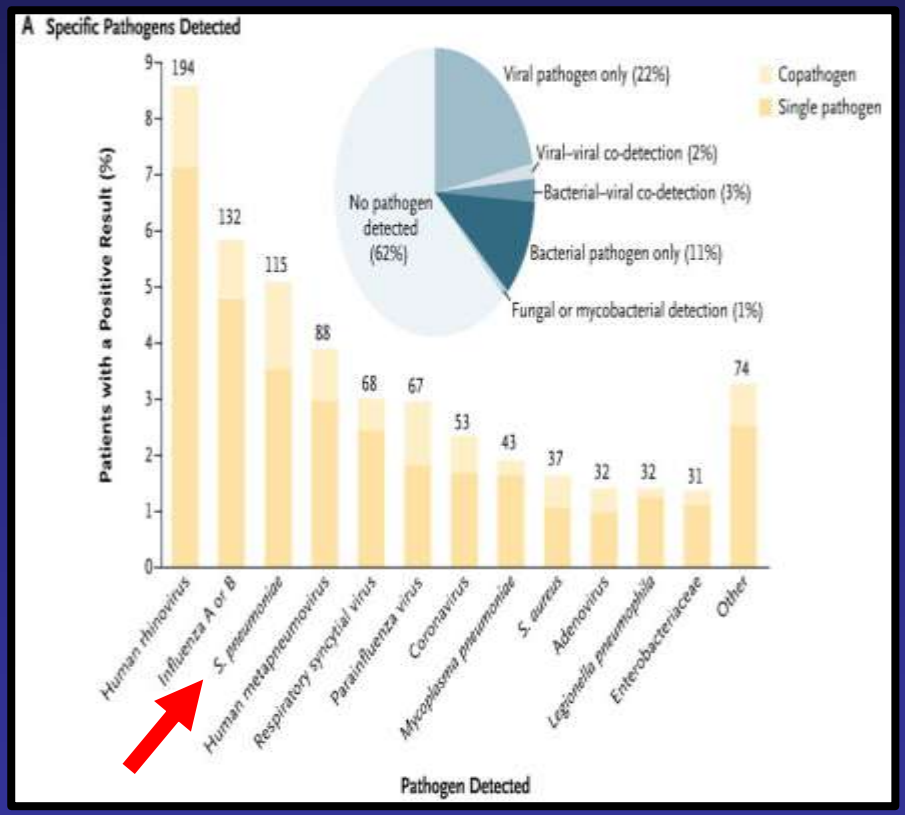
| Aetiological category | Pathogen | PCV13 (*n*) | Placebo (*n*) | Total (*n*) | % of total (*n* = 1653) |
|---|---|---|---|---|---|
| Bacterial | *Streptococcus pneumoniae* | 107 | 137 | 244 | 14.8% |
| | *Haemophilus (para)influenzae* | 25 | 24 | 49 | 3.3% |
| | *Staphylococcus aureus* | 8 | 14 | 22 | 1.3% |
| | *Pseudomonas aeruginosa* and *Pseudomonas* spp. | 6 | 14 | 20 | 1.2% |
| | *Escherichia coli* | 4 | 7 | 11 | 0.7% |
| | *Polymicrobial* | 8 | 3 | 11 | 0.7% |
| | Other | 21 | 21 | 42 | 2.5% |
| | Total | 179 | 220 | 399 | 24.1% |
| Viral | Human rhinovirus | 43 | 35 | 78 | 4.7% |
| | Influenza virus A or B[a] | 14 | 24 | 38 | 2.3% |
| | Human coronavirus | 13 | 17 | 30 | 1.8% |
| | Human metapneumovirus | 8 | 16 | 24 | 1.5% |
| | RSV | 16 | 7 | 23 | 1.4% |
| | Two viral pathogens | 3 | 5 | 8 | 4.8% |
| | Other | 11 | 9 | 20 | 1.2% |
| | Total | 108 | 113 | 221 | 13.4% |
| Bacterial–viral co-infection | *S. pneumoniae* & human rhinovirus | 12 | 15 | 27 | 1.6% |
| | *S. pneumoniae* & human coronavirus | 6 | 10 | 16 | 1.0% |
| | *S. pneumoniae* & influenza virus A or B[a] | 5 | 7 | 12 | 0.7% |
| | *S. pneumoniae* & RSV | 4 | 7 | 11 | 0.7% |
| | *H. influenzae* & human rhinovirus | 3 | 8 | 11 | 0.7% |
| | Other bacteria & influenza virus A or B[a] | 4 | 2 | 6 | 0.4% |
| | Other bacteria & other virus | 27 | 11 | 38 | 2.3% |
| | Total | 61 | 60 | 121 | 7.3% |
| No pathogen | | 458 | 454 | 912 | 55.2% |
| | Overall total | 1154 | 1240 | 1653 | 100% |

# Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults

N Engl J Med. 2015, 373(5): 415–427

S. Jain, W.H. Self, R.G. Wunderink, S. Fakhran, R. Balk, A.M. Bramley, C. Reed, C.G. Grijalva, E.J. Anderson, D.M. Courtney, J.D. Chappell, C. Qi, E.M. Hart, F. Carroll, C. Trabue, H.K. Donnelly, D.J. Williams, Y. Zhu, S.R. Arnold, K. Ampofo, G.W. Waterer, M. Levine, S. Lindstrom, J.M. Winchell, J.M. Katz, D. Erdman, E. Schneider, L.A. Hicks, J.A. McCullers, A.T. Pavia, K.M. Edwards, and L. Finelli for the CDC EPIC Study Team*




- Despite current diagnostic tests, no pathogen was detected in the majority of patients (62%)
- Respiratory viruses were detected more frequently than bacteria (27% vs 14%)

# Viral infection in community-acquired pneumonia: a systematic review and meta-analysis

Eur Respir Rev 2016; 25: 178–188

Michael Burk[1], Karim El-Kersh[1], Mohamed Saad[1], Timothy Wiemken[2], Julio Ramirez[2] and Rodrigo Cavallazzi[1]

- The pooled proportion of patients with viral infection was 24.5%
- Among the individual studies, it ranged from 8.6% to 56.2%.
- It was 12.1% in a study with an outpatient population
- 22.4% in studies with mixed inpatients and outpatients

- Influenza and rhinovirus were the most commonly detected viruses
- The analysis of the evidence shows a significant increase in mortality in CAP patients with dual bacterial and viral infection

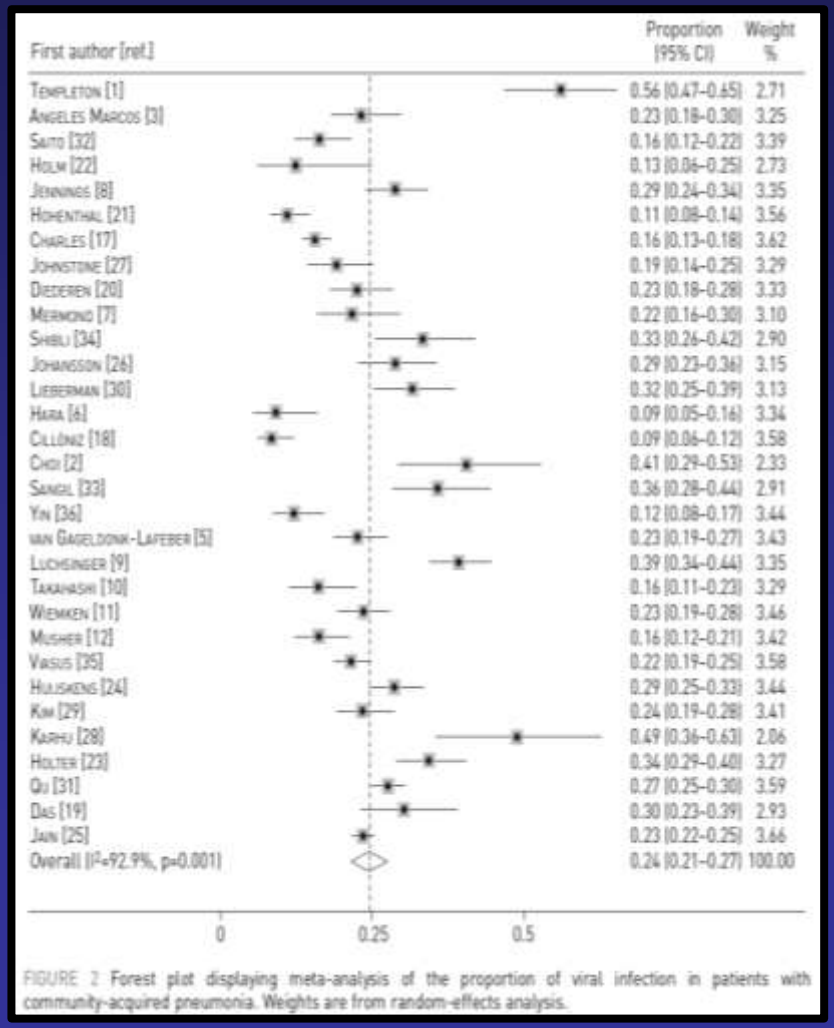
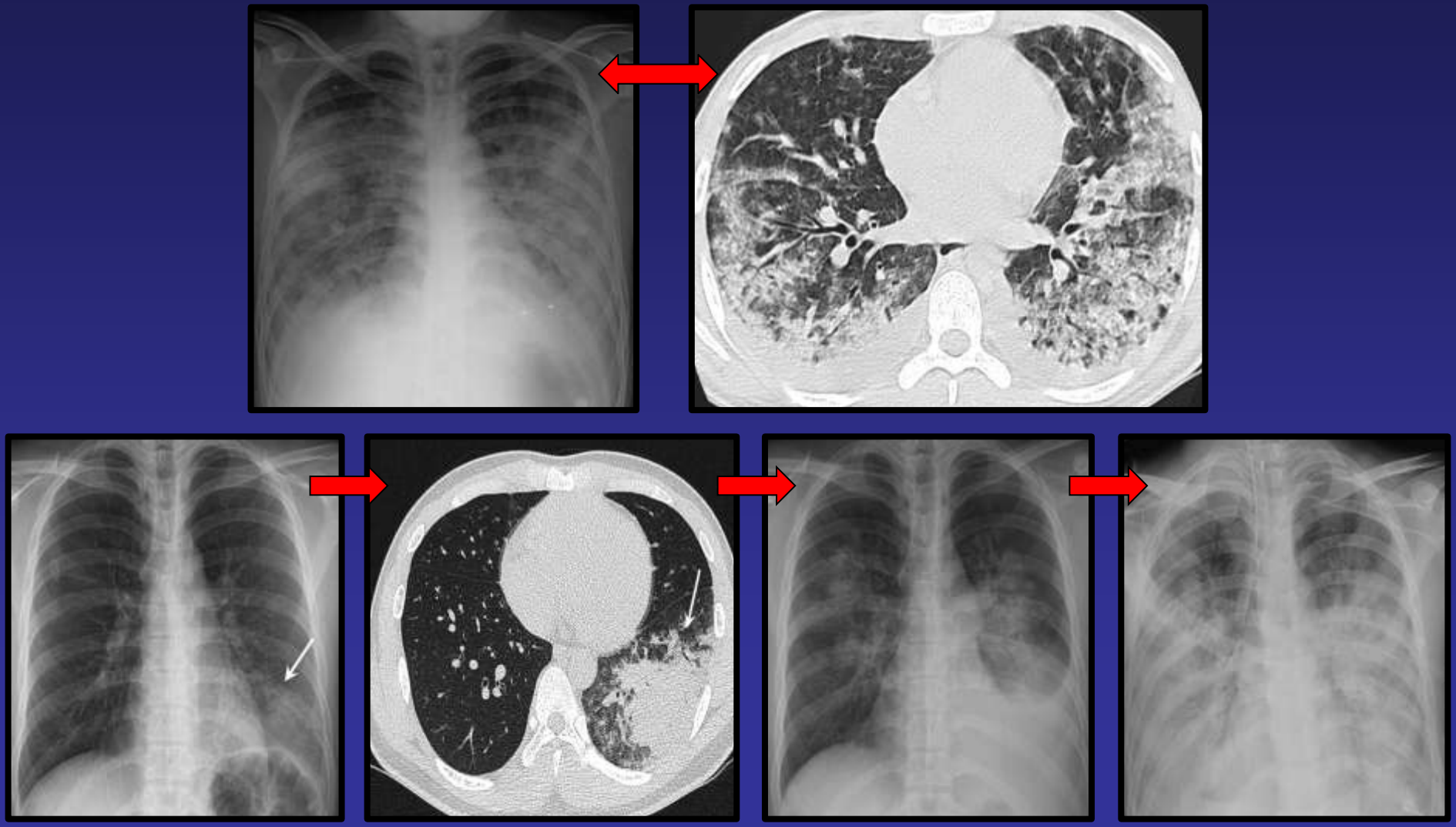



