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Manuela Carugati

Infectious Diseases, Luigi Sacco Hospital.

Stefano Aliberti

Università degli Studi di Milano, Italy.

Luis Felipe Reyes

Infectious Diseases, Luigi Sacco Hospital.

Ricardo Franco Sadud

Infectious Diseases, Luigi Sacco Hospital.

Muhammad Irfan

Aga Khan University, muhammad.irfan@aku.edu

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Microbiological testing of adults hospitalised with community-acquired pneumonia: an international study

Manuela Carugati ^{1,2,3}, Stefano Aliberti ^{4,5}, Luis Felipe Reyes^{6,7}, Ricardo Franco Sadud⁸, Muhammad Irfan⁹, Cristina Prat¹⁰, Nilam J. Soni¹¹, Paola Faverio¹², Andrea Gori^{3,4}, Francesco Blasi^{4,5}, Marcos I. Restrepo¹¹ and the GLIMP collaborators¹³

Affiliations: ¹Division of Infectious Diseases, San Gerardo Hospital, ASST Monza, Monza, Italy. ²Division of Infectious Diseases and International Health, Duke University, Durham, NC, USA. ³Internal Medicine Dept, Infectious Diseases Unit, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico Milano, Milan, Italy. ⁴Dept of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy. ⁵Internal Medicine Dept, Respiratory Unit and Adult Cystic Fibrosis Center, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico Milano, Milan, Italy. ⁶Dept of Microbiology, Universidad de La Sabana, Chia, Colombia. ⁷Dept of Critical Care Medicine, Clinica Universidad de La Sabana, Chia, Colombia. ⁸Dept of Medicine, University of Central Florida, Naples, FL, USA. ⁹Section of Pulmonary and Critical Care Medicine, Dept of Medicine, Aga Khan University, Karachi, Pakistan. ¹⁰Dept of Microbiology, Hospital Universitari Germans Trias i Pujol, Institut d'Investigació Germans Trias i Pujol, Universitat Autònoma de Barcelona, CIBER Enfermedades Respiratorias, Badalona, Spain. ¹¹South Texas Veterans Health Care System and University of Texas Health San Antonio, San Antonio, TX, USA. ¹²Cardio-Thoracic-Vascular Dept, University of Milan Bicocca, Respiratory Unit, San Gerardo Hospital, ASST Monza, Monza, Italy. ¹³A full list of the GLIMP collaborators and their affiliations can be found at the end of this article.

Correspondence: Stefano Aliberti, Dept of Pathophysiology and Transplantation, Università degli Studi di Milano, Via Francesco Sforza 35, Milan, 20122, Italy. E-mail: stefano.aliberti@unimi.it

ABSTRACT This study aimed to describe real-life microbiological testing of adults hospitalised with community-acquired pneumonia (CAP) and to assess concordance with the 2007 Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) and 2011 European Respiratory Society (ERS) CAP guidelines.

This was a cohort study based on the Global Initiative for Methicillin-resistant *Staphylococcus aureus* Pneumonia (GLIMP) database, which contains point-prevalence data on adults hospitalised with CAP across 54 countries during 2015.

In total, 3702 patients were included. Testing was performed in 3217 patients, and included blood culture (71.1%), sputum culture (61.8%), *Legionella* urinary antigen test (30.1%), pneumococcal urinary antigen test (30.0%), viral testing (14.9%), acute-phase serology (8.8%), bronchoalveolar lavage culture (8.4%) and pleural fluid culture (3.2%). A pathogen was detected in 1173 (36.5%) patients. Testing attitudes varied significantly according to geography and disease severity. Testing was concordant with IDSA/ATS and ERS guidelines in 16.7% and 23.9% of patients, respectively. IDSA/ATS concordance was higher in Europe than in North America (21.5% versus 9.8%; $p < 0.01$), while ERS concordance was higher in North America than in Europe (33.5% versus 19.5%; $p < 0.01$).

Testing practices of adults hospitalised with CAP varied significantly by geography and disease severity. There was a wide discordance between real-life testing practices and IDSA/ATS/ERS guideline recommendations.



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Testing practices vary based on geography and disease severity, and IDSA/ATS/ERS testing recommendations are rarely followed <http://ow.ly/80Iy30lxo1c>

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Introduction

Community-acquired pneumonia (CAP) is a leading cause of hospitalisation worldwide. Mortality rates for patients hospitalised with CAP approach 30%, especially in those admitted to an intensive care unit (ICU) [1–4]. Diagnostic testing in CAP has the potential to improve individual patient management, reducing the risk of clinical failure and death, and to generate epidemiological data, informing the selection of appropriate empirical antibiotic therapy. Unfortunately, these advantages are counterbalanced by high healthcare costs associated with diagnostic testing and low sensitivity of these tests to identify pathogens causing CAP [5, 6].

