CAP 2023

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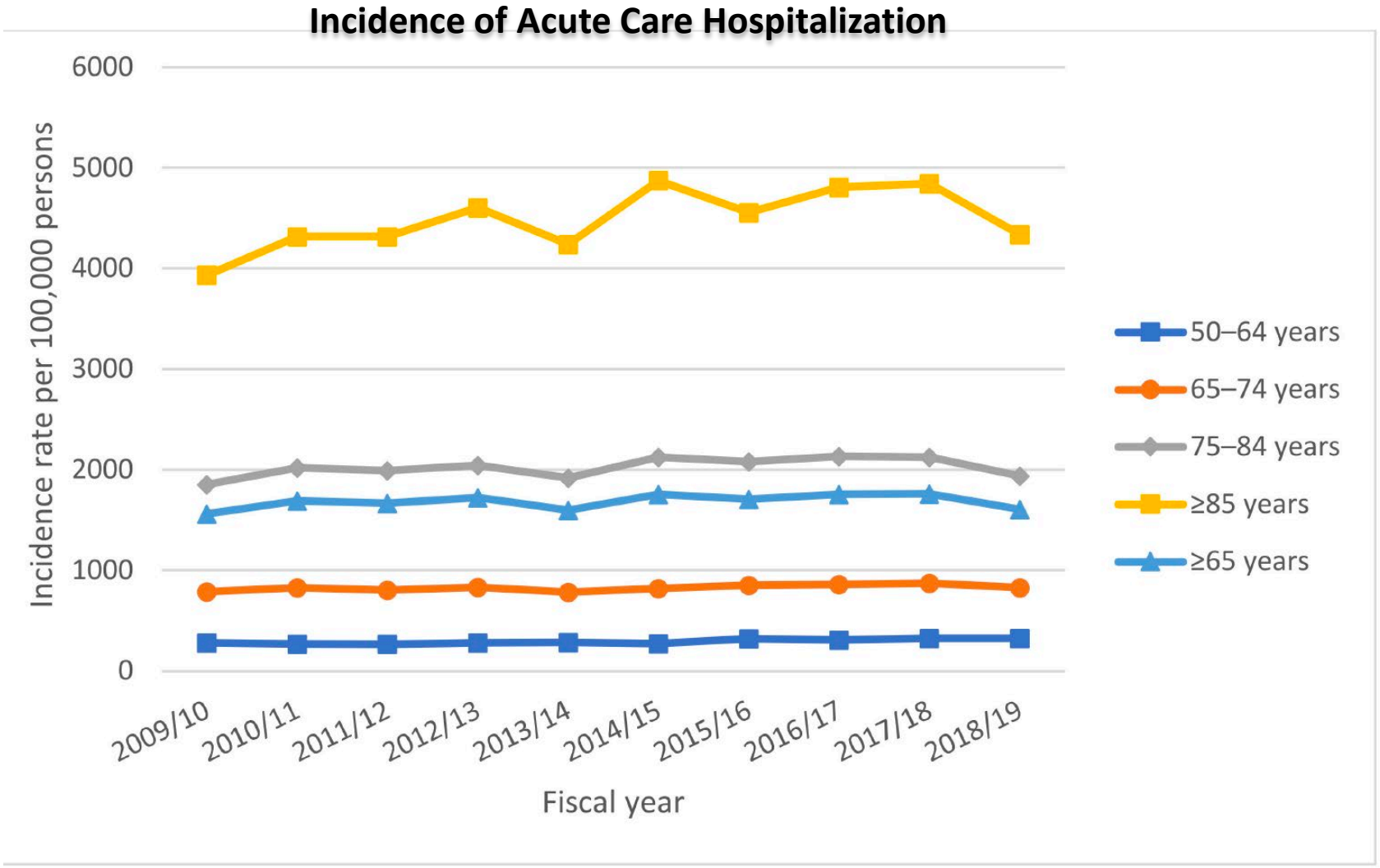
Consultant/Advisory Board/Speaker fees

- Pfizer, MSD, Angelini
- Thermo Fisher, Shionogi
- BioTest, Nordic Pharma, InfectoPharma
- Gilead Sciences, GSK
- Hikma, Advanz, Correvio
- Tillots, Menarini

- **Research grant**
  - Pfizer, MSD, Shionogi

Acute-Care Hospitalization for CAP in Canadian Adults >50yo: Most Responsible Diagnosis Tells Only Part of the Story

Grajales Beltrán AG et al. Vaccines (Basel) 2023;11(4):748



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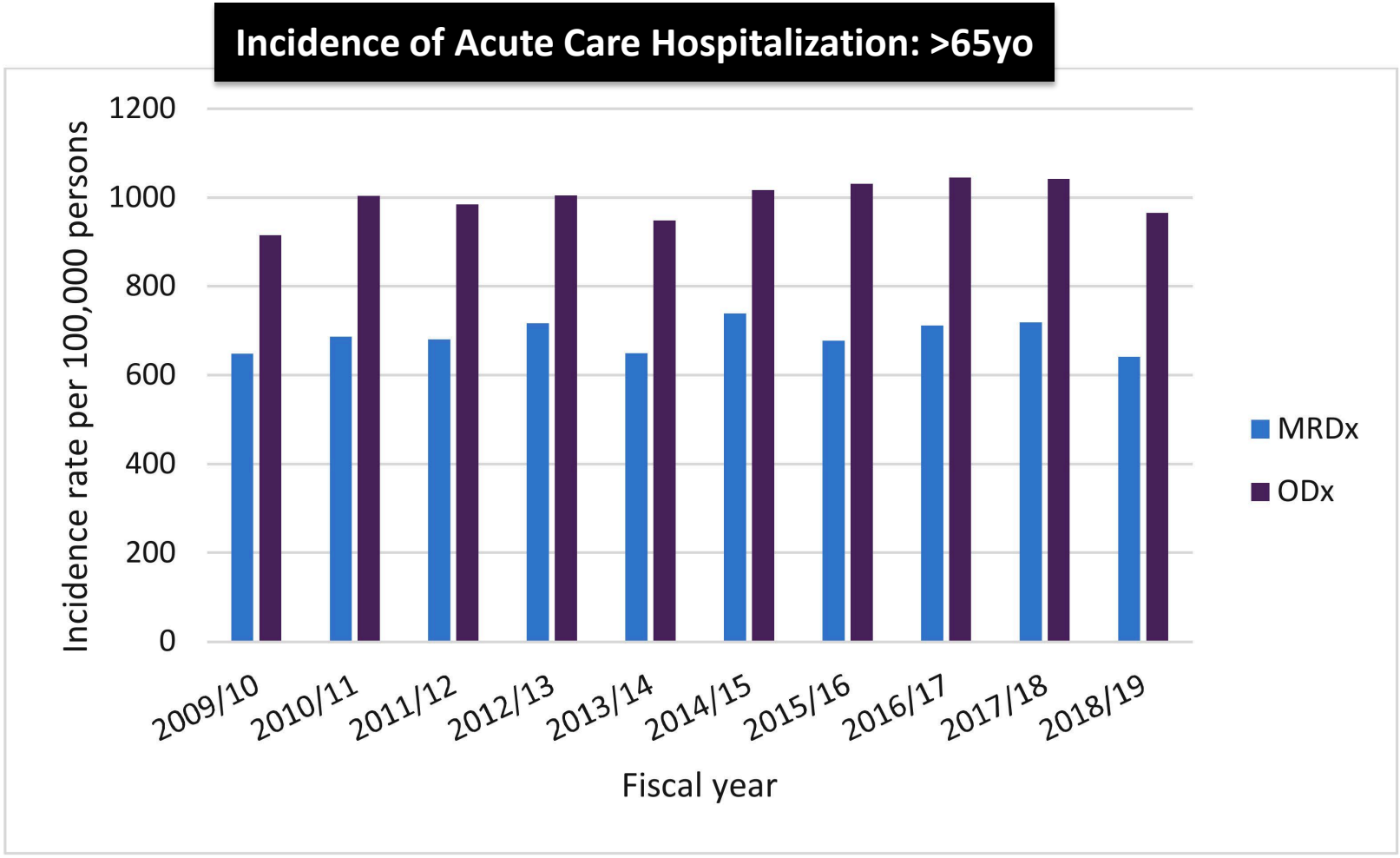