FIGURE 2 Forest plot displaying meta-analysis of the proportion of viral infection in patients with community-acquired pneumonia. Weights are from random-effects analysis.

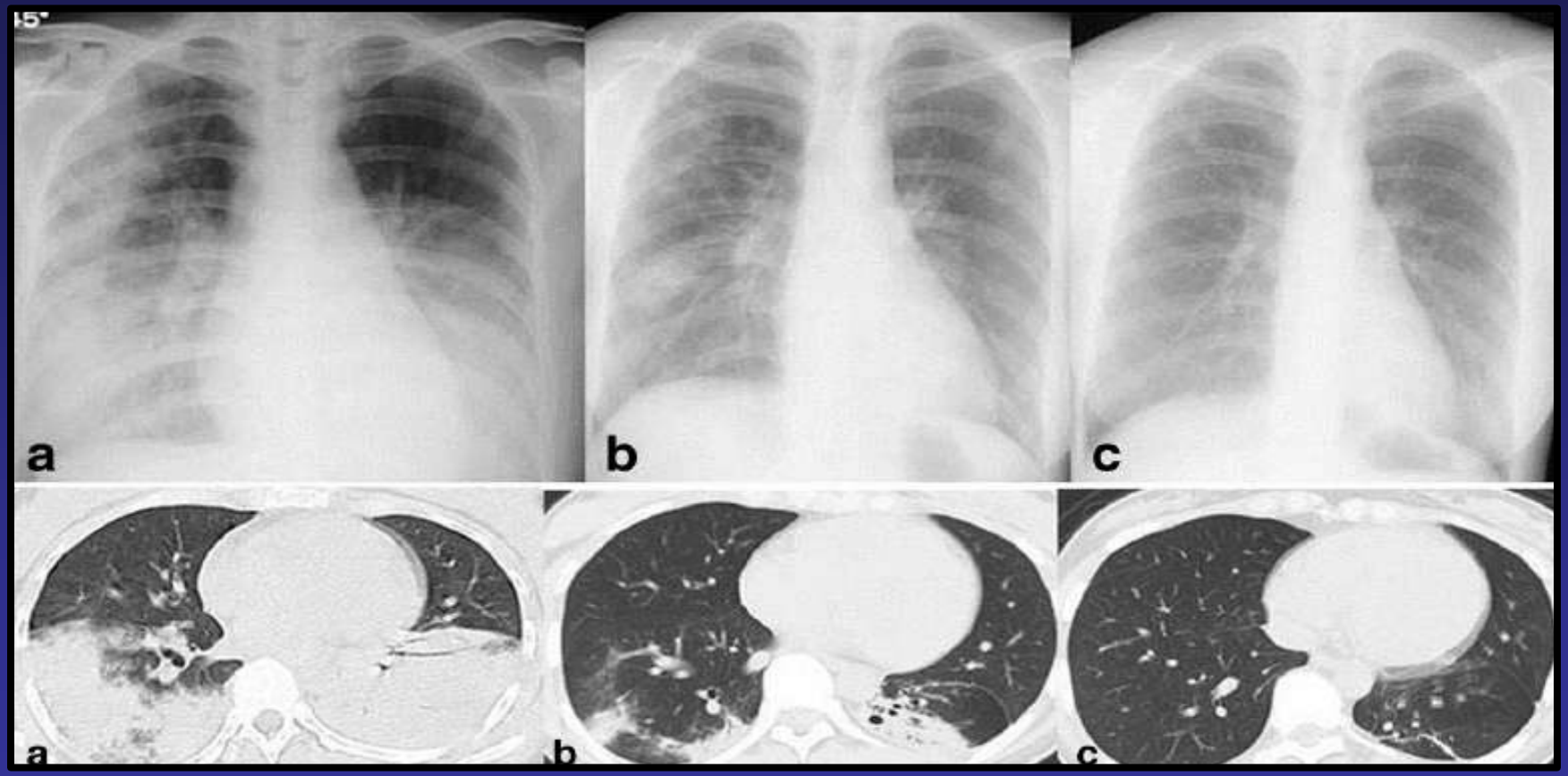
# Πνευμονία από αδενοϊούς με εξέλιξη σε ARDS

Jae Cha M, et al. Korean J Radiol 2016



# Δευτεροπαθής οργανούμενη πνευμονία κατόπιν βαριάς λοίμωξης από τον ιό της γρίπης

Asai N, et al. BMC infect Dis 2017

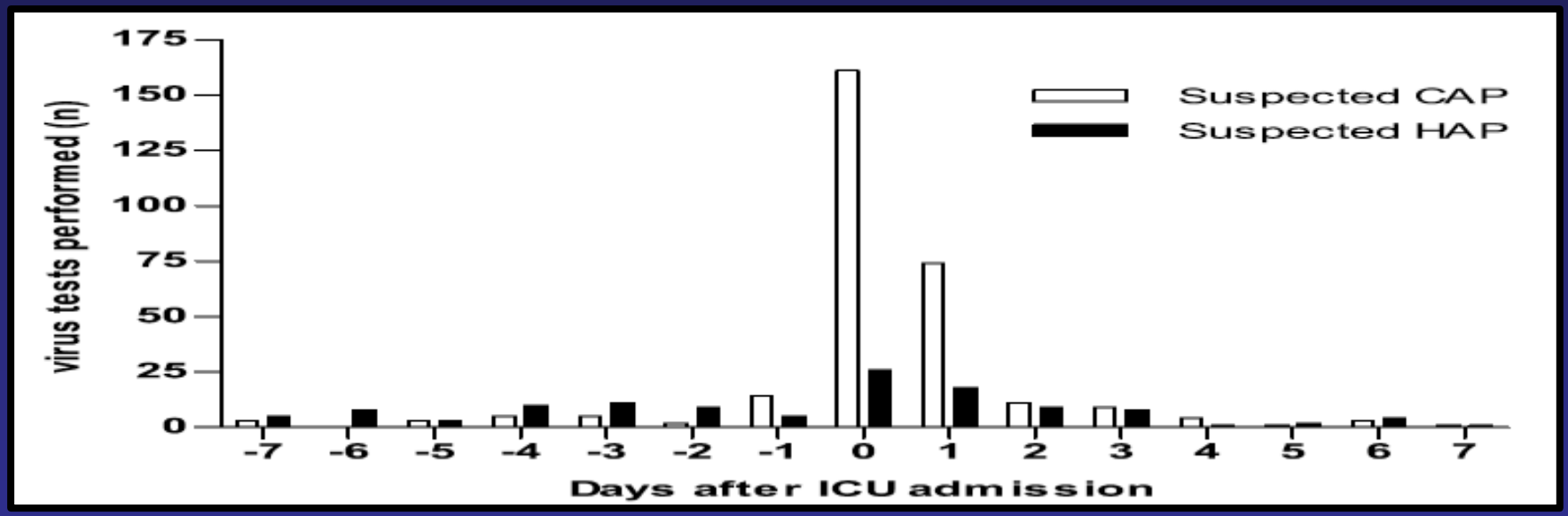



Chest X-ray showed bilateral infiltrates on admission (a upper). After starting corticosteroid therapy on day 25, infiltrates were improved (b upper). Abnormal shadows on chest X-ray disappeared 6 months after starting corticosteroid therapy (c upper). Chest CT showed consolidations on both lungs on admission (a lower) and the shadows were improved on day 25 after starting corticosteroid therapy (b lower). Six months after starting corticosteroid therapy, the consolidations disappeared (c lower)

# Clinical practice of respiratory virus diagnostics in critically ill patients with a suspected pneumonia: A prospective observational study

Frank van Someren Gréve (MD)[a,b,*,1], David S.Y. Ong (MD, PharmD, PhD)[c,d,e,**,1], Olaf L. Cremer (MD, PhD)[c], Marc J.M. Bonten (MD, PhD)[d,e], Lieuwe D.J. Bos (PhD)[a], Menno D. de Jong (MD, PhD)[b], Marcus J. Schultz (MD, PhD)[a], Nicole P. Juffermans (MD, PhD)[a], on behalf of: the MARS consortium[2]

Journal of Clinical Virology 83 (2016) 37–42




- In the influenza season, viruses were found in 34% of suspected CAP patients, and in 34% of suspected HAP patients
- Outside the influenza season, 19% of suspected CAP patients and 16% of suspected HAP patients tested positive for at least 1 virus.
- Less than half (46%) of patients admitted to the ICU with suspected pneumonia were tested for the presence of viral pathogens in the influenza season and 32% outside the season

# Respiratory viral infections are underdiagnosed in patients with suspected sepsis

Eur J Clin Microbiol Infect Dis (2017) 36:1767–1776

L. R. Ljungström[1,3] · G. Jacobsson[1,3] · B. E. B. Claesson[2] · R. Andersson[3] · H. Enroth[4,5]

- Samples from study patients with suspected sepsis are compared with all clinically requested samples for influenza A virus in all hospitalized patients

- There were very few clinical requests for influenza A virus testing during the first four weeks of the de facto influenza season, indicating a lack of systemic awareness and clinical suspicion even during a rapid escalation in cases