Considering both the benefits and limitations of diagnostic testing, several international scientific societies have published guidelines on effective diagnostic testing strategies for hospitalised patients with CAP. However, important differences exist between recommendations of different societies [7]. These recommendations are mainly based on expert opinion given the scarcity of published evidence. In particular, substantial differences can be found between the two most cited international guidelines on CAP: the 2007 Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) and the 2011 European Respiratory Society (ERS) guidelines [8, 9]. Limited data are available of real-life diagnostic testing practices for hospitalised patients with CAP and whether real-life diagnostic testing practices are concordant with the 2007 IDSA/ATS and 2011 ERS guideline recommendations [10–12].

This study aimed to describe real-life microbiological testing of adults hospitalised with CAP, evaluate the influence of geography and disease severity on microbiological testing practices, and assess the concordance of real-life microbiological testing with the two most cited international guidelines, specifically the 2007 IDSA/ATS and the 2011 ERS guidelines.

Methods

Study design, setting and participants

We performed a secondary analysis of an international, multicentre, observational, prospective cohort study using the Global Initiative for Methicillin-resistant *Staphylococcus aureus* Pneumonia (GLIMP) database [13]. GLIMP was conducted among 222 hospitals in 54 countries over 4 days, with 1 day per month randomly selected during March, April, May and June 2015. All adult patients (aged >18 years) hospitalised for CAP at the participating centres during the four study days were screened by GLIMP investigators and included in this secondary analysis. Patients hospitalised with a diagnosis of hospital-acquired or ventilator-associated pneumonia were excluded. The GLIMP coordinating centre was located at the University of Texas Health San Antonio (San Antonio, TX, USA). The coordinating centre received expedited project approval by the institutional review board (number HSC20150184E). The review board waived the need for receipt of informed consent due to the nature of the study. Institutional review board approval was obtained by the site investigators at each individual centre. A detailed description of the GLIMP organisation and methodologies has been previously published [13].

Study outcomes

The primary outcome of this study was describing real-life microbiological testing among patients hospitalised with CAP, including the frequency of testing, laboratory technique used and patients' characteristics by testing status (tested patients *versus* not tested patients). This study had also two secondary outcomes. The first was to evaluate the influence of geography and disease severity on testing practices. ICU admission, invasive mechanical ventilation, vasopressors, and combined administration of vasopressors and invasive mechanical ventilation were used as measures of disease severity. The second was to evaluate the concordance of real-life microbiological testing with the 2007 IDSA/ATS and the 2011 ERS guidelines for CAP.

Study definitions

CAP was defined by evidence of new pulmonary infiltrates on thoracic imaging (chest radiograph, computed tomography or ultrasound) during the first 48 h of hospitalisation and at least one of the following criteria: new or increased cough with or without sputum production or with purulent respiratory secretions; fever or hypothermia (documented rectal or oral temperature $\geq 37.8^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$, respectively); and evidence of systemic inflammation, such as abnormal white blood cell count (leukocytosis ($> 10\,000\text{ cells}\cdot\text{mL}^{-1}$), leukopenia ($< 4000\text{ cells}\cdot\text{mL}^{-1}$) or bandaemia ($> 10\%$)) and increased C-reactive protein or procalcitonin concentrations above the local upper limit of normal. Hospitalisation was defined as admission at an inpatient service and subsequent stay for $\geq 24\text{ h}$. Methicillin-resistant *Staphylococcus aureus* was defined according to the Clinical and Laboratory Standards Institute (CLSI) guidelines, in which the minimum inhibitory concentration was $\geq 4\text{ }\mu\text{g}\cdot\text{mL}^{-1}$ to oxacillin. Production of

TABLE 1 Tests considered as recommended or not recommended by the Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines

	IDSA/ATS recommendations	ERS recommendations
Blood culture	Recommended in case of ICU admission, leukopenia, alcohol abuse, chronic severe liver disease, asplenia, positive pneumococcal urinary antigen test and presence of pleural effusion	Recommended in all patients hospitalised with CAP
Sputum culture	Recommended in case of ICU admission, alcohol abuse, severe obstructive or structural lung disease, positive <i>Legionella</i> urinary antigen test, positive pneumococcal urinary antigen test and presence of pleural effusion	Recommended in case of purulent sputum sample
Bronchoalveolar lavage culture	Recommended in case of intubation	Recommended in case of intubation
<i>Legionella</i> urinary antigen test	Recommended in case of ICU admission, alcohol abuse and presence of pleural effusion	Recommended in all patients hospitalised with severe CAP
Pneumococcal urinary antigen test	Recommended in case of ICU admission, leukopenia, alcohol abuse, chronic severe liver disease, asplenia and pleural effusion	Recommended in all patients hospitalised with severe CAP
Acute-phase serology for <i>Chlamydomphila pneumoniae</i>, <i>Mycoplasma pneumoniae</i>, and <i>Legionella</i> species	Not recommended	Not recommended

ICU: intensive care unit; CAP: community-acquired pneumonia.

extended-spectrum β -lactamase was defined according to the CLSI guidelines *via* broth microdilution or disk diffusion clavulanate inhibition test.

Diagnostic testing was defined as concordant with the 2007 IDSA/ATS guidelines if recommended tests were performed and non-recommended tests were not performed. Similarly, diagnostic testing was defined as concordant with the 2011 ERS guidelines if recommended tests were performed and non-recommended tests were not performed. The tests considered in this study as recommended or non-recommended by the IDSA/ATS and ERS guidelines are presented in table 1. Over-testing was defined as a condition where tests not required were performed. Under-testing was defined as a condition where required tests were not performed.

Statistical analysis

Continuous variables were presented as medians with interquartile range. Categorical variables were presented as frequencies and percentages of the specified group. Comparisons between groups were made with the Fisher exact test or the Kruskal–Wallis test, as appropriate. A two-sided p-value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS Statistics, version 24, software (IBM, Armonk, NY, USA).

Results

Among 3702 patients, 3217 (86.9%) had at least one diagnostic test performed, with 1173 (36.5%) patients with at least one pathogen detected by diagnostic testing. Variables significantly associated with the performance of diagnostic testing are presented in table 2. When patients from whom at least one pathogen was detected were compared with patients from whom no pathogens were detected, we found the former group more commonly presented the following conditions: bronchiectasis, tracheostomy, at least one respiratory comorbidity, hypertension, HIV infection, previous infections, previous healthcare exposure, severe CAP, ICU admission, mechanical ventilation and use of vasopressors (table 2).

TABLE 2 Baseline characteristics of adult inpatients with community-acquired pneumonia by testing status and by pathogen detection