(b)

Acute-Care Hospitalization for CAP in Canadian Adults >50yo: Most Responsible Diagnosis Tells Only Part of the Story

Grajales Beltrán AG et al. Vaccines (Basel) 2023;11(4):748

- **CAP estimates at admission using ICD codes (2009-2019):**
  - **MRDx:** CAP as the most responsible diagnosis
  - **ODx:** CAP as other than most responsible diagnosis
    - Also "Pre-admit comorbidity type 1"
- **Reported outcomes:**
  - Pneumonia incidence rate, in-hospital mortality
  - Hospital length of stay, cost
- **CAP incidence increased from 805.66 to 896.94 per 100,000**
  - 55-58% of cases had pneumonia coded as ODx
  - ODx had longer hospital stays & costs & higher in-hospital mortality
- **→ The burden of CAP not solely focusing on MRDx**

Outcomes of CAP: PSI Vs. CURB-65 in Routine Practice of Emergency Departments

Kaal AG et al. ERJ Open Res 2023 May 2;9(3):00051-2023

- **Nationwide retrospective cohort Study, Netherlands**
- **Main outcomes:**
  - Hospital admission rates, ICU admissions, length of hospital stay, delayed admissions, readmissions, all-cause 30-day mortality
- **50.984 CAP patients**
  - 21157 **CURB-65 hospitals**
  - 17279 **PSI hospitals**
  - 12548 **No-consensus hospitals**
- **→ 30-day mortality**
  - Significantly lower in CURB-65 hospitals versus PSI hospitals
    - 8.6% and 9.7%, adjusted odds ratio (aOR) 0.89, 95% CI: 0.83-0.96, p=0.003

Practical Severity Assessment Model: CURB 65

- 6 point (0-5) score. One each for:

Confusion	Resp rate	Age > 65
Urea	Blood Pressure	

CURB 65

- % Mortality (30 day), points (CURB-65)
  - 0--0.7
  - 1--3.2
  - 2--3
  - 3--17
  - 4--41.5
  - 5---57

Lim et al. Thorax 2003; 58: 377

Outcomes of CAP: PSI Vs. CURB-65 in Routine Practice of Emergency Departments

Kaal AG et al. ERJ Open Res 2023 May 2;9(3):00051-2023

	CURB-65 hospital	PSI hospital	No-consensus hospital	Total
Total patients	21 157 (41.5)	17 279 (33.9)	12 548 (24.6)	50 984 (100)
Female patients	10 096 (47.7)	8019 (46.4)	5947 (47.4)	24 062 (47.2)
Age years	72 (60–81)	72 (60–81)	72 (61–82)	72 (60–81)
Age range years				
18–49 years	2838 (13.4)	2184 (12.6)	1493 (11.9)	6515 (12.8)
50–64 years	4185 (19.8)	3469 (20.1)	2458 (19.6)	10 112 (19.8)
65–74 years	5083 (24.0)	4203 (24.3)	3008 (24.0)	12 294 (24.1)
75–84 years	5500 (26.0)	4471 (25.9)	3339 (26.6)	13 310 (26.1)
>85 years	3551 (16.8)	2952 (17.1)	2250 (17.9)	8753 (17.2)
SES score				
Quartile 1	5020 (23.7)	6219 (36.0)	3299 (26.3)	14 538 (28.5)
Quartile 2	6011 (28.4)	4166 (24.1)	3716 (29.6)	13 893 (27.2)
Quartile 3	5533 (26.2)	3861 (22.4)	2973 (23.7)	12 367 (24.3)
Quartile 4	4593 (21.7)	3033 (17.6)	2560 (20.4)	10 186 (20.0)
Comorbidities				
History of neoplastic disease[#]	3849 (18.2)	3212 (18.6)	2192 (17.5)	9253 (18.1)
Liver disease[#]	292 (1.4)	229 (1.3)	134 (1.1)	655 (1.3)
Congestive heart failure[#]	1993 (9.4)	1764 (10.2)	1279 (10.2)	5036 (9.9)
Cerebrovascular disease[#]	1574 (7.4)	1285 (7.4)	923 (7.4)	3782 (7.4)
Chronic renal disease[#]	1153 (5.5)	997 (5.8)	635 (5.1)	2785 (5.5)
Cardiovascular disease[¶]	4250 (20.1)	3716 (21.5)	2559 (20.4)	10 525 (20.6)
Pulmonary disease[+]	4048 (19.1)	3455 (20.0)	2468(19.7)	9971 (19.6)
Diabetes mellitus[§]	3713 (17.6)	3278 (19.0)	2285 (18.2)	9276 (18.2)
Immunocompromised[ƒ]	576 (2.7)	515 (3.0)	367 (2.9)	1458 (2.9)
Neurological disease[##]	457 (2.2)	403 (2.3)	288 (2.3)	1148 (2.3)
HIV infection[¶]	66 (0.3)	32 (0.2)	15 (0.1)	113 (0.2)
Treated at pulmonology department	15 051 (71.1)	12 387 (71.7)	8905 (71.0)	36 343 (71.3)
Treated at teaching hospital	12 796 (60.5)	10 722 (62.1)	5075 (40.4)	28 593 (56.1)
Main clinical outcomes				
Admission	16 331 (77.2)	13 807 (79.9)	10 230 (81.5)	40 368 (79.2)
ICU admission	1869 (8.8)	1395 (8.1)	1077 (8.6)	4341 (8.5)
30-day mortality	1827 (8.6)	1682 (9.7)	1119 (8.9)	4628 (9.1)

Outcomes of CAP: PSI Vs. CURB-65 in Routine Practice of Emergency Departments

Kaal AG et al. ERJ Open Res 2023 May 2;9(3):00051-2023

TABLE 2 Multilevel analysis of outcomes of patients with community-acquired pneumonia using CURB-65 *versus* Pneumonia Severity Index (PSI)