Table 1 Findings in nasopharyngeal swabs by multiplex PCR from 432 patients with suspected sepsis

| Pathogen | Number of findings | Percent of total (%) |
|---|---|---|
| Influenza A virus | 96 | 22 |
| Human metapneumovirus | 23 | 5 |
| Coronavirus types OC43, 229E, and HKU1 | 19 (14, 2, 3) | 4 |
| Respiratory syncytial virus types A and B | 12 (6, 6) | 3 |
| Rhinovirus and enteroviruses | 10 | 2 |
| Parainfluenza viruses types 1, 2, 3, and 4 | 3 (2, 1) | 0.6 |
| Human bocavirus | 2 | 0.4 |
| Adenovirus | 1 | 0.2 |
| *Mycoplasma pneumoniae* | 5 | 1 |
| Total | 171 | |

# Επιδημιολογικά στοιχεία της ιογενούς πνευμονίας

Jokinen C, et al. Am J Epidemiol 1993 – Ruuskanen O, et al. Lancet 2011

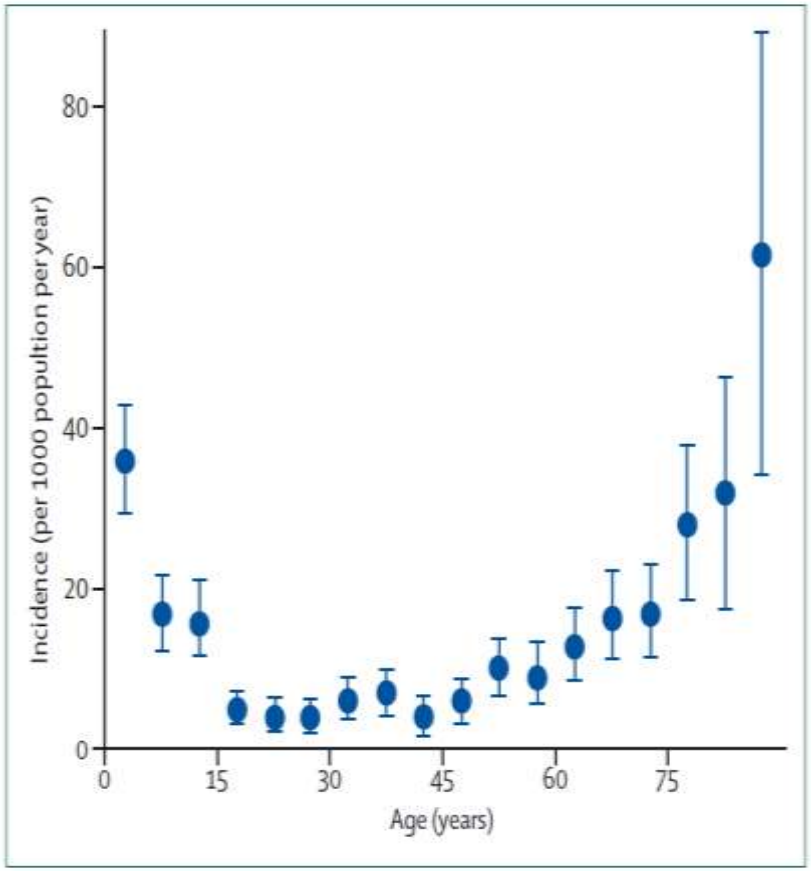



*Figure 1*: Age-specific incidence of community-acquired pneumonia

***Panel*: Viruses linked to community-acquired pneumonia in children and adults**

- Respiratory syncytial virus
- Rhinovirus
- Influenza A, B, and C viruses
- Human metapneumovirus
- Parainfluenza viruses types 1, 2, 3, and 4
- Human bocavirus*
- Coronavirus types 229E, OC43, NL63, HKU1, SARS
- Adenovirus
- Enteroviruses
- Varicella-zoster virus
- Hantavirus
- Parechoviruses
- Epstein-Barr virus
- Human herpesvirus 6 and 7
- Herpes simplex virus
- Mimivirus
- Cytomegalovirus†
- Measles†

*Mostly in children. †Mostly in developing countries.

# Οι ιοί που προκαλούν συχνότερα πνευμονία στην Ευρώπη

Alimi Y, et al. J Clin Virol 2017

| Virus type | Pooled% | 95% CI | No. of studies (and patients) included in pathogen-specific *meta*-analysis | $I^2$(%) |
|---|---|---|---|---|
| Influenza (A or B) | 9 | 7–12 | 17 (6487) | 93.45 |
| Rhinovirus | 5 | 4–7 | 12 (3324) | 88.22 |
| Coronavirus | 4 | 2–7 | 7 (1343) | 80.37 |
| Parainfluenza | 3 | 2–5 | 14 (5600) | 88.35 |
| Human metapneumovirus (hMPV) | 2 | 1–2 | 10 (1779) | 7.49 |
| Respiratory syncytial virus (RSV) | 2. | 1–3 | 17 (5968) | 82.42 |
| Adenovirus | 1 | 0 – 1 | 13 (3166) | 32.88 |

Enterovirus, poliovirus, cytomegalovirus, coxsackie virus, varicella-zoster virus, human bocavirus and herpes simplex virus were detected in < 1% of adult patients with CAP.

- Στοιχεία από 22 μελέτες
- Ανίχνευση ιών στο 22% και με τη συμβολή της PCR στο 29%

# The impact of virus infections on pneumonia mortality is complex in adults: a prospective multicentre observational study

BMC Infectious Diseases (2017) 17:755

Naoko Katsurada[1,2], Motoi Suzuki[3*], Masahiro Aoshima[1], Makito Yaegashi[4], Tomoko Ishifuji[3], Norichika Asoh[5], Naohisa Hamashige[6], Masahiko Abe[7], Koya Ariyoshi[3], Konosuke Morimoto[3] and on behalf of the Adult Pneumonia Study Group-Japan

**Table 5** Viral and bacterial infection status and in-hospital mortality among pneumonia patients by comorbidity status

| | Without comorbidities, $n = 574$ | | With chronic respiratory disease, $n = 790$ | | With other comorbidities[a], $n = 1253$ | |
|---|---|---|---|---|---|---|
| | No. death/no. cases (% mortality) | ARR[b] (95% CI) | No. death/no. cases (% mortality) | ARR[b] (95% CI) | No. death/no. cases (% mortality) | ARR[b] (95% CI) |
| HRV | 2/53 (3.8) | 0.73 (0.18–2.96) | 4/83 (4.8) | 0.78 (0.28–2.14) | 8/98 (8.2) | 0.97 (0.48–1.96) |
| Inf A/B | 0/22 (0.0) | 0.00 (0.00–0.00) | 6/31 (19.4) | 3.38 (1.54–7.42) | 4/57 (7.0) | 0.73 (0.26–2.02) |
| Paramyxovirus (RSV/hMPV/PIV1–4) | 1/32 (3.1) | 0.47 (0.07–3.26) | 3/71 (4.2) | 0.66 (0.20–2.13) | 1/109 (0.9) | 0.10 (0.01–0.70) |
| Other viruses (HAdV/HBoV/HCoV) | 0/4 (0.0) | 0.00 (0.00–0.00) | 1/5 (20.0) | 4.55 (0.58–35.5) | 1/9 (11.1) | 1.33 (0.21–8.66) |
| Multiple viruses | 0/7 (0.0) | 0.00 (0.00–0.00) | 1/6 (16.7) | 3.98 (0.68–23.24) | 3/18 (16.7) | 1.68 (0.56–5.03) |
| No virus | 26/456 (5.7) | Reference | 44/594 (7.4) | Reference | 88/962 (9.2) | Reference |
| | | ARR[c](95% CI) | | ARR[c](95% CI) | | ARR[c](95% CI) |
| Only viruses | 1/64 (1.6) | 0.24 (0.03–1.78) | 9/108 (8.3) | 1.28 (0.59–2.81) | 9/187 (4.8) | 0.51 (0.26–1.01) |
| Only bacterial pathogens | 8/179 (4.5) | 0.83 (0.36–1.93) | 16/227 (7.1) | 1.13 (0.61–2.09) | 27/340 (7.9) | 0.84 (0.54–1.31) |
| Viral-bacterial co-infection | 2/54 (3.7) | 0.58 (0.14–2.38) | 6/88 (6.8) | 1.29 (0.55–3.06) | 8/104 (7.7) | 0.77 (0.38–1.59) |
| No viral or bacterial pathogens | 18/277 (6.5) | Reference | 28/367 (7.6) | Reference | 61/622 (9.8) | Reference |
| | | ARR[b] (95% CI) | | ARR[b] (95% CI) | | ARR[b] (95% CI) |
| Multiple viruses | 0/7 (0.0) | 0.00 (0.00–0.00) | 1/6 (16.7) | 3.22 (0.52–19.81) | 3/18 (16.7) | 2.98 (0.91–9.78) |
| Single virus | 3/111 (2.7) | Reference | 14/190 (7.4) | Reference | 14/273 (5.1) | Reference |

*ARR* adjusted risk ratio, *CI* confidence interval, *HRV* human rhinovirus, *InfA* influenza A virus, *RSV* respiratory syncytial virus, *PIV1–4* human parainfluenza virus type 1–4, *HMPV* human metapneumovirus, *InfB* influenza B virus, *HCoV* human coronavirus (229E/OC43), *HAdV* human adenovirus, *HBoV* human bocavirus

[a] Other comorbidities include diabetes mellitus, cerebrovascular disease, dementia, neuromuscular disease, cardiac failure, ischaemic heart disease, collagen disease, malignancy, renal disease, and liver disease

[b] Adjusted for age, study site, duration of symptoms, month of diagnosis, antibiotic use and presence of bacteria

[c] Adjusted for age, study site, duration of symptoms, month of diagnosis, and antibiotic use

# Viral etiology of community-acquired pneumonia among adolescents and adults with mild or moderate severity and its relation to age and severity

**BMC Infectious Diseases (2015)**

Jiu-Xin Qu[1†], Li Gu[1†], Zeng-Hui Pu[2], Xiao-Min Yu[1], Ying-Mei Liu[1], Ran Li[1], Yi-Min Wang[1], Bin Cao[1*], Chen Wang[3] and For Beijing Network for Adult Community-Acquired Pneumonia (BNACAP)

**Table 2 Etiology of study population with CAP**

| Pathogen identified | n (%) |
|---|---|
| At least one pathogen | 393 (41.2) |
| Respiratory viruses (RVs) | 262 (27.5) |
| Influenza virus A | 94 (9.9) |
| Pandemic H1N1 (pH1N1) | 60 (6.3) |
| Seasonal H3N2 (sH3N2) | 30 (3.1) |
| pH1N1 and sH3N2 | 4 (0.4) |
| Human rhinovirus | 41 (4.3) |
| Adenovirus | 40 (4.2) |
| Human metapneumovirus | 17 (1.8) |
| Parainfluenza virus type 1 | 16 (1.7) |
| Parainfluenza virus type 3 | 14 (1.5) |
| Parainfluenza virus type 2 | 11 (1.2) |
| Influenza virus B | 6 (0.6) |
| Enterovirus | 5 (0.5) |
| Respiratory syncytial virus type A | 5 (0.5) |
| Respiratory syncytial virus type B | 4 (0.4) |
| Human coronavirus types OC43/HKU1 | 4 (0.4) |
| Human coronavirus types 229E/NL63 | 4 (0.4) |
| Parainfluenza virus type 4 | 1 (0.1) |
| Bocavirus | 0 (0) |
| Bacteria | 219 (23.0) |
| *Mycoplasma pneumoniae* | 168 (17.6) |
| *Legionella pneumophila* | 4 (0.4) |
| Typical bacteria | 47 |

Data are expressed as n (%).