	Testing status			Pathogen detection		
	Not tested	Tested	p-value	Not detected	Detected	p-value
Patients	485	3217		2044	1173	
Demographic characteristics						
Age	71.0 (54.0–81.0)	68.0 (54.0–80.0)	0.03	70.0 (55.0–81.0)	65.0 (50.0–77.0)	<0.01
Male sex	255 (52.6)	1888 (58.7)	0.01	1173 (57.4)	715 (61.0)	0.04
Underweight	14 (5.2)	152 (7.4)	0.19	83 (6.5)	69 (8.8)	0.06
Obesity	64 (13.2)	513 (15.9)	0.12	314 (15.4)	199 (17.0)	0.23
Respiratory past medical history						
Active lung cancer	17 (3.5)	92 (2.9)	0.43	62 (3.0)	30 (2.6)	0.44
Asthma	26 (5.4)	235 (7.3)	0.12	149 (7.3)	86 (7.3)	0.97
Bronchiectasis	9 (1.9)	169 (5.3)	<0.01	76 (3.7)	93 (7.9)	<0.01
Chronic aspiration	39 (8.0)	218 (6.8)	0.31	137 (6.7)	81 (6.9)	0.83
COPD	96 (19.8)	840 (26.1)	0.01	517 (25.3)	323 (27.5)	0.16
Current or former smoker	121 (24.9)	1124 (34.9)	<0.01	709 (34.7)	415 (35.4)	0.69
Interstitial lung disease	4 (0.8)	91 (2.8)	0.01	65 (3.2)	26 (2.2)	0.11
Obstructive sleep apnoea	7 (1.4)	123 (3.8)	0.01	78 (3.8)	45 (3.8)	0.98
Home oxygen therapy	14 (2.9)	210 (6.5)	<0.01	123 (6.0)	87 (7.4)	0.12
Lung transplant	0 (0.0)	7 (0.2)	0.30	2 (0.1)	5 (0.4)	0.06
Tracheostomy	3 (0.6)	50 (1.6)	0.11	14 (0.7)	36 (3.1)	<0.01
At least one respiratory comorbidity	235 (48.5)	1917 (59.6)	<0.01	1434 (56.7)	718 (61.2)	0.01
Cardiovascular past medical history						
Arrhythmia	69 (14.2)	458 (14.2)	1.00	307 (15.0)	151 (12.9)	0.09
Coronary artery disease	69 (14.2)	528 (16.4)	0.22	325 (15.9)	203 (17.3)	0.30
Heart failure	64 (13.2)	421 (13.1)	0.95	270 (13.2)	151 (12.9)	0.79
Hypertension	201 (41.4)	1454 (45.2)	0.12	973 (47.6)	481 (41.0)	<0.01
Stroke	55 (11.3)	251 (7.8)	0.01	168 (8.2)	83 (7.1)	0.25
Immunosuppressive conditions						
Active solid tumour	40 (8.2)	247 (7.7)	0.66	164 (8.0)	83 (7.1)	0.33
AIDS	8 (1.6)	57 (1.8)	0.85	24 (1.2)	33 (2.8)	<0.01
Aplastic anaemia	1 (0.2)	13 (0.4)	0.51	8 (0.4)	5 (0.4)	0.88
Asplenia	0 (0.0)	12 (0.4)	0.18	5 (0.2)	7 (0.6)	0.12
Chemotherapy in the last 3 months	9 (1.9)	136 (4.2)	0.01	83 (4.1)	53 (4.5)	0.54
Haematological malignancy	11 (2.3)	151 (4.7)	0.02	93 (4.5)	58 (4.9)	0.61
HIV infection	16 (3.3)	107 (3.3)	0.98	56 (2.7)	51 (4.3)	0.01
Neutropenia	4 (0.8)	44 (1.4)	0.32	29 (1.4)	15 (1.3)	0.74
Steroids use	24 (4.9)	270 (8.4)	0.01	174 (8.5)	96 (8.2)	0.75
At least one immunosuppressive condition	74 (15.3)	591 (18.4)	0.09	356 (17.4)	235 (20.0)	0.07
Other chronic medical conditions						
Chronic renal failure	50 (10.3)	350 (10.9)	0.71	241 (11.8)	109 (9.3)	0.03
Cirrhosis	6 (1.2)	64 (2.0)	0.26	36 (1.8)	28 (2.4)	0.22
Diabetes mellitus	92 (19.0)	690 (21.4)	0.21	448 (21.9)	242 (20.6)	0.39
Haemodialysis	1 (0.2)	51 (1.6)	0.02	32 (1.6)	19 (1.6)	0.91
Liver disease	11 (2.3)	129 (4.0)	0.06	75 (3.7)	54 (4.6)	0.19
Mental illness	33 (6.8)	221 (6.9)	0.96	146 (7.1)	75 (6.4)	0.42
Dementia	74 (15.3)	334 (10.4)	<0.01	228 (11.2)	106 (9.0)	0.06
Previous infections						
Prior ESBL	0 (0.0)	55 (1.7)	<0.01	27 (1.3)	28 (2.4)	0.03
Prior MRSA	5 (1.0)	81 (2.5)	0.04	34 (1.7)	47 (4.0)	<0.01
Prior mycobacterial disease	7 (1.4)	89 (2.8)	0.09	42 (2.1)	47 (4.0)	<0.01
Prior <i>Pseudomonas</i>	4 (0.8)	97 (3.0)	<0.01	32 (1.6)	65 (5.5)	<0.01
Previous healthcare exposure[#]						
Lower respiratory tract infection	106 (21.9)	935 (29.1)	<0.01	667 (26.4)	374 (31.9)	<0.01
Emergency room admission	120 (24.7)	981 (30.5)	0.01	708 (28.0)	393 (33.5)	<0.01
Hospitalisation	128 (26.4)	1035 (32.2)	0.01	771 (30.5)	392 (33.4)	0.07
Home antibiotic infusion therapy	21 (4.3)	141 (4.4)	0.96	94 (3.7)	68 (5.8)	<0.01
Intravenous antibiotics	89 (18.4)	816 (25.4)	<0.01	569 (22.5)	336 (28.6)	<0.01
Oral antibiotics	166 (34.2)	1226 (38.1)	0.10	917 (36.3)	475 (40.5)	0.01

Continued

TABLE 2 Continued

	Testing status			Pathogen detection		
	Not tested	Tested	p-value	Not detected	Detected	p-value
Current pneumonia episode						
ICU admission	33 (6.8)	601 (18.7)	<0.01	275 (13.5)	326 (27.8)	<0.01
Mechanical ventilation	28 (5.8)	634 (19.7)	<0.01	312 (15.3)	322 (27.5)	<0.01
Vasopressors	9 (1.9)	233 (7.2)	<0.01	91 (4.5)	142 (12.1)	<0.01

Data are presented as n, median (interquartile range) or n (%), unless otherwise stated. COPD: chronic obstructive pulmonary disease; ESBL: extended-spectrum β -lactamase; MRSA: methicillin-resistant *Staphylococcus aureus*; ICU: intensive care unit. #: in the previous 12 months. Bold indicates statistical significance at p<0.05.