	CURB-65	PSI	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Patients n	21 157	17 279		
Admission	16 331 (77.2)	13 807 (79.9)	0.81 (0.64–1.02)	0.81 (0.64–1.02)
Readmission[#]	410 (2.5)	329 (2.3)	1.03 (0.86–1.24)	1.02 (0.85–1.22)
Delayed admission[¶]	371 (7.7)	275 (7.9)	0.98 (0.79–1.21)	0.99 (0.80–1.22)
ICU admission[+]	1869 (8.8)	1395 (8.1)	1.10 (0.93–1.31)	1.14 (0.96–1.35)
30-day mortality[+]	1827 (8.6)	1682 (9.7)	0.88 (0.81–0.96)	0.89 (0.83–0.96)

Data are presented as n (%) unless stated otherwise. Readmission was defined as patients who were discharged from the hospital but readmitted within 7 days. Delayed admission was defined as emergency department pneumonia patients initially treated as outpatients, but who were admitted to the hospital within 7 days. ICU: intensive care unit. [#]: percentage out of the total number of (delayed) admissions; [¶]: percentage out of the total number of initial outpatients; [+]: percentage out of the total number of patients.

Outcomes of CAP: PSI Vs. CURB-65 in Routine Practice of Emergency Departments

Kaal AG et al. ERJ Open Res 2023 May 2;9(3):00051-2023

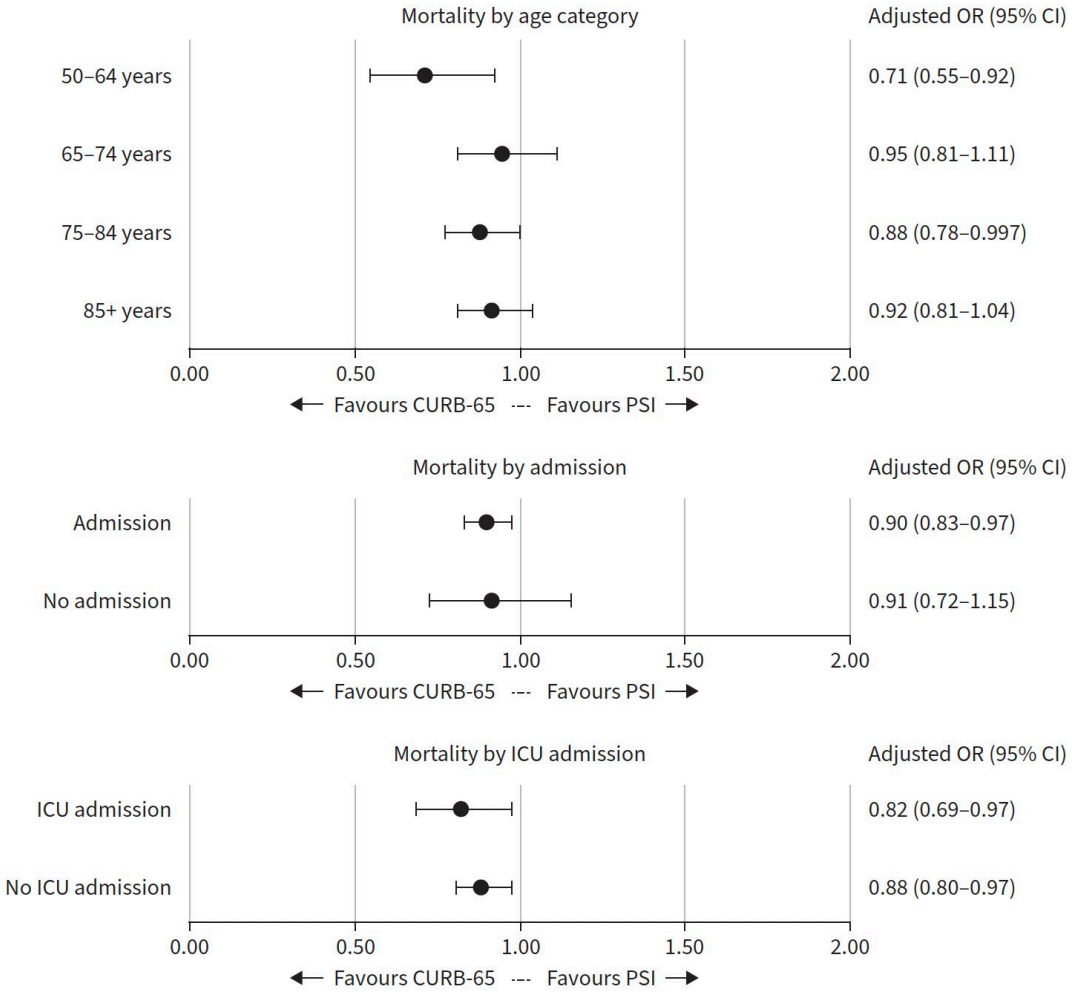

FIGURE 2 Subgroup analysis for the primary outcome 30-day mortality in patients with community-acquired pneumonia: CURB-65 *versus* Pneumonia Severity Index (PSI). ICU: intensive care unit.

Limited Clinical Impact of Ultralow-Dose CT in Suspected CAP: OPTIMAC Trial

van Engelen TSR et al Open Forum Infect Dis 2023 Apr 20;10(5):ofad215

- **Patients suspected of CAP were randomized:**
  - Ultralow-dose chest computed tomography (ULDCT): 261 patients
  - Chest radiograph (CXR): 231 patients
- **Main Message:**
  - No evidence of any antibiotic treatment policy change
  - No different patient outcomes
- **But:**
- **In a subgroup of afebrile patients**

  → More patients diagnosed with CAP in the ULDCT group (P = .001)
  - ULDCT, 106 of 608 patients
  - CXR, 71 of 654 patients

BAL in Elderly Patients with CAP: Clinical Characteristics and Pathogen Analysis

Guo RN et al. Immun Inflamm Dis 2023 Apr;11(4):e813

- **92 cases:**
  - 44 patients >75 year-old and 48 patients 65-74 year-old
- **The elderly over 75-yo with diabetes are:**
  - More likely to suffer from CAP — 35.42% vs. 63.64%, p = 0.007
  - More likely with mixed infections — 6.25% vs. 22.73%, p = 0.023
  - More likely to have larger lesions — 45.83% vs. 68.18%, p = 0.031
  - Prolonged hospital stays — 39.58% vs. 63.64%, p = 0.020
- **→ Clinical symptoms & signs not so typical**
- **→ Infection is more serious**
- **→ Prediction of prognosis:**
  - Hypoalbuminemia & high d-dimer

Factors affecting Hospital Discharge Outcomes in CAP: A Retrospective Epidemiological Study (2014-2021)