**Table 3 Distribution of co-infections**

| Associations | n (%) |
|---|---|
| **Dual infections** | **65 (6.8)** |
| **RV + Bacterium** | **48** |
| IFV A + Bacterium | 19 |
| HRV + Bacterium | 9 |
| PIVs + Bacterium | 8 |
| AdV + MP | 4 |
| hCoVs + MP | 2 |
| IFV B + MP | 2 |
| RSVs + MP | 2 |
| hMPV + Bacterium | 2 |
| **RV + RV** | **11** |
| IFV A + hCoVs | 2 |
| IFV A + PIVs | 2 |
| HRV + PIVs | 2 |
| hMPV + PIVs | 2 |
| AdV + RSV A | 1 |
| AdV + PIVs | 1 |
| AdV + hCoVs | 1 |
| **Bacterium + Bacterium** | **6** |
| **Triple infections** | **8 (0.84)** |
| IFV A (sH3N2) + PIV1 + PIV2 | 1 |
| IFV A (sH3N2) + PIV2 + PIV3 | 1 |
| IFV A (pH1N1) + two Bacteria | 1 |
| HRV + PIV1 + PIV3 | 1 |
| HRV + two bacteria | 1 |
| PIV1 + EV + bacterium | 1 |
| PIV1 + PIV3 + bacterium | 1 |
| IFV B + AdV + PIV3 | 1 |
| **Quadruple infection** | **1 (0.1)** |
| PIV1 + PIV3 + two bacteria | 1 |
| **Quintuple infections** | **1 (0.1)** |
| HRV + PIV1 + PIV2 + PIV3 + RSV B | 1 |
| **Total** | **75/954 (7.9)** |

Note: Influenza virus (IFV) types A and B, human rhinovirus (HRV), adenovirus (AdV), human metapneumovirus (hMPV), parainfluenza virus (PIV) types 1, 2, 3 and 4, enterovirus (EV), respiratory syncytial virus (RSV) types A and B, human coronaviruses (hCoVs), *Mycoplasma pneumoniae* (MP).

**The proportion of RVs in CAP is higher than previously reported. Influenza A virus pneumonia are usually found in patients older than 45 years, while adenovirus pneumonia are common in adolescents and young adults**

# Επιδημιολογικά στοιχεία και προγνωστικοί παράγοντες ενδονοσοκομειακής θνητότητας σε ασθενείς με ιογενή πνευμονία

Crotty MP, et al. Medicine 2015

| n (%) | Univariate Analysis | | Multivariate Analysis | | *P* Value |
|---|---|---|---|---|---|
| | OR | *P*-value | aOR | 95% CI | *P* Value |
| ICU admission | 42.3 | < 0.01 | 14.3 | 1.76, 116 | 0.01 |
| Multiple Respiratory Viruses | 2.63 | 0.08 | 4.87 | 1.09, 21.8 | 0.04 |
| Stem-cell Transplant | 2.62 | 0.01 | 4.22 | 1.57, 11.3 | 0.01 |
| Vasopressors | 6.05 | <0.01 | 2.68 | 1.27, 5.64 | 0.01 |
| APACHE II | 1.16 | <0.01 | 1.11 | 1.04, 1.18 | 0.01 |
| Solid organ Transplant | 0.287 | 0.03 | 0.28 | 0.07, 1.14 | 0.08 |
| Fungal RCI | 3.58 | 0.02 | 3.23 | 0.87, 12.0 | 0.08 |
| Outside hospital Transfer | 2.21 | 0.01 | 2.08 | 0.98, 4.44 | 0.06 |
| RSV | 1.72 | 0.16 | — | — | — |
| Bacterial infection (Any) | 1.79 | 0.04 | — | — | — |
| CMV RCI | 2.15 | 0.18 | — | — | — |
| Mechanical Ventilation | 5.41 | < 0.01 | — | — | — |
| CCI | 1.16 | 0.01 | — | — | — |

aOR = adjusted odds ratio, APACHE = Acute Physiology and Chronic Health Evaluation, CCI = Charlson's comorbidity index, CI = confidence interval, CMV = cytomegalovirus, ICU = intensive care unit, OR = odds ratio, RCI = respiratory co-infection, RSV = respiratory syncytial virus.

- The majority of the patients (51.8%) were immunocompromised
- 29.6% of the patients were found to have a RCI with 57.6% having a bacterial RCI. Viral RCI with HSV, CMV, or both occurred in 33.3% fungal (16.7%) and other RCIs (7.1%) were less common.
- Many patients required mechanical ventilation (54%) and vasopressor support (36%)
- Overall in-hospital mortality was high (23.2%) and readmissions were common with several patients re-hospitalized within 30 (21.1%) and 90 days (36.7%) of discharge

# Viral-bacterial coinfection affects the presentation and alters the prognosis of severe community-acquired pneumonia

Guillaume Voiriot[1,7*], Benoit Visseaux[2], Johana Cohen[1], Liem Binh Luong Nguyen[3], Mathilde Neuville[1], Caroline Morbieu[3], Charles Burdet[3], Aguila Radjou[1], François-Xavier Lescure[3], Roland Smonig[1], Laurence Armand-Lefèvre[4], Bruno Mourvillier[1], Yazdan Yazdanpanah[3,5], Jean-François Soubirou[1], Stephane Ruckly[6], Nadhira Houhou-Fidouh[2] and Jean-François Timsit[1,5]

Critical Care (2016) 20:375

**Table 1** Baseline characteristics, behavior during ICU stay, and outcome of 174 patients with severe CAP, according to the microbiological diagnosis

| Patients | All patients (n = 174) | Bacterial group (n = 46) | Viral group (n = 53) | Mixed group (n = 45) | No etiology group (n = 30) | *p* value[a] |
|---|---|---|---|---|---|---|
| Organ supports during ICU stay | | | | | | |
| Noninvasive ventilation | 55 (31.8) | 14 (30.4) | 21 (40.4) | 12 (26.7) | 8 (26.7) | 0.44 |
| Mechanical ventilation | 98 (56.3) | 28 (60.9) | 22 (41.5) | 36 (80) | 12 (40) | <0.01 |
| ARDS | 60 (34.5) | 17 (37) | 13 (24.5) | 22 (48.9) | 8 (26.7) | 0.06 |
| Dialysis | 37 (21.3) | 10 (21.7) | 10 (18.9) | 12 (26.7) | 5 (16.7) | 0.72 |
| Vasopressors | 80 (46.2) | 22 (47.8) | 19 (36.5) | 27 (60) | 12 (40) | 0.12 |
| Outcome | | | | | | |
| Length of mechanical ventilation, d | 9 [5;13] | 6.5 [3;12.5] | 7 [4;12] | 9 [6;14] | 10 [7.5;17.5] | 0.34 |
| Follow-up duration, d[f] | 15 [10 ; 29] | 14 [5;23] | 18 [12;32] | 16 [11;31] | 14.5 [12;19] | 0.25 |
| Hospital mortality | 30 (17.2) | 6 (13) | 6 (11.3) | 13 (28.9) | 5 (16.7) | 0.10 |
| Complicated course[g] | 74 (42.5) | 18 (39.1) | 15 (28.3) | 31 (68.9) | 10 (33.3) | <0.01 |

# Η επίδραση του είδους των παθογόνων στη θνητότητα της πνευμονίας

Quah J et al. BMC Infect Dis 2018

**Table 3** Distribution of microbial pathogens detected in study cohort

| Microbial Pathogens | Study Cohort, *n* = 117 (%) |
|---|---|
| Viruses | |
| *Influenza A** | 28 (24.0) |
| *Influenza B* | 5 (4.3) |
| *Rhinovirus* | 6 (5.1) |
| *Human Metapneumovirus* | 5 (4.3) |
| *Adenovirus* | 3 (2.6) |
| *Coronavirus* | 2 (1.7) |
| *Respiratory Syncytial Virus* | 2 (1.7) |
| *Parainfluenza* | 1 (0.9) |
| Bacteria | |
| *Streptococcus pneumoniae* | 19 (16.3) |
| *Staphylococcus aureus* | 6 (5.1) |
| *Klebsiella pneumoniae* | 5 (4.3) |
| *Pseudomonas aeruginosa* | 4 (3.4) |
| *Haemophilus influenzae* | 3 (2.6) |
| *Moraxella catahamlis* | 2 (1.7) |
| *Achromobacter* | 1 (0.9) |
| *Escherichia coli* | 1 (0.9) |
| *Burkholderia pseudomallei* | 1 (0.9) |
| *Nocardia* | 1 (0.9) |
| Atypical organisms | |
| *Mycoplasma pneumoniae* | 4 (3.4) |
| *Legionella* | 3 (2.6) |
| *Mycobacterium tuberculosis* | 3 (2.6) |

Data are presented as number (%). *9 out of 28 *Influenza A* samples were serotype H1N1