Of the 3702 patients hospitalised with CAP and included in this study, diagnostic testing was as follows: 2633 (71.1%) had blood cultures, 2287 (61.8%) had sputum cultures, 1113 (30.1%) had *Legionella* urinary antigen testing, 1110 (30.0%) had pneumococcal urinary antigen testing, 553 (14.9%) had viral testing, 325 (8.8%) had acute-phase serology, 312 (8.4%) had bronchoalveolar lavage (BAL) cultures and 117 (3.2%) had pleural fluid cultures. Blood, sputum, BAL cultures, pleural fluid cultures and viral testing were more frequently obtained among patients undergoing invasive mechanical ventilation compared to patients not receiving invasive mechanical ventilation. In contrast, when ICU admission, vasopressor administration, or combined vasopressor and invasive mechanical ventilation administration were used as measures of disease severity, only blood cultures, BAL cultures and viral testing were significantly more common among patients with a severe disease (table 3). Of the 8450 diagnostic tests performed, 12.9% yielded a positive result. Specifically, 38.8% of the BAL cultures, 28.2% of the viral testing, 19.4% of acute-phase serology testing, 17.7% of sputum cultures, 11.7% of pneumococcal urinary antigen testing, 11.1% of pleural fluid cultures, 6.7% of blood cultures and 2.2% of *Legionella* urinary antigen testing led to the detection of at least one pathogen, for a total of 1362 pathogens detected. Bacteria, viruses and fungi accounted for 83.0%, 14.1% and 2.9% of the pathogens detected, respectively. *Streptococcus pneumoniae* was the most frequently encountered pathogen (n=268), followed by *Staphylococcus aureus* (n=188), influenza viruses (n=154) and *Pseudomonas aeruginosa* (n=133).

When the performance of diagnostic testing was compared among patients admitted at participating hospitals in North America, South America, Africa, Asia, Europe and Oceania, significant differences were identified (table 4). Performance of at least one test ranged from 82.1% among patients hospitalised in Africa to 97.8% among patients hospitalised in Asia. While blood cultures were obtained in approximately 70–90% of patients hospitalised in North America, South America, Europe, Asia and Oceania, only 41.7% of patients in participating African hospitals had blood cultures (p<0.01). Similarly, viral testing was performed in 10–20% of patients hospitalised in North America, South America, Europe, Asia and

TABLE 3 Microbiological tests performed among adult inpatients with community-acquired pneumonia by disease severity

	Total	ICU		p-value	Invasive mechanical ventilation and vasopressors		p-value
		No	Yes		No	Yes	
Patients	3702	3068	634		3529	173	
Blood culture	2633 (71.1)	2110 (68.8)	523 (82.5)	<0.01	2477 (70.2)	156 (90.2)	<0.01
Sputum culture	2287 (61.8)	1895 (61.8)	392 (61.8)	0.98	2182 (61.8)	105 (60.7)	0.76
Bronchoalveolar lavage culture	312 (8.4)	179 (5.8)	133 (21.0)	<0.01	268 (7.6)	44 (25.4)	<0.01
Pleural fluid culture	117 (3.2)	90 (2.9)	27 (4.3)	0.08	108 (3.1)	9 (5.2)	0.12
Pneumococcal urinary antigen	1110 (30.0)	939 (30.6)	171 (27.0)	0.07	1054 (29.9)	56 (32.4)	0.48
Legionella urinary antigen	1113 (30.1)	939 (30.6)	174 (27.4)	0.11	1051 (29.8)	62 (35.8)	0.09
Acute-phase serology	325 (8.8)	258 (8.4)	67 (10.6)	0.08	307 (8.7)	18 (10.4)	0.44
Viral testing	553 (14.9)	390 (12.7)	163 (25.7)	<0.01	482 (13.7)	71 (41.0)	<0.01

Data are presented as n or n (%), unless otherwise stated. ICU: intensive care unit. Bold indicates statistical significance at p<0.05.