Chen S et al Am J Med Sci 2023

- **1008 patients with CAP, 247 patients discharged as remission**
- **Multivariate logistic regression:**
  - **Independent ssociation of poor discharge outcomes** All P<0.05
    - Age >65 years
    - Smoking history
    - Co-morbidities: COPD, chronic heart disease, diabetes, malignancy, cerebrovascular disease
    - Pleural effusion, hypoxemia, electrolyte disturbances
    - Severe pneumonia, respiratory failure
  - **Protective factor**
    - Pathogen-targeted therapy OR: 0.32, 95% CI: 0.16-0.62
- →→
- **CAP with defined etiology are more likely to be cured**
- **Accurate & efficient pathogen testing <u>essential for admitted CAP</u>**

Molecular Point-of-care Testing for Lower Respiratory Tract Pathogens Improves Safe Antibiotic de-escalation in Patients with Pneumonia in the ICU: Results of a Randomised Controlled Trial

Poole S et al J Infect 2022;85:625-633

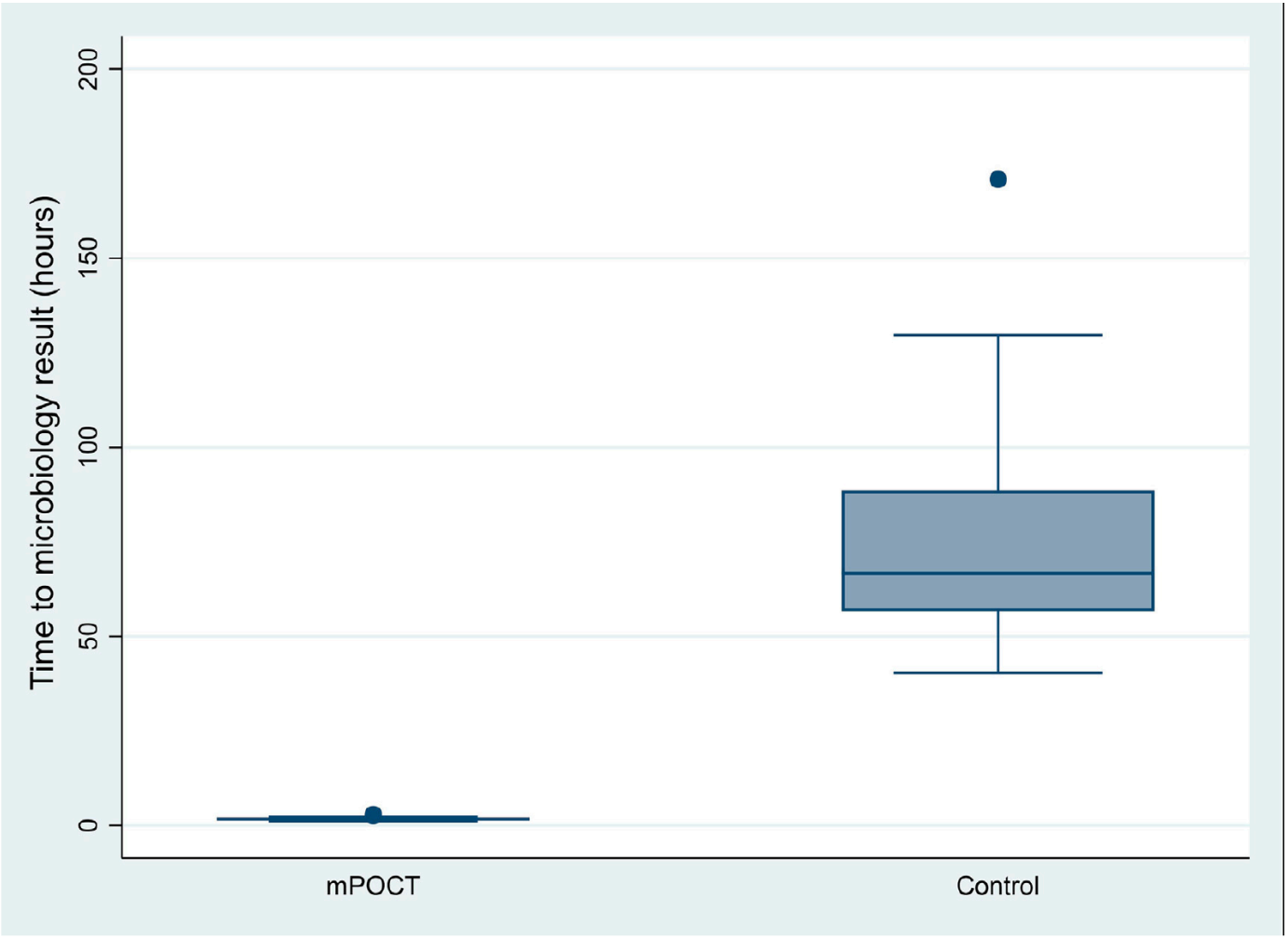

Fig. 2. Time to microbiology results.

Molecular Point-of-care Testing for Lower Respiratory Tract Pathogens Improves Safe Antibiotic de-escalation in Patients with Pneumonia in the ICU: Results of a Randomised Controlled Trial

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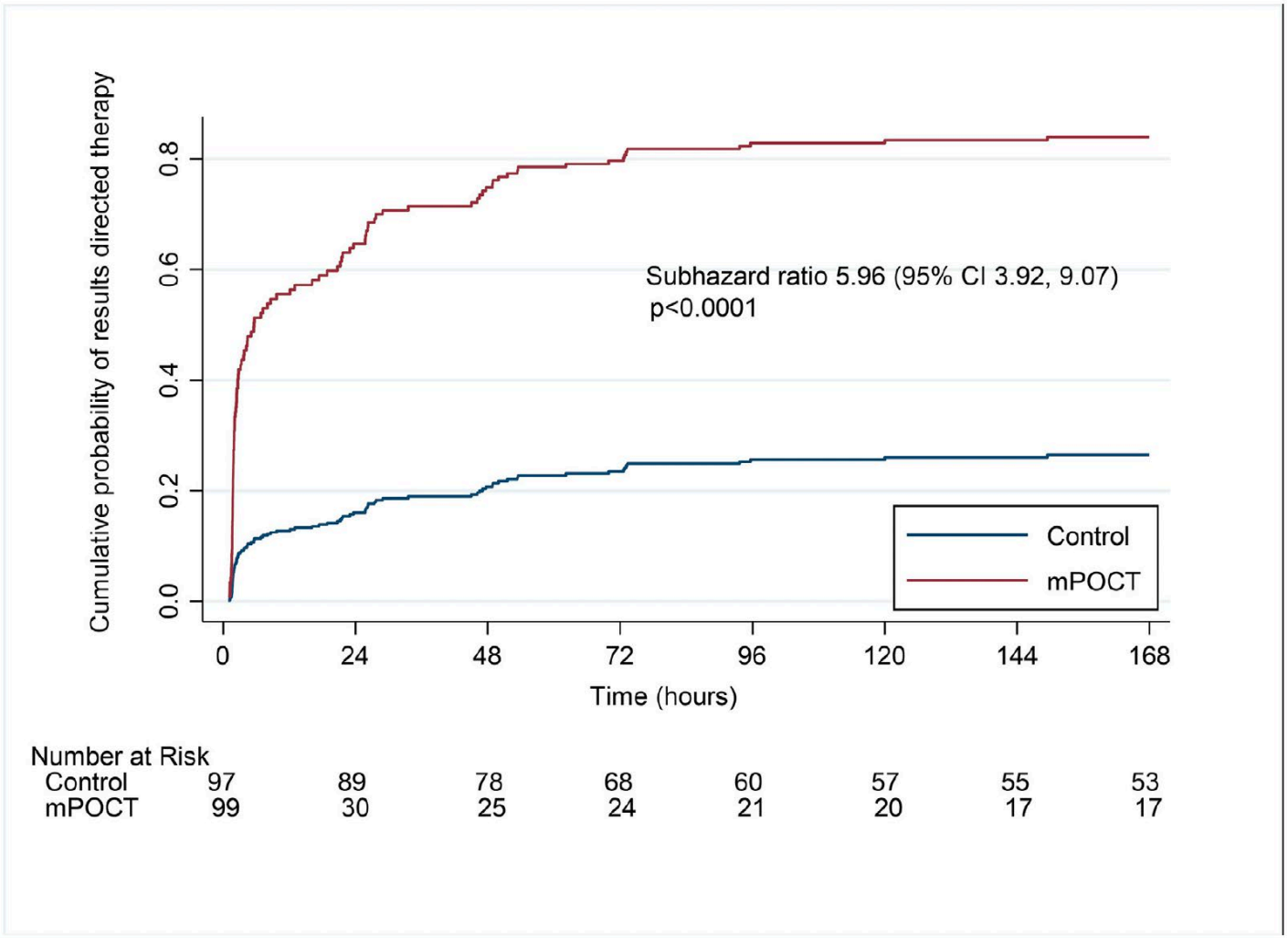