**Table 4** Univariate and multivariate logistic regression for hospital mortality

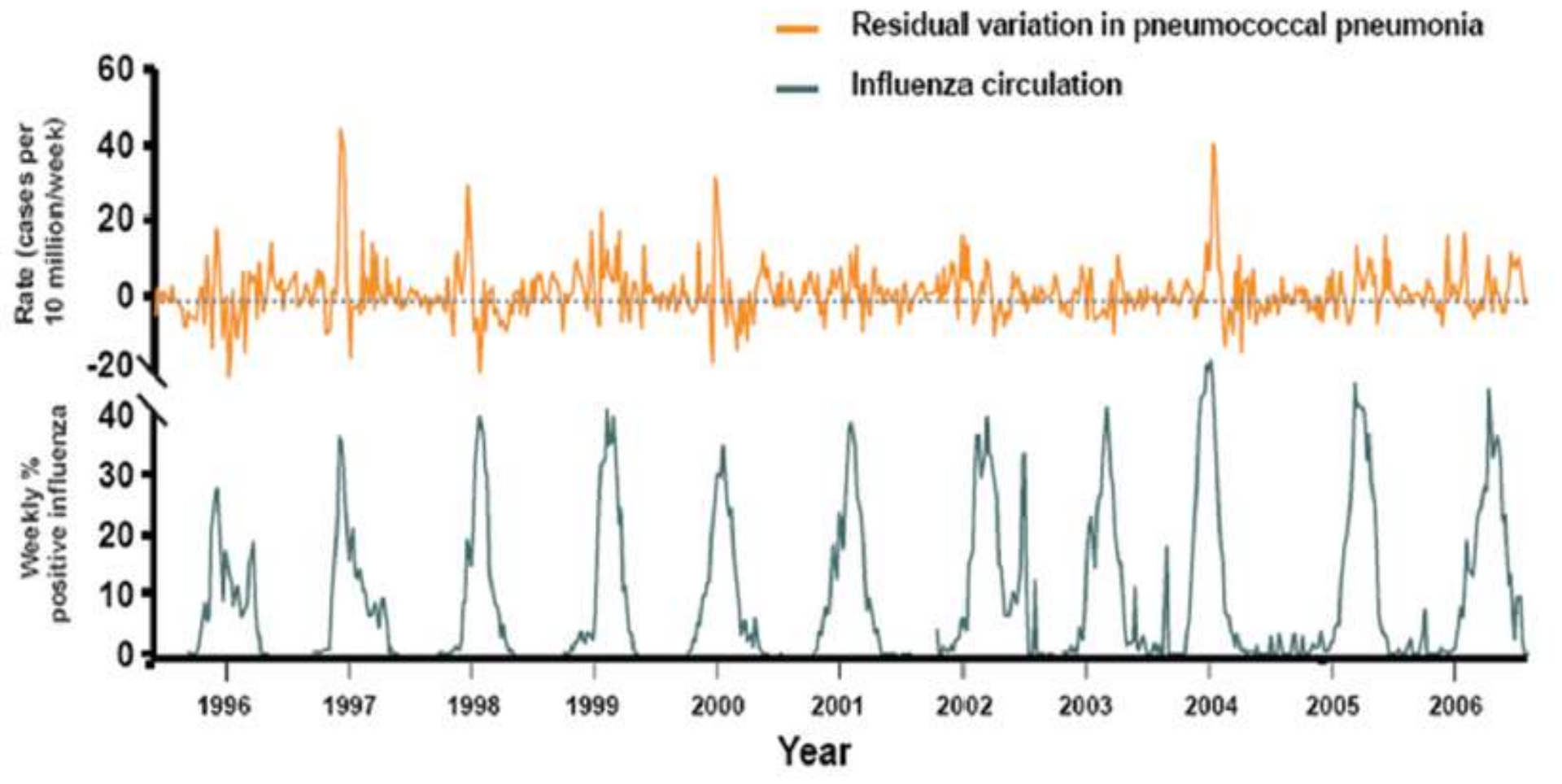
| Variable | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | O.R (95% CI) | *p*-value | Adjusted O.R (95% CI) | *p*-value |
| -Bacteria only | 0.30 (0.03, 3.07) | 0.312 | 0.14 (0.004,2.27) | 0.143 |
| -Viruses only | 1.85 (0.40, 8.49) | 0.428 | 4.63 (0.47, 45.53) | 0.189 |
| Mixed viral-bacterial co-infections | 6.36 (1.39, 29.1) | 0.017 | 13.99 (1.30, 151.05) | 0.03 |
| -Atypical infection | Omitted | | Omitted | |

- Respiratory viruses were as commonly found as bacteria (42.7% vs 38.5%), as an etiological pathogen
- Mixed viral-bacterial co-infections occurred in 15.4% of patients and was associated with an adjusted odds ratio of 13.99 for hospital mortality

# Influenza Circulation and the Burden of Invasive Pneumococcal Pneumonia during a Non-pandemic Period in the United States

Clinical Infectious Diseases 2010; 50:175–83

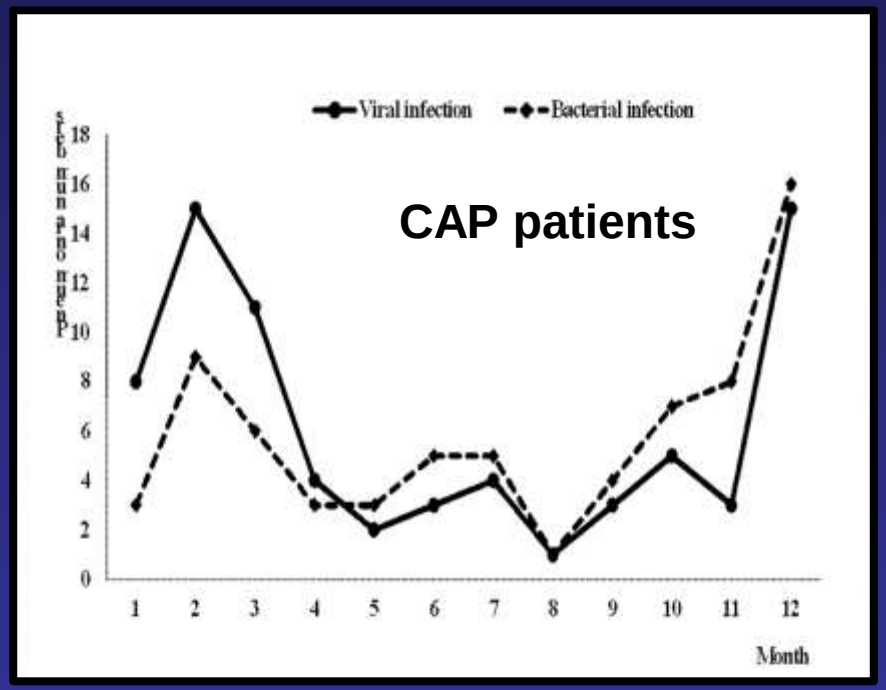
Nicholas D. Walter,[1,2,a] Thomas H. Taylor, Jr,[3] David K. Shay,[4] William W. Thompson,[4] Lynnette Brammer,[4] Scott F. Dowell,[5] Matthew R. Moore [2]; for the Active Bacterial Core Surveillance Team

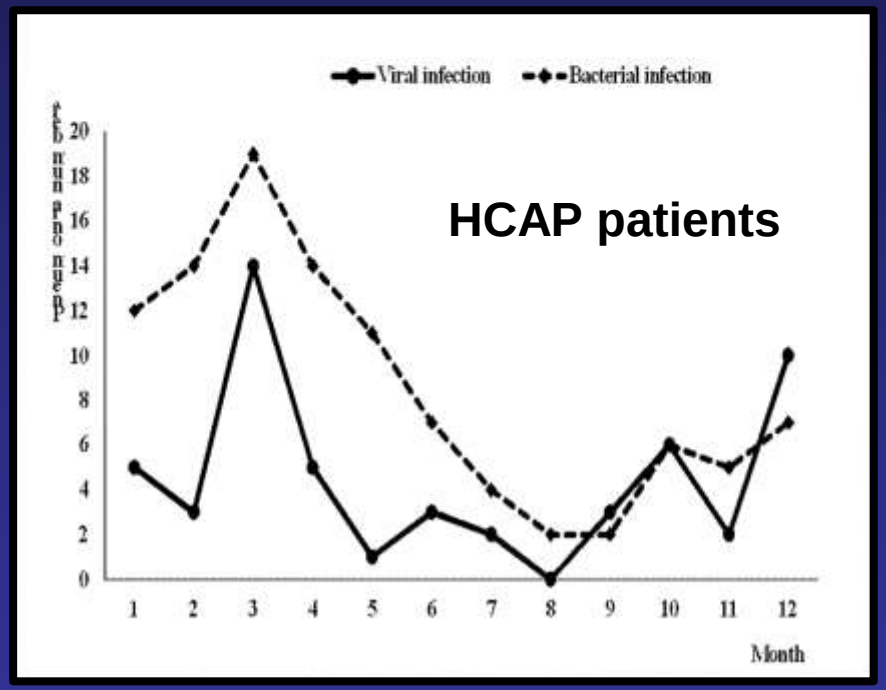


# Comparison of viral infection in healthcare-associated pneumonia (HCAP) and community-acquired pneumonia (CAP)

PLOS ONE February 15, 2018

Eun Sun Kim[1,2], Kyoung Un Park[3], Sang Hoon Lee[1,2], Yeon Joo Lee[1,2], Jong Sun Park[1,2], Young-Jae Cho[1,2], Ho Il Yoon[1,2], Choon-Taek Lee[1,2], Jae Ho Lee[1,2]*



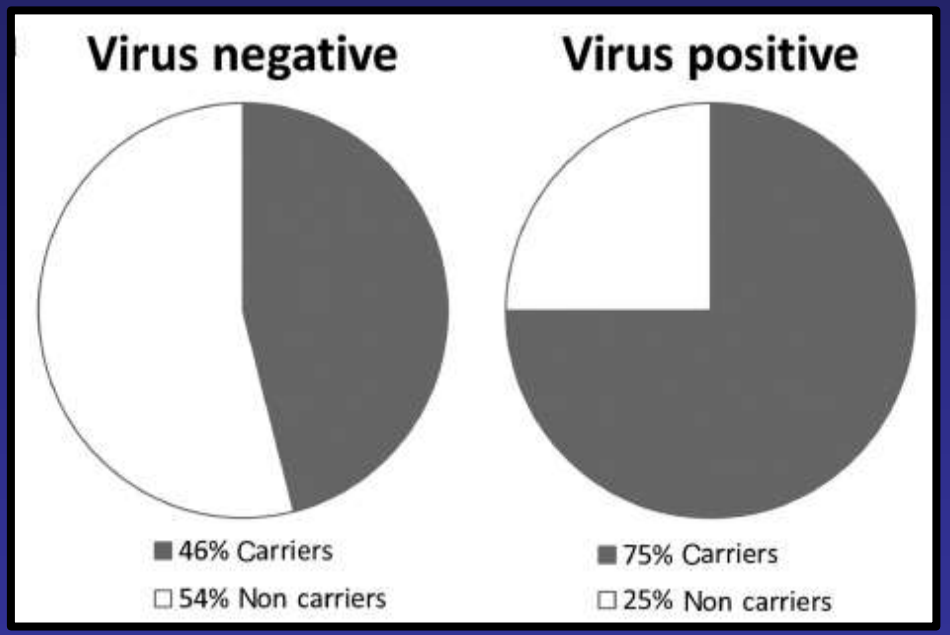




- The prevalence of viral infection in patients with HCAP was lower than that in patients with CAP, and resulted in a similar prognosis as viral-bacterial coinfection or bacterial infection
- Multi-bacterial or MDR bacterial infection was the most important concern in patients with HCAP

# Modulation of nasopharyngeal innate defenses by viral coinfection predisposes individuals to experimental pneumococcal carriage

**Glennie S, et al. Mucosal Immunology 2016**

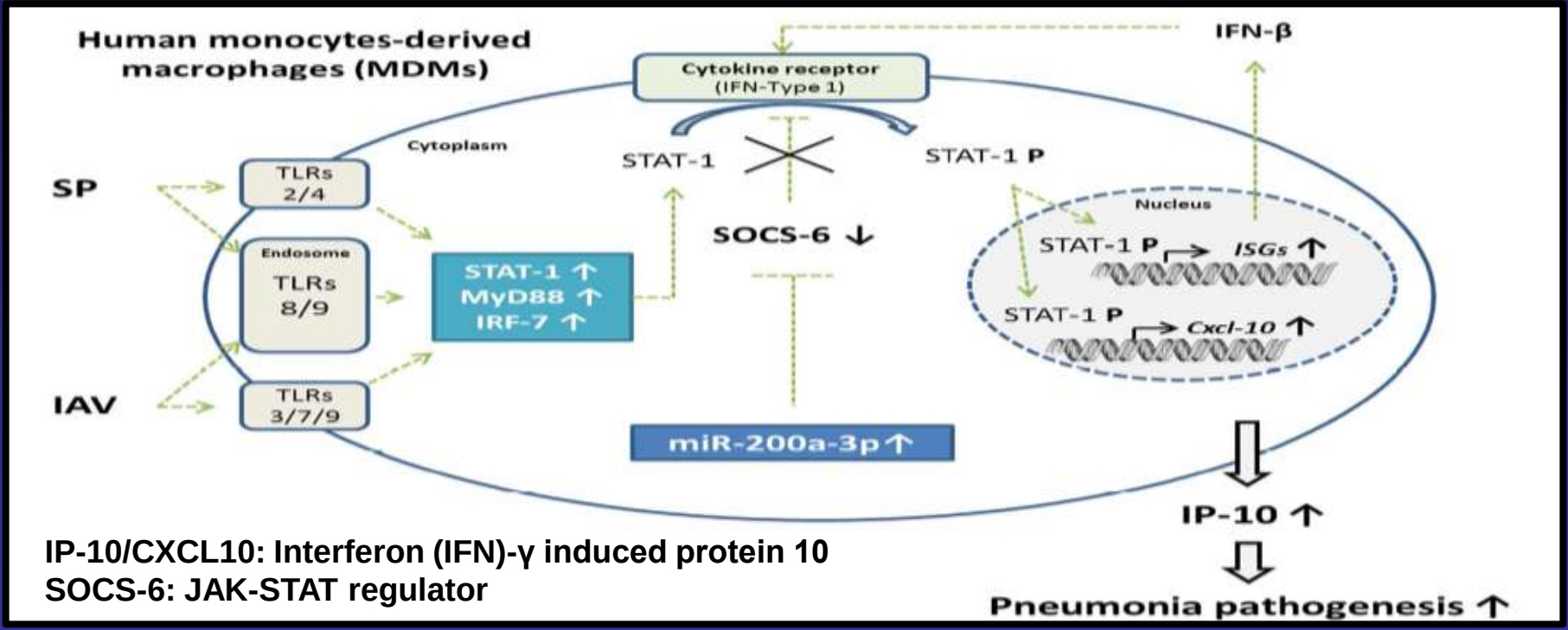
- **Upper respiratory tract viral infection is associated with a 2.8-fold increase in the odds of becoming colonized by *S. pneumoniae***
- **Viral infections reduce mucociliary velocity, denude epithelial surfaces, expose basement membranes, and modulate chemokine and innate defenses**
- **Viral infections transform this normally harmless commensal organism into a potentially fatal pathogen by increasing:**
  **- transmission**
  **- carriage density**
  **- the host disease susceptibility**



# Viral and bacterial co-infection in severe pneumonia triggers innate immune responses and specifically enhances IP-10: a translational study

www.nature.com/scientificreports

Jonathan Hoffmann[1], Daniela Machado[1], Olivier Terrier[2], Stephane Pouzol[1], Mélina Messaoudi[1], Wilma Basualdo[3], Emilio E Espínola[4], Rosa M. Guillen[4], Manuel Rosa-Calatrava[2], Valentina Picot[1], Thomas Bénet[5], Hubert Endtz[1], Graciela Russomando[4] & Gláucia Paranhos-Baccalà[1]




**IP-10/CXCL10: Interferon (IFN)-γ induced protein 10**
**SOCS-6: JAK-STAT regulator**

**Viral and bacterial coinfection modulates the JAK-STAT signaling pathway and leads to exacerbated IP-10 expression, which could play a major role in the pathogenesis of pneumonia**

# Η μετάδοση των ιών

- Από το περιβάλλον (αδενοϊοί, εντεροϊοί, ρινοϊοί) *
- Με την άμεση επαφή με μολυσμένα αντικείμενα (VZV)
- Μέσω της μεταμόσχευσης μολυσμένων οργάνων ή της μετάγγισης αίματος (CMV)
- Μέσω της εισρόφησης σιέλου που περιέχει ασυμπτωματικά τους ιούς (CMV, HSV)
- Με επανενεργοποίηση λανθάνουσας λοίμωξης (HSV, CMV)
- Αιματογενώς (CMV)
- Μέσω του προσωπικού των υπηρεσιών υγείας (SARS, ιλαρά, αδενοϊοί, ιοί parainfluenza, RSV) *

* Πολλοί ιοί μεταδίδονται εύκολα κατά τη διάρκεια νοσηλείας

Οι αδενοϊοί, οι ιοί parainfluenza και RSV είναι υπεύθυνοι για το 70% των νοσοκομειακών λοιμώξεων από ιούς

# Χαρακτηριστικά των σημαντικότερων ιών που προκαλούν πνευμονία

Galvan JM, et al. Arch Broncopneumol 2015

| Virus | Family | Subtype | Incidence of CAP | | Risk factors | | Seasonality | Differential clinical factors | Treatment |
|---|---|---|---|---|---|---|---|---|---|
| | | | Children | Adults | Infection | Poor evolution | | | |
| Rhinovirus | *Picornaviridae* | – | ≈18% | ≈6% | All ages, but more in children | Asthma. Cellular immunosuppression | All year (more in autumn) | Upper airway symptoms: rhinorrhea, cough and nasal congestion | Pleconaril (compassionate use) |
| Syncytial respiratory virus (SRV) | *Paramyxoviridae* | 1 and 2 | ≈11% | ≈3% | Newborn and premature babies. Immunosuppression | COPD. Asthma. Stem cell transplant. Immunosuppression | End of autumn, beginning of Winter | Marked bronchial reactivity | Inhaled ribavirin (children), IV ribavirin (immunosuppression) |
| Influenza virus (IV) | *Orthomyxoviridae* | A and B seasonal | ≈10% | ≈8% | Children and geriatrics | >65 years. Comorbidities. Gestation. BMI ↑ | End of autumn and winter | General asthenia. Influenza-like syndrome | NAI (OSE±resistant) Amantadines (not in B) |
| | | H1N1 09 pandemic | – | – | <65 years | Gestation. Homeless. Obesity | Specific outbreaks in waves | More pneumonias, ICU and mortality | NAI (ZAN and PER in critical patients) |
| | | H5N1 | – | – | Contact with birds | Neutropenia and delayed diagnosis | Outbreaks throughout the year | Thrombocytopenia and kidney failure | High does NAI. Amantadines not beneficial |
| Parainfluenza virus (PIV) | *Paramyxoviridae* | 1, 2, 3 and 4 | ≈8% | ≈2% | Geriatric care homes | Lung and stem cell transplant. Fragile elderly | Autumn (PIV1-2) Spring (PIV-3) | Laryngeal croup (children with PIV-1) | Ribavirin iv (immunosuppression) |
| Metapneumovirus | *Paramyxoviridae* | – | ≈8% | ≈1% | Children<5 years | SRV coinfection. Immunosuppression | End of Winter and Spring | Wheezing. Asthma exacerbations | Ribavirin iv (immunosuppression) |
| Coronavirus | *Coronaviridae* | 229E, NL63 OC43, KU1 | ≈7% | ≈5% | Geriatric care homes | Asthma. Immunosuppression | Winter | Diarrhea (OC43, and intermittent) | No proven treatment. Chloroquine |
| | | SARS | – | – | Bats and civets in Asia. Healthcare personnel | Elderly. DM. Hepatitis B. (Pediatric population protective factor) | Outbreaks throughout the year | Prodrome with fever and myalgia followed by a respiratory distress | No specific treatment. Corticosteroids used |
| Adenovirus | *Adenoviridae* | 7, 14, 16 | ≈3% | ≈2% | Prisons (outbreaks) | Pneumococcus | All year | Conjunctivitis, diarrhea, encephalitis | Cidofovir (proven in immunosuppression) |
| Bocavirus | *Parvoviridae* | – | ≈5% | <1% | Children<2 years | Poorly defined | End of autumn, beginning of winter | Otitis media and pneumonia (few studies) | No specific treatment |

BMI: body mass index; COPD: chronic obstructive pulmonary disease; IV: intravenous; NAI: neuraminidase inhibitors (OSE: oseltamivir; PER: peramivir; ZAN: zanamivir).

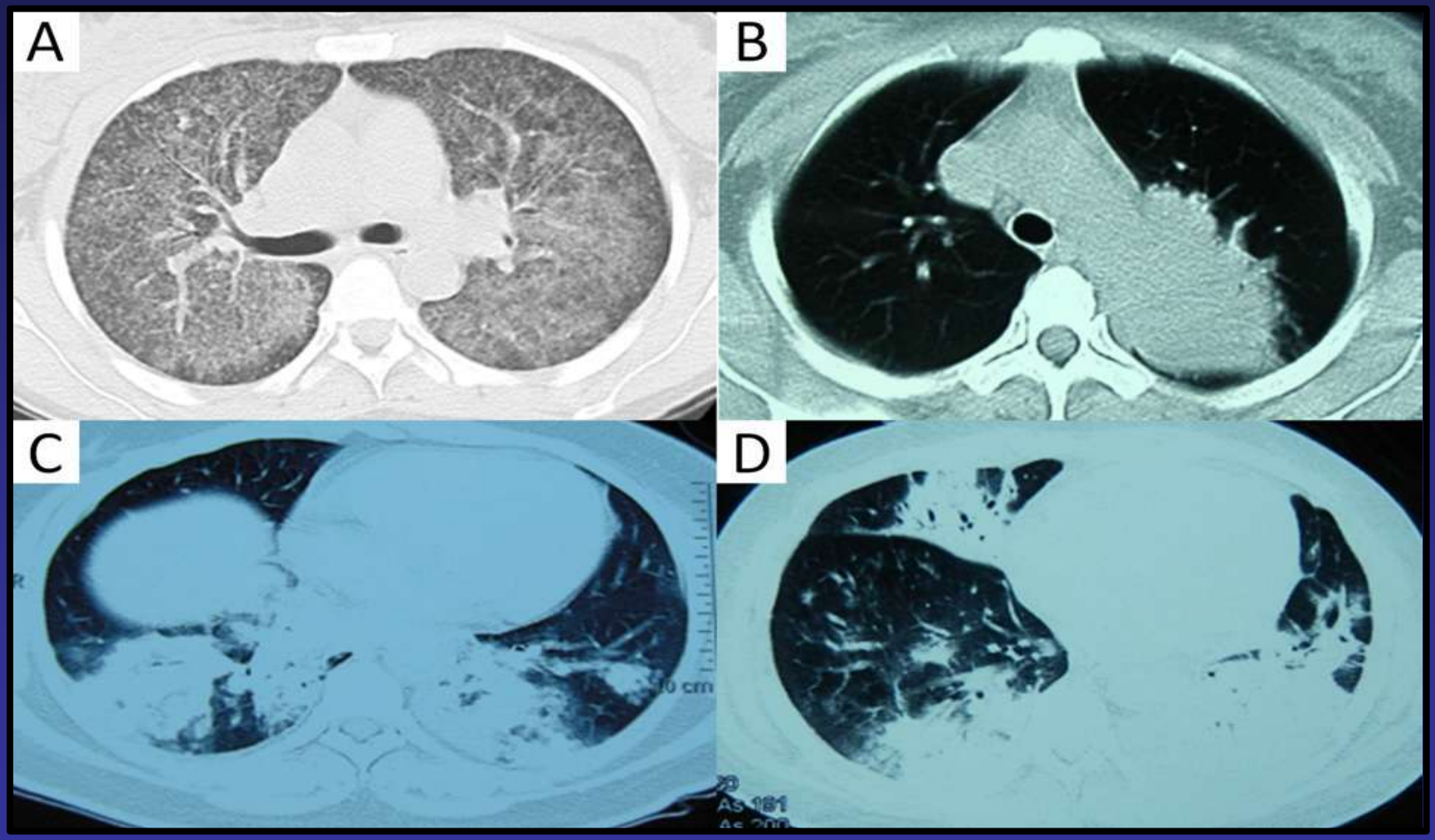
# Παράμετροι για την διαφορική διάγνωση της ιογενούς από τη βακτηριακή πνευμονία