Fig. 3. Time-to-event curve for results-directed antimicrobial therapy.

Molecular Point-of-care Testing for Lower Respiratory Tract Pathogens Improves Safe Antibiotic de-escalation in Patients with Pneumonia in the ICU: Results of a Randomised Controlled Trial

Poole S et al J Infect 2022;85:625-633

- **Pragmatic, randomised trial of 200 critically ill adults with pneumonia**
  - 1:1 randomization to molecular testing at the point-of-care (mPOCT) or routine clinical care
  - **Primary outcome:** proportion of results-directed antimicrobial therapy
- **CAP: 85 patients (42 Vs. 43)**
- **HAP: 69 patients (30 Vs. 39)**
- **VAP: 46 patients (28 Vs. 18)**
- **Median [IQR] time to results (h)**
  - 1.7 [1.6-1.9] Vs. 66.7 [56.7-88.5] (difference of -65.0 h, 95% CI -68.0 to -62.0; $p < 0.0\ 0\ 01$)
- **Pathogens detected therapy:**
  - 71 Vs. 51 (51%) (difference of 20%, 95% CI 7 to 33; $p = 0.004$)
- **Results-directed therapy: 80 Vs. 29 (80% Vs. 29%)**
- **Time to results-directed therapy: 2.3 [1.8-7.2] Vs. 46.1 hours**
- **De-escalation: 42 Vs. 8 (42% Vs. 8%)**
- **Time to de-escalation: 4.8 [2.4-13.0] Vs. 46.5 hours [26.3-48.6]**
  - Difference of -41.4 h, 95% CI -53 to -29.7; $p < 0.0001$)

Molecular Point-of-care Testing for Lower Respiratory Tract Pathogens Improves Safe Antibiotic de-escalation in Patients with Pneumonia in the ICU: Results of a Randomised Controlled Trial

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Table 3
Pathogens detected according to type of pneumonia.

	CAP mPOCT $n = 42$	CAP Control $n = 43$	HAP mPOCT $n = 30$	HAP Control $n = 39$	VAP mPOCT $n = 28$	VAP Control $n = 18$
Any pathogen	25 (60)	20 (47)	20 (67)	18 (46)	26 (93)	13 (72)
Single pathogen	15/25 (60)	17/20 (85)	8/20 (40)	15/18 (83)	15/26 (58)	8/13 (62)
Multiple pathogens	10/25 (40)	3/20 (15)	12/20 (60)	3/18 (17)	11/26 (42)	5/3 (38)*
Frequency of detection of individual pathogens						
S. pneumoniae	1	0	2	2	1	1
S. aureus	6	6	7	0	2	3
H. influenzae	5	0	3	2	2	1
M. catarrhalis	0	0	1	0	0	0
H. parainfluenzae	0	1	0	0	0	1
L. pneumophilia	0	1	0	0	0	0
K. pneumoniae group	1	2	2	3	2	3
E. coli	3	1	6	3	6	1
S. marcescens	2	0	3	2	2	1
E. cloacae complex	1	0	1	2	1	0
K. aerogenes	1	1	2	0	0	0
K. oxytoca	2	0	1	1	5	1
S. maltophilia	0	0	0	1	0	0
P. mirabilis	1	0	0	1	3	1
Citrobacter spp	1	1	0	0	1	0
P. aeruginosa	5	1	3	3	15	3
Rhinovirus/enterovirus	3	2	1	0	0	0
RSV	1	0	0	1	0	0
Parainfluenza virus	1	0	0	0	0	0
Seasonal coronavirus†	0	0	2	0	0	0
SARS-CoV-2‡	6	7	0	0	0	0

All data are presented as n (%). mPOCT, molecular point-of-care testing. CAP, Community acquired pneumonia. HAP, Hospital acquired pneumonia. VAP, ventilator associated pneumonia. RSV, respiratory syncytial virus.

* One culture reported as mixed coliforms.

† Seasonal human coronavirus includes; HKU1, 229E, NL63 and OC43. SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2.

‡ SARS-CoV-2 is not a target on the FilmArray Pneumonia panel and was tested using laboratory PCR. This data applies only to initial diagnostic testing for this episode of pneumonia (i.e. for HAP/VAP developing subsequently in a patient hospitalised with COVID-19, the SARS-CoV-2 PCR result is not included, but is recorded with baseline characteristics).

Open Forum Infectious Diseases

MAJOR ARTICLE

A Phase 3 Study to Compare Delafloxacin With Moxifloxacin for the Treatment of Adults With Community-Acquired Bacterial Pneumonia (DEFINE-CABP)

Juan P. Horcajada,[1] Robert A. Salata,[2] Rodolfo Álvarez-Sala,[3] Floarea Mimi Nitu,[4] Laura Lawrence,[5] Megan Quintas,[5] Chun-Yen Cheng,[6] and Sue Cammarata[5]; for the DEFINE-CABP Study Group[*]

[1]Hospital del Mar, Institut Hospital del Mar d'Investigacions Mèdiques (IMIM), Universitat Autònoma de Barcelona and Universitat Pompeu Fabra, Barcelona, Spain, [2]Case Western Reserve University, Cleveland, Ohio, USA, [3]University Hospital la Paz, Madrid, Spain, [4]Victor Babes Clinical Hospital of Infectious Diseases and Pneumophtisiology, Craiova, Romania, [5]Melinta Therapeutics, Lincolnshire, Illinois, USA, and [6]Firma Clinical Research, Hunt Valley, Maryland, USA

Background. The clinical and economic burden of community-acquired bacterial pneumonia (CABP) is significant and is anticipated to increase as the population ages and pathogens become more resistant. Delafloxacin is a fluoroquinolone antibiotic approved in the United States for the treatment of adults with acute bacterial skin and skin structure infections. Delafloxacin's shape and charge profile uniquely impact its spectrum of activity and side effect profile. This phase 3 study compared the efficacy and safety of delafloxacin with moxifloxacin for the treatment of CABP.

Methods. A randomized, double-blind, comparator-controlled, multicenter, global phase 3 study compared the efficacy and safety of delafloxacin 300 mg twice daily or moxifloxacin 400 mg once daily in adults with CABP. The primary end point was early clinical response (ECR), defined as improvement at 96 (±24) hours after the first dose of study drug. Clinical response at test of cure (TOC) and microbiologic response were also assessed.

Results. In the intent-to-treat analysis population (ITT), ECR rates were 88.9% in the delafloxacin group and 89.0% in the moxifloxacin group. Noninferiority of delafloxacin compared with moxifloxacin was demonstrated. At TOC in the ITT population, the success rates were similar between groups. Treatment-emergent adverse events that were considered at least possibly related to the study drug occurred in 65 subjects (15.2%) in the delafloxacin group and 54 (12.6%) in the moxifloxacin group.

Conclusions. Intravenous/oral delafloxacin monotherapy is effective and well tolerated in the treatment of adults with CABP, providing coverage for Gram-positive, Gram-negative, and atypical pathogens.

ClinicalTrials.gov Identifier. NCT03534622.

Keywords. CABP; delafloxacin; fluoroquinolone; moxifloxacin; pneumonia.

Delafloxacin in CAP

Lee A et al. Drugs 2022

Table 2 Comparative in vitro antimicrobial activity of delafloxacin against selected bacterial isolates

	Isolates[a]	MIC_{90} range across studies in mg/L [% susceptible; FDA breakpoints]				
		Delafloxacin	Levofloxacin	Moxifloxacin	Ceftaroline	Ceftriaxone
Gram-positive isolates						
Staphylococcus aureus [11, 26, 34]	5867	0.004–0.25	>4		1	
Levofloxacin-resistant [34]	1252	1				
MSSA [11, 15, 26, 34, 35]	5293	0.004–0.12 [91.8]	2–4 [88.3]	1 [88.6]	0.25	
Levofloxacin-resistant MSSA [34]	213	1				
MRSA [15, 16, 26, 34]	2596	0.5–4	>4–>16		1	
Levofloxacin-resistant MRSA [34]	1039	1				
Streptococcus pneumoniae [11, 13, 26, 35–37]	6536	0.015–0.03 [97.6]	1–2 [99.4]	0.25 [99.6]	0.12	0.5–1
MDR [11, 36–38]	431	0.015–0.03	1–2	0.25	0.12	2
Levofloxacin-resistant [37, 39]	203	0.12–0.5	>4	4	0.12	2
Penicillin nonsuseptible [36, 38]	1544	0.03	1–2	0.25		
Erythromycin nonsuseptible [36]	651	0.03	2	0.25		

Steroids & CAP

Date	Paper
• May 25, 2023	• Dequin NEJM, CAPE COD Trial, France, "Severe CAP"→ hydrocortisone
• April-December 2022	• ESICM Guidelines
• August 2022	• Meduri GU, Intens Care Med, USA, "Critically Ill patients with severe CAP"→ methylprednisolone
• April 2023	• Pitre T et al. J Gen Intern Med Metanalysis

Hydrocortisone in Severe CAP: CAPE COD Trial (2015-2020 in France)

Dequin PF et al. NEJM 2023 May 25;388(21):1931-1941

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Hydrocortisone (N = 400)	Placebo (N = 395)
Median age (IQR) — yr	67 (58–77)	67 (58–78)
Sex — no. (%)		
Male	281 (70.2)	271 (68.6)
Median Pulmonary Severity Index (IQR)†	127 (102–153)	130 (103–150)
Distribution — no./total no. (%)		
Class I	5/396 (1.3)	4/392 (1.0)
Class II	15/396 (3.8)	15/392 (3.8)
Class III	45/396 (11.4)	47/392 (12.0)
Class IV	150/396 (37.9)	133/392 (33.9)
Class V	181/396 (45.7)	193/392 (49.2)

Inclusion Criteria:

Respiratory failure with the initiation of at least high-flow oxygen
ICU admission
Absence of septic shock
No influenza

Hydrocortisone in Severe CAP

CAPE COD Trial (2015-2020 in France)

Dequin PF et al. NEJM 2023 May 25;388(21):1931-1941

Median SAPS II score (IQR)‡	37 (30–45)	38 (31–47)
Median SOFA score (IQR)§	4 (3–6)	4 (3–6)
Treatment with vasopressors — no. (%)	41 (10.2)	51 (12.9)
Laboratory data		
C-reactive protein		
Median (IQR) — mg/dl	26.3 (11.7–35.6)	23.8 (11.7–35.0)
Value of >15 mg/dl — no./total no. (%)	208/298 (69.8)	215/312 (68.9)
Median procalcitonin (IQR) — ng/ml	3.2 (0.5–16.4)	4.1 (0.6–16.0)
Median cortisol (IQR) — nmol/liter	302 (24–785)	307 (25–697)
Timing of treatment		
Median interval from hospital admission to ICU admission (IQR) — hr	5.5 (2.8–10.9)	5.2 (2.4–10.9)
Median interval from ICU admission to initiation of trial agent (IQR) — hr	15.3 (7.0–20.5)	14.6 (5.9–20.5)

Hydrocortisone in Severe CAP

CAPE COD Trial (2015-2020 in France)