Ruuskanen O, et al. Lancet 2011

| | Suggests viral cause | Suggests bacterial cause |
|---|---|---|
| Age | Younger than 5 years | Adults |
| Epidemic situation | Ongoing viral epidemic | .. |
| History of illness | Slow onset | Rapid onset |
| Clinical profile | Rhinitis, wheezing | High fever, tachypnoea |
| Biomarkers | | |
| Total white-blood cell count | $<10\times10^9$ cells per L | $>15\times10^9$ cells per L |
| C-reactive protein concentration in serum | <20 mg/L | >60 mg/L |
| Procalcitonin concentration in serum | <0·1 µg/L | >0·5 µg/L |
| Chest radiograph findings | Sole interstitial infiltrates, bilaterally | Lobar alveolar infiltrates |
| Response to antibiotic treatment | Slow or non-responsive | Rapid |

# Η ακτινολογική εικόνα της ιογενούς πνευμονίας εμφανίζει ποικιλομορφία

Tan D, et al. PLOS One 2016



# Clinical Characteristics of Influenza-Associated Pneumonia of Adults: Clinical Features and Factors Contributing to Severity and Mortality

YALE JOURNAL OF BIOLOGY AND MEDICINE 90 (2017), 165-181.

Takashi Ishiguro, MD, PhD[a,*], Naho Kagiyama, MD, PhD[a], Ryuji Uozumi, MS[b], Kyuto Odashima, MD[a], Yotaro Takaku, MD, PhD[a], Kazuyoshi Kurashima, MD, PhD[a], Satoshi Morita, PhD[b], and Noboru Takayanagi, MD, PhD[a]

**Background:** Pneumonia is a major complication of influenza that contributes to mortality. Clinical characteristics and factors of influenza virus contributing to the severity and mortality of pneumonia have not been fully elucidated.

**Objective:** The objective was to clarify clinical characteristics and factors contributing to the severity and mortality of influenza-associated pneumonia (flu-p†).

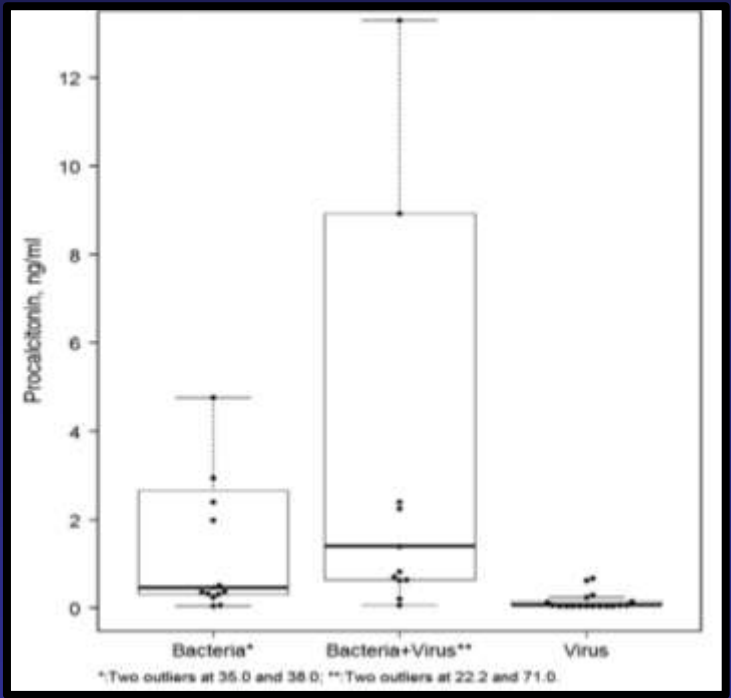
**Methods:** Retrospectively analyzed patients with flu-p.

**Results:** From December 1999 to March 2016, 210 patients with a median age of 69 (range, 17 to 92) years with flu-p based on positive rapid antigen tests, increased antibody titers of paired sera, or positive results of reverse transcription polymerase chain reaction were admitted. A multivariate analysis found that advanced age (≥ 65 years), pneumonia subtypes (unclassified), diabetes mellitus, and acute kidney injury complicated with flu-p were independent factors associated with disease severity, whereas pneumonia subtypes (mixed viral and bacterial pneumonia and unclassified), healthcare-associated pneumonia, acute kidney injury complicated with flu-p, and severity on admission (severe) were independent factors associated with non-survival.

**Conclusion:** The clinical characteristics of flu-p are varied, and the contribution of several factors to the severity and mortality of flu-p suggest their importance in either preventing flu-p or managing flu-p after it develops.

# Η συμβολή της PCT και της Film Array Multiplex PCR (FAM-PCR) στην αιτιολογική διάκριση της πνευμονίας

Gelfer G, et al. Diagn Microbiol Infect Dis 2015 – Self WH, et al. Clin Infect Dis 2017




| Pathogen identified | Standard (24 patients) | FilmArray (22 patients) |
|---|---|---|
| Patients with viral pathogen only | | |
| Adenovirus | 0 | 1 |
| Coronavirus | 0 | 5 |
| Human metapneumovirus | 3 | 2 |
| Influenza | 3 | 0 |
| Parainfluenza | 0 | 0 |
| Respiratory syncytial virus | 1 | 3 |
| Rhinovirus | 0 | 0 |
| Patients with bacterial pathogen only | | |
| *Streptococcus anginosus* | 1 | 0 |
| *S. pneumoniae* | 5 | 2 |
| *S. pneumoniae* + MRSA | 0 | 1 |
| *Streptococcus pneumoniae* + MSSA | 1 | 0 |
| MRSA only | 2 | 0 |
| *C. pneumoniae* | | 1 |
| *L. pneumophila* | 1 | 0 |
| Patients with both viral and bacterial pathogens | | |
| Influenza + elevated PCT | 3 | |
| *S. pneumoniae* + influenza | 0 | 0 |
| *S. pneumoniae* + adenovirus | 1 | 1 |
| *S. pneumoniae* + hMPV | 1 | 1 |
| *S. pneumoniae* + rhinovirus | 0 | 1 |
| *S. pneumoniae* + RSV | 1 | 1 |
| MRSA + hMPV | | 1 |
| *M. catarrhalis* + coronavirus | | 1 |
| MRSA + RSV | 1 | |

- Patients with a PCT of 10 ng/mL were 4 times more likely to have a bacterial pathogen detected than those with an undetectable PCT <0.05 ng/mL
- No PCT threshold allowed for perfect discrimination between viral and bacterial detection, as demonstrated by 23% of patients with typical bacterial pathogens having PCT <0.25 ng/mL and 12% having PCT <0.1 ng/mL
- The Film Array PCR platform detected more viruses than the laboratory-generated bundle and did so in less than 2 hours

# The Use of Polymerase Chain Reaction Amplification for the Detection of Viruses and Bacteria in Severe Community-Acquired Pneumonia

Respiration 2016;92:286–294

Wen Ting Siow[a, c] Evelyn Siew-Chuan Koay[b, d] Chun Kiat Lee[d] Hong Kai Lee[d]
Venetia Ong[a, c] Wang Jee Ngerng[a, c] Hui Fang Lim[a, c] Adeline Tan[e]
Julian Wei-Tze Tang[f, g] Jason Phua[a, c]

**Table 5.** Outcomes

| Characteristics | All patients (n = 100) | Virus detected (n = 32) | Virus not detected (n = 68) | p value |
|---|---|---|---|---|
| Mortality | | | | |
| Hospital | 15 (15.0) | 1 (3.1) | 14 (20.6) | 0.03 |
| ICU | 9 (9.0) | 0 (0) | 9 (13.2) | 0.05 |
| Duration | | | | |
| Hospital length of stay, days | 8 (6–16) | 9 (6–14) | 8 (5.0–17) | 0.94 |
| ICU length of stay, days | 4 (2–7) | 5 (2–7) | 4 (2–7) | 0.46 |
| Invasive mechanical ventilation[1], days | 4 (2–7) | 4 (3–7) | 4 (2–7) | 0.70 |

Data are presented as number (%) and median (interquartile range). ICU = Intensive care unit.

[1] Eighty-one patients on invasive mechanical ventilation.