Dequin PF et al. NEJM 2023 May 25;388(21):1931-1941

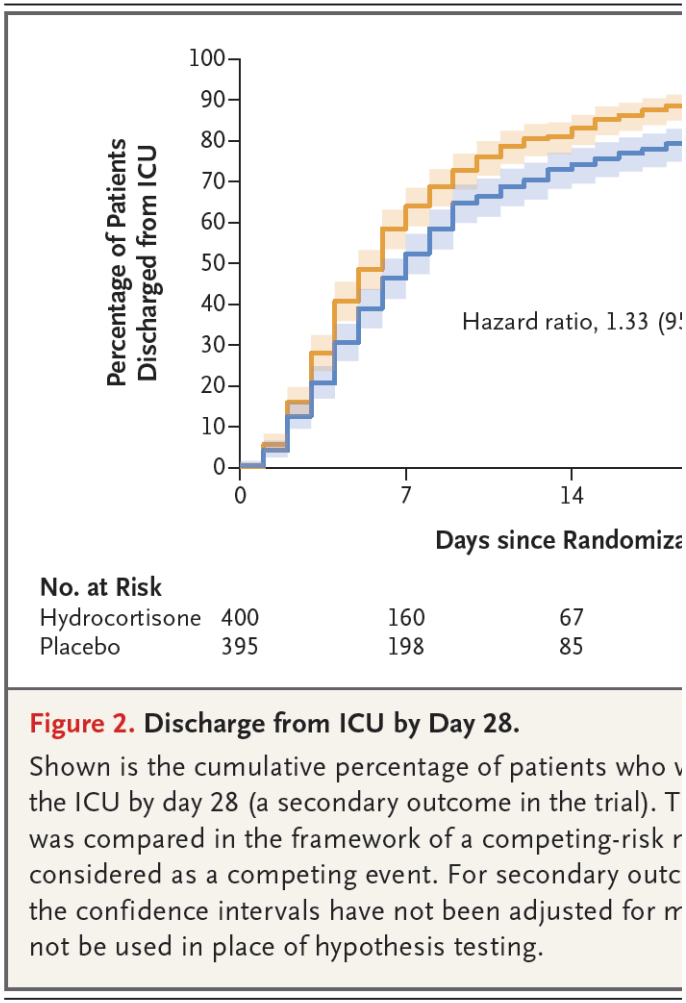
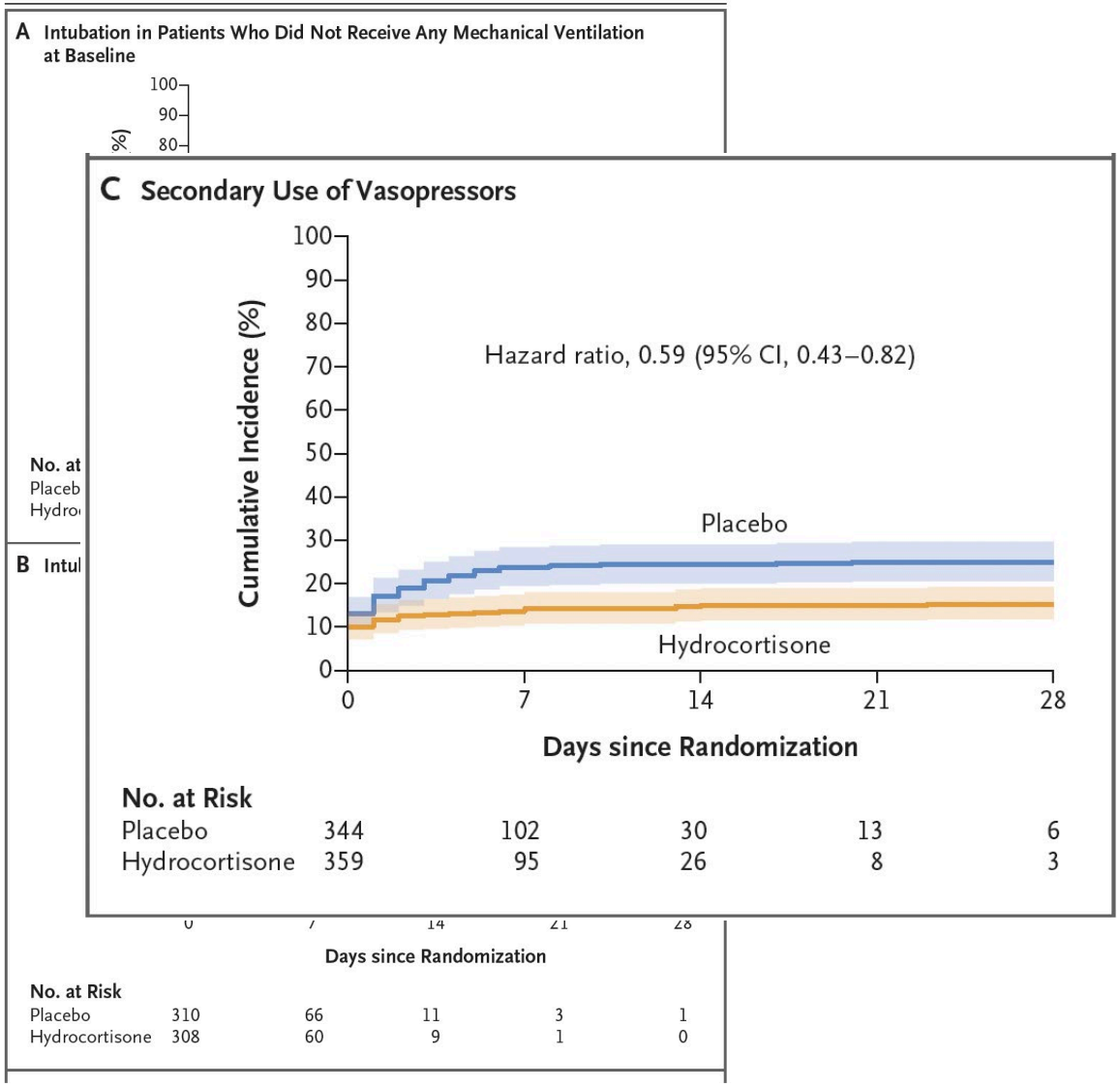


Figure 2. Discharge from ICU by Day 28.

Shown is the cumulative percentage of patients who v
the ICU by day 28 (a secondary outcome in the trial). T
was compared in the framework of a competing-risk r
considered as a competing event. For secondary outc
the confidence intervals have not been adjusted for m
not be used in place of hypothesis testing.



Hydrocortisone in Severe CAP

CAPE COD Trial (2015-2020 in France)

Dequin PF et al. NEJM 2023 May 25;388(21):1931-1941

- **800 patients randomization → trial stopped → 795 patients**
- **Day 28 mortality in hydrocortisone Vs. placebo group:**
  - 25 of 400 patients (6.2%) Vs. 47 of 395 patients (11.9%)
  - Absolute difference -5.6 percentage points; 95% CI -9.6 to -1.7; P = 0.006
- **Endotra… …e**
  - 40 of…
  - Haza…
- **If not re… …8**
  - 55 of…
  - Haza…
- **Adverse…**
  - Similar hospital-acquired infections and gastrointestinal bleeding,
  - Hydrocortisone group → higher daily doses of insulin during the first week of treatment
- **→ Hydrocortisone had a lower risk of death by day 28**

Bias:

PD of steroids: HD 200mg by continuous infusion (4-7d)

Early initiation of treatment

Septic shock excluded

30% of Females

Rate of Ashtma, COPD, Immunosuppression

Rate of definite etiology

ERS/ESICM/ESCMID/ALAT Guidelines for the Management of severe CAP

Martin-Loeches M et al Eur Resp J 2023

TABLE 1 Summary of research questions and recommendations

Questions	Recommendations
Question 1: In patients with sCAP, should rapid microbiological techniques be added to current testing of blood and respiratory tract samples?	If the technology is available, we suggest sending a lower respiratory tract sample (either sputum or endotracheal aspirates) for multiplex PCR testing (virus and/or bacterial detection) whenever non-standard sCAP antibiotics are prescribed or considered (conditional recommendation, very low quality of evidence)
Question 2: In hypoxaemic patients with sCAP, can either NIV or HFNO be used initially – rather than supplemental standard oxygen administration – to avoid intubation and reduce mortality?	In patients with sCAP and acute hypoxaemic respiratory failure not needing immediate intubation, we suggest using HFNO instead of standard oxygen (conditional recommendation, very low quality of evidence) NIV might be an option in certain patients with persistent hypoxaemic respiratory failure not needing immediate intubation, irrespective of HFNO (conditional recommendation, low quality of evidence)
Question 3: When using initial empirical therapy for sCAP, should a macrolide or fluoroquinolone be used as part of combination therapy, to reduce mortality and adverse clinical outcomes?	We suggest the addition of macrolides, not fluoroquinolones, to beta-lactams as empirical antibiotic therapy in hospitalised patients with sCAP (conditional recommendation, very low quality of evidence)
Question 4: In patients with sCAP, can serum PCT be used to reduce the duration of antibiotic therapy and improve other outcomes in comparison to standard of care not guided by serial biomarker measurements?	We suggest the use of PCT to reduce the duration of antibiotic treatment in patients with sCAP (conditional recommendation, low quality of evidence)

ERS/ESICM/ESCMID/ALAT Guidelines for the Management of severe CAP

Martin-Loeches M et al Eur Resp J 2023

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Question 5: Should oseltamivir be added to standard therapy in patients with sCAP and confirmed influenza?	We suggest the use of oseltamivir for patients with sCAP due to influenza confirmed by PCR (conditional recommendation, very low quality of evidence) When PCR is not available to confirm influenza, we suggest the use of empirical oseltamivir during the influenza season (conditional recommendation, very low quality of evidence)
Question 6: Does the addition of steroids to antibiotic therapy in specific sCAP populations lead to better outcomes in comparison to when steroid therapy is not used?	In patients with sCAP, we suggest the use of corticosteroids if shock is present (conditional recommendation, low quality of evidence)
Question 7: Does the use of a prediction score for drug-resistant pathogens lead to more appropriate therapy and improved outcomes (mortality, treatment failure, duration of antibiotic therapy, prolonged ICU stay)?	We suggest integrating specific risk factors (eventually computed into clinical scores) based on local epidemiology and previous colonisation to guide decisions regarding drug-resistant pathogens (excluding those immunocompromised) and empirical antibiotic prescription in sCAP patients (conditional recommendation, moderate quality of evidence)
Question 8: Do patients with sCAP and aspiration risk factors have better outcomes (mortality, length of stay, treatment failure) if treated with a risk-based therapy regimen instead of standard sCAP antibiotics?	In patients with sCAP and aspiration risk factors we suggest standard CAP therapy regimen and not specific therapy targeting anaerobic bacteria (ungraded, good practice statement)

sCAP: severe community-acquired pneumonia; NIV: non-invasive ventilation; HFNO: high-flow nasal oxygen; PCT: procalcitonin; ICU: intensive care unit; CAP: community-acquired pneumonia.

How Contemporary are Guidelines Efforts

Low-dose Methylprednisolone Treatment in Critically Ill Patients with Severe CAP

Meduri GU et al. Intensive Care Med 2022 Aug; 48: 1009-23

- **Randomized trial, 2012-2016**
  - 42 Veterans Affairs medical centers US
  - 586 patients with severe CAP in the ICU, (mostly Males)
- **Treatment:**
  - Methylprednisolone iv (40 mg/die for 7 days, tapering in 20 days)
  - Placebo
- **Primary outcome = 60-day mortality:**
  - 16% vs. 18%, P = 0.61
  - Methylprednisolone Vs. control group
- **Prespecified analyses →**
  - No subgroup identified which benefited from glucocorticoids

Corticosteroids in CAP (1): Systematic Review, Pairwise and Dose-Response Meta-Analysis Pitre T et al. J Gen Intern Med. 2023 Apr 19:1-14

- **Pair-wise & dose-response metanalysis**
  - REML-GRADE-ICEMAN methodology
  - 18 eligible studies that included 4661 patients
- **Corticosteroids effect:**
  - Probable reduction of mortality in more severe CAP
    - RR 0.62 [95% CI 0.45 to 0.85]; moderate certainty)
  - Possible null effect in less severe CAP
    - RR 1.08 [95% CI 0.83 to 1.42]; low certainty
- **Non-linear dose-response relationship with mortality**
  - Optimal dose: 6 mg of dexamethasone (or equivalent) for 7 days
    - RR 0.44 [95% 0.30 to 0.66]

Corticosteroids in CAP (2): Systematic Review, Pairwise and Dose-Response Meta-Analysis Pitre T et al. J Gen Intern Med 2023 Apr 19:1-14

- **Probable reduction of risks (moderate certainty):**
  - Invasive mechanical ventilation
    - RR 0.56 [95% CI 0.42 to 74]
  - ICU admission
    - RR 0.65 [95% CI 0.43 to 0.97]
- **Possible reduction (low certainty):**
  - Duration of hospitalization and ICU stay
- **Possible increase (low certainty):**
  - Risk of hyperglycemia (RR 1.76 [95% CI 1.46 to 2.14])

S. pneumoniae Serotyping & Antimicrobial Susceptibility: Assessment for Vaccine Efficacy in Canada after PCV13 Zhanel GG et al JAC 2023

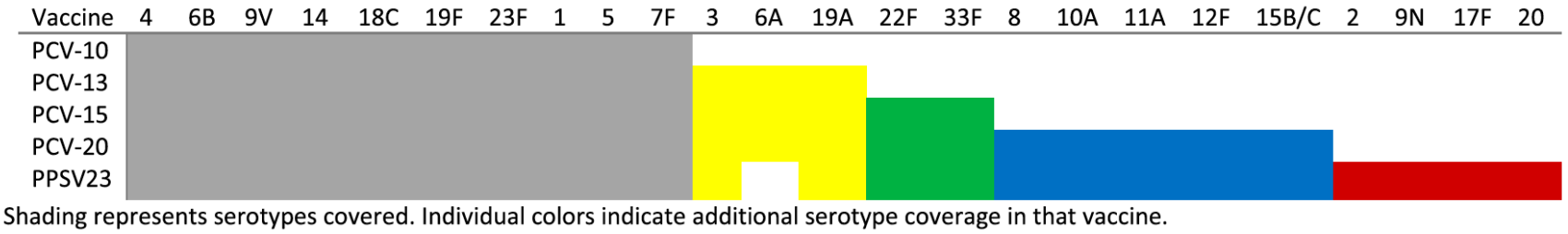

Figure 1. Serotypes contained in various conjugated and polysaccharide vaccines. Shading represents serotypes covered. Individual colours indicate additional serotype coverage in that vaccine. This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

- **The data highlight the evolution of *S. pneumoniae* under pressure by vaccination and antimicrobial usage, as well as vaccine coverage**

Conclusions

- **CAP remains a serious healthcare problem**
- **Multiple areas of concern**
  - Diagnosis & rapid diagnosis
  - Imaging & BAL
  - Admission / ICU Admission / MRDx-ODx
  - Treatment / de-escalation
- **Stewardship**
- **Steroids & CAP & COPD & ...**