- **The use of PCR amplification in addition to routine microbiological investigations including cultures vastly improves the ability to detect both viral and bacterial pathogens in severe CAP**
- **Viral infection appears to be independently associated with lower hospital mortality**

# Serology Enhances Molecular Diagnosis of Respiratory Virus Infections Other than Influenza in Children and Adults Hospitalized with Community-Acquired Pneumonia

J Clin Microbiol 2017; Vol 55 (1): 79-89

Yange Zhang,[a,h] Senthilkumar K. Sakthivel,[a,h] Anna Bramley,[a] Seema Jain,[a] Amber Haynes,[a] James D. Chappell,[b] Weston Hymas,[c] Noel Lenny,[d,e] Anami Patel,[d,e] Chao Qi,[f] Krow Ampofo,[c] Sandra R. Arnold,[d,e] Wesley H. Self,[b] Derek J. Williams,[b] David Hillyard,[c] Evan J. Anderson,[i] Carlos G. Grijalva,[b] Yuwei Zhu,[b] Richard G. Wunderink,[f] Kathryn M. Edwards,[b] Andrew T. Pavia,[c] Jonathan A. McCullers,[d,e,g] Dean D. Erdman[a]

**TABLE 2** Comparison of RT-PCR and serology for CAP patients by cycle threshold value

| | RSV | | | HMPV | | | PIV1, -2, -3 | | | AdV | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| RT-PCR $C_T$[a] | No. positive by RT-PCR | No. (%) positive by RT-PCR and serology | No. (%) positive by RT-PCR and negative by serology | No. positive by RT-PCR | No. (%) positive by RT-PCR and serology | No. (%) positive by RT-PCR and negative by serology | No. positive by RT-PCR | No. (%) positive by RT-PCR and serology | No. (%) positive by RT-PCR and negative by serology | No. positive by RT-PCR | No. (%) positive by RT-PCR and serology | No. (%) positive by RT-PCR and negative by serology |
| ≤20 | 37 | 27 (73.0) | 10 (27.0) | 2 | 1 (50.0) | 1 (50.0) | 5 | 4 (80.0) | 1 (20.0) | 13 | 11 (84.6) | 2 (15.4) |
| >20 ≤ 25 | 111 | 85 (76.6) | 26 (23.4) | 37 | 27 (73.0) | 10 (27.0) | 18 | 13 (72.2) | 5 (27.8) | 8 | 3 (37.5) | 5 (62.5) |
| >25 ≤ 30 | 78 | 60 (76.9) | 18 (23.1) | 62 | 43 (69.4) | 19 (30.6) | 26 | 18 (69.2) | 8 (30.8) | 17 | 4 (23.5) | 13 (76.5) |
| >30 ≤ 35 | 45 | 25 (55.6) | 20 (44.4) | 48 | 30 (62.5) | 18 (37.5) | 23 | 8 (34.8) | 15 (65.2) | 33 | 6 (18.2) | 27 (81.8) |
| >35 < 40 | 16 | 3 (18.8) | 13 (81.2) | 23 | 3 (13.0) | 20 (87.0) | 23 | 4 (17.4) | 19 (82.6) | 41 | 2 (4.9) | 38 (92.7) |
| Total | 287 | 200 (69.7) | 87 (30.3) | 172 | 104 (60.5) | 68 (39.5) | 95 | 47 (49.5) | 48 (50.5) | 111 | 26 (23.2) | 85 (76.6) |

**RT-PCR provided the highest number of positive detections overall, but serology increased diagnostic yield for RSV by 11.8%, human metapneumovirus (HMPV) by 25.0%, adenovirus (AdV) by 32.4%, and parainfluenza virus (PIV) by 48.9%**

Clinical Infectious Diseases 2016;62(7):817–23

# Comprehensive Molecular Testing for Respiratory Pathogens in Community-Acquired Pneumonia

Naomi J. Gadsby,[1] Clark D. Russell,[1,2] Martin P. McHugh,[1] Harriet Mark,[1] Andrew Conway Morris,[3] Ian F. Laurenson,[1] Adam T. Hill,[4] and Kate E. Templeton[1]

- A large number of additional factors influence antimicrobial selection (e.g. severity of illness, concurrent infection at sites other than the lower respiratory tract, drug allergy, antimicrobial susceptibility testing, inflammatory markers)
- It is highly likely that enhancing the detection of pathogens and reporting of bacterial loads would have a major impact on the clinical decision-making process

**Table 3. Estimated Potential Impact of Comprehensive Molecular Testing on Antimicrobial Prescribing in Patients With Community-Acquired Pneumonia (n = 320)**

| Potential Modification | Antibiotic Agent | N (%) |
|---|---|---|
| De-escalation | | 247 (77.2) |
| Remove 1 agent | | 113 |
| | CLR | 108 |
| | AMC | 2 |
| | Other[a] | 3 |
| Remove 2 agents | | 12 |
| | CLR + AMX | 6 |
| | CLR + DOX | 6 |
| Reduce spectrum of agent | | 12 |
| | AMC to DOX | 8 |
| | AMC to AMX | 2 |
| | Other[b] | 2 |
| Reduce number and spectrum | | 110 |
| | AMC + CLR to DOX | 61 |
| | AMC + CLR to AMX | 22 |
| | AMX + CLR to AMC | 12 |
| | AMX + CLR to DOX | 5 |
| | CRO + CLR to DOX | 4 |
| | AMC + CLR to LEV | 2 |
| Other[c] | | 4 |
| Escalation | | 19 (5.9) |
| Add 1 agent | | 2 |
| | CIP | 1 |
| | DOX | 1 |
| Increase spectrum of agent | | 15 |
| | CLR to DOX | 6 |
| | CLR to CIP | 3 |
| | DOX to AMC | 3 |
| | Other[d] | 3 |
| Increase number and spectrum | | 2 |
| | AMX to DOX + CLR | 1 |
| | CLR to AMX + CIP | 1 |
| No change | | 54 (16.9) |

Abbreviations: AMC, amoxicillin-clavulanic acid; AMX, amoxicillin; AZM, azithromycin; CIP, ciprofloxacin; CLR, clarithromycin; CRO, ceftriaxone; DOX, doxycycline; LEV, levofloxacin.

J Infect Dis 2017;216:936–44

# Multiplex Respiratory Virus Testing for Antimicrobial Stewardship: A Prospective Assessment of Antimicrobial Use and Clinical Outcomes Among Hospitalized Adults

Makeda Semret,[1] Ian Schiller,[2] Barbara Ann Jardin,[2] Charles Frenette,[1] Vivian G. Loo,[1] Jesse Papenburg,[1] Shelly A. McNeil,[4] and Nandini Dendukuri[3]

**Table 4. Change in Management of Antivirals and Antibiotics After Respiratory Virus Panel (RVP) Testing Among Patients Treated Empirically (Before Testing), by RVP Result**

| Treatment, Pneumonia Suspicion | Influenza Virus Positive | Other Virus Positive | Virus Negative |
|---|---|---|---|
| Antivirals | | | |
| Suspicion | | | |
| Patients | 47[a] | 4 | 18 |
| Antiviral continued[b] | 37 (79) | 0 (0) | 1 (6) |
| No suspicion | | | |
| Patients | 100[a] | 5 | 12 |
| Antiviral continued[c] | 81 (81) | 1 (20) | 6 (50) |
| Antibiotics | | | |
| Suspicion | | | |
| Patients[d] | 57 | 15 | 90 |
| Antibiotic continued[e] | 35 (61) | 12 (80) | 63 (70) |
| No suspicion | | | |
| Patients[d] | 53 | 7 | 42 |
| Antibiotic continued[f] | 21 (40) | 1 (14) | 26 (62) |

- Influenza virus positivity is associated with shorter durations of hospitalization and leads to appropriate management decisions, including instituting antivirals and a rend toward antibiotic de-escalation
- Rapid testing for a broad array of viruses does not appear, by itself, to be useful for stewardship interventions among hospitalized adult patients, unless it can be combined with additional means of ruling out bacterial coinfections

# Θεραπευτικοί και προφυλακτικοί παράγοντες για τη βαριά ιογενή πνευμονία

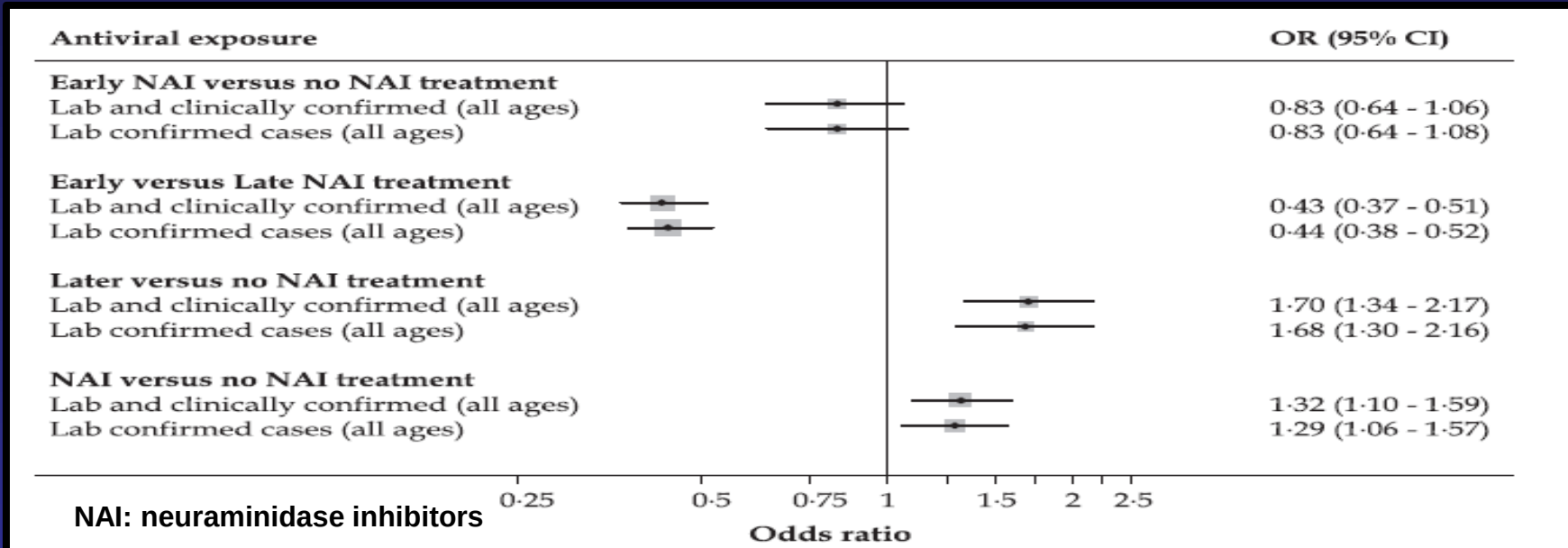
Ruuskanen O, et al. Lancet 2011

| | Treatment | Prevention |
|---|---|---|
| Influenza A and B viruses | Oseltamivir (oral); zanamivir (inhalation, intravenous); peramivir (intravenous) | Vaccines (inactivated, live); oseltamivir; zanamivir |
| Influenza A virus | Amantadine (oral); rimantadine (oral) | .. |
| Respiratory syncytial virus | Ribavirin (inhalation, intravenous) | Palivizumab (intramuscular) |
| Adenovirus | Cidofovir (intravenous) | Vaccine for types 4 and 7* |
| Rhinovirus | Pleconaril† | Alfa interferon (intranasal) |
| Enteroviruses | Pleconaril† | .. |
| Human metapneumovirus | Ribavirin (intravenous) | .. |
| Hantavirus | Ribavirin (intravenous) | .. |
| Varicella-zoster virus | Aciclovir (intravenous) | Vaccine |

*Long successful use in US military conscripts, no production now. †Has been used for compassionate cases.

# Impact of neuraminidase inhibitors on influenza A(H1N1) pdm09-related pneumonia: an individual participant data meta-analysis

Mathouri SG, et al. (2016) Influenza and Other Respiratory Viruses, 2016 10(3) 192–204




NAI: neuraminidase inhibitors

- Early NAI treatment probably reduces the likelihood of influenza-related pneumonia (IRP)
- NAI treatment compared with no NAI treatment was associated with an increased likelihood of IRP (due to late administration, in response to pneumonia?)
- In patients with IRP, early NAI treatment versus later reduced the need for ventilatory support and subsequent mortality


Καλές γιορτές!