TABLE 4 Microbiological tests performed among adult inpatients with community-acquired pneumonia by geographic area

	Continent	Rest of the world	p-value
Blood culture			
North America	434 (82.0)	2199 (69.3)	<0.01
South America	202 (92.7)	2431 (69.8)	<0.01
Africa	65 (41.7)	2568 (72.4)	<0.01
Asia	294 (70.8)	2339 (71.2)	0.89
Europe	1609 (68.6)	1024 (75.4)	<0.01
Oceania	29 (72.5)	2604 (71.1)	0.85
Sputum culture			
North America	286 (54.1)	2001 (63.1)	<0.01
South America	95 (43.6)	2192 (62.9)	<0.01
Africa	92 (59.0)	2195 (61.9)	0.46
Asia	305 (73.5)	1982 (60.3)	<0.01
Europe	1496 (63.8)	791 (58.2)	<0.01
Oceania	13 (32.5)	2274 (62.1)	<0.01
Bronchoalveolar lavage culture			
North America	68 (12.9)	244 (7.7)	<0.01
South America	15 (6.9)	297 (8.5)	0.40
Africa	10 (6.4)	302 (8.5)	0.35
Asia	48 (11.6)	264 (8.0)	0.02
Europe	171 (7.3)	141 (10.4)	<0.01
Oceania	0 (0.0)	312 (8.5)	0.05
Pleural fluid culture			
North America	13 (2.5)	104 (3.3)	0.32
South America	13 (6.0)	104 (3.3)	0.02
Africa	12 (7.7)	105 (3.0)	<0.01
Asia	12 (2.9)	105 (3.2)	0.74
Europe	67 (2.9)	50 (3.7)	0.17
Oceania	0 (0.0)	117 (3.2)	0.25
Pneumococcal urinary antigen			
North America	55 (10.4)	1055 (33.2)	<0.01
South America	17 (7.8)	1093 (31.4)	<0.01
Africa	2 (1.3)	1108 (31.2)	<0.01
Asia	22 (5.3)	1088 (33.1)	<0.01
Europe	1014 (43.3)	96 (7.1)	<0.01
Oceania	0 (0.0)	1110 (30.3)	<0.01
Legionella urinary antigen			
North America	93 (17.6)	1020 (32.1)	<0.01
South America	1 (0.5)	1112 (31.9)	<0.01
Africa	1 (0.6)	1112 (31.4)	<0.01
Asia	30 (7.2)	1083 (32.9)	<0.01
Europe	988 (42.2)	125 (9.2)	<0.01
Oceania	0 (0.0)	1113 (30.4)	<0.01
Acute-phase serology			
North America	22 (4.2)	303 (9.5)	<0.01
South America	11 (5.0)	314 (9.0)	0.04
Africa	9 (5.8)	316 (8.9)	0.18
Asia	17 (4.1)	308 (9.4)	<0.01
Europe	263 (11.2)	62 (4.6)	<0.01
Oceania	3 (7.5)	322 (8.8)	0.77
Viral testing			
North America	83 (15.7)	470 (14.8)	0.60
South America	25 (11.5)	528 (15.2)	0.14
Africa	2 (1.3)	551 (15.5)	<0.01
Asia	78 (18.8)	475 (14.5)	0.02
Europe	361 (15.4)	192 (14.1)	0.30
Oceania	4 (10.0)	549 (15.0)	0.38

Continued

TABLE 4 Continued			
	Continent	Rest of the world	p-value
At least one test done			
North America	489 (92.4)	2728 (86.0)	<0.01
South America	204 (93.6)	3013 (86.5)	<0.01
Africa	128 (82.1)	3089 (87.1)	0.07
Asia	406 (97.8)	2811 (85.5)	<0.01
Europe	1955 (83.4)	1262 (92.9)	<0.01
Oceania	35 (87.5)	3182 (86.9)	0.91

Data are presented as n (%), unless otherwise stated. Bold indicates statistical significance at p<0.05.

Oceania, and in 1.3% of patients admitted to African hospitals (p<0.01). Pneumococcal and *Legionella* urinary antigen tests were performed in >40% of the patients admitted in European hospitals and in <20% of the patients hospitalised in the remaining continents (p<0.01). Acute-phase serology for *Chlamydomphila pneumoniae*, *Mycoplasma pneumoniae* and *Legionella* species was more common in Europe (11.2%) than elsewhere (4.6%) (p<0.01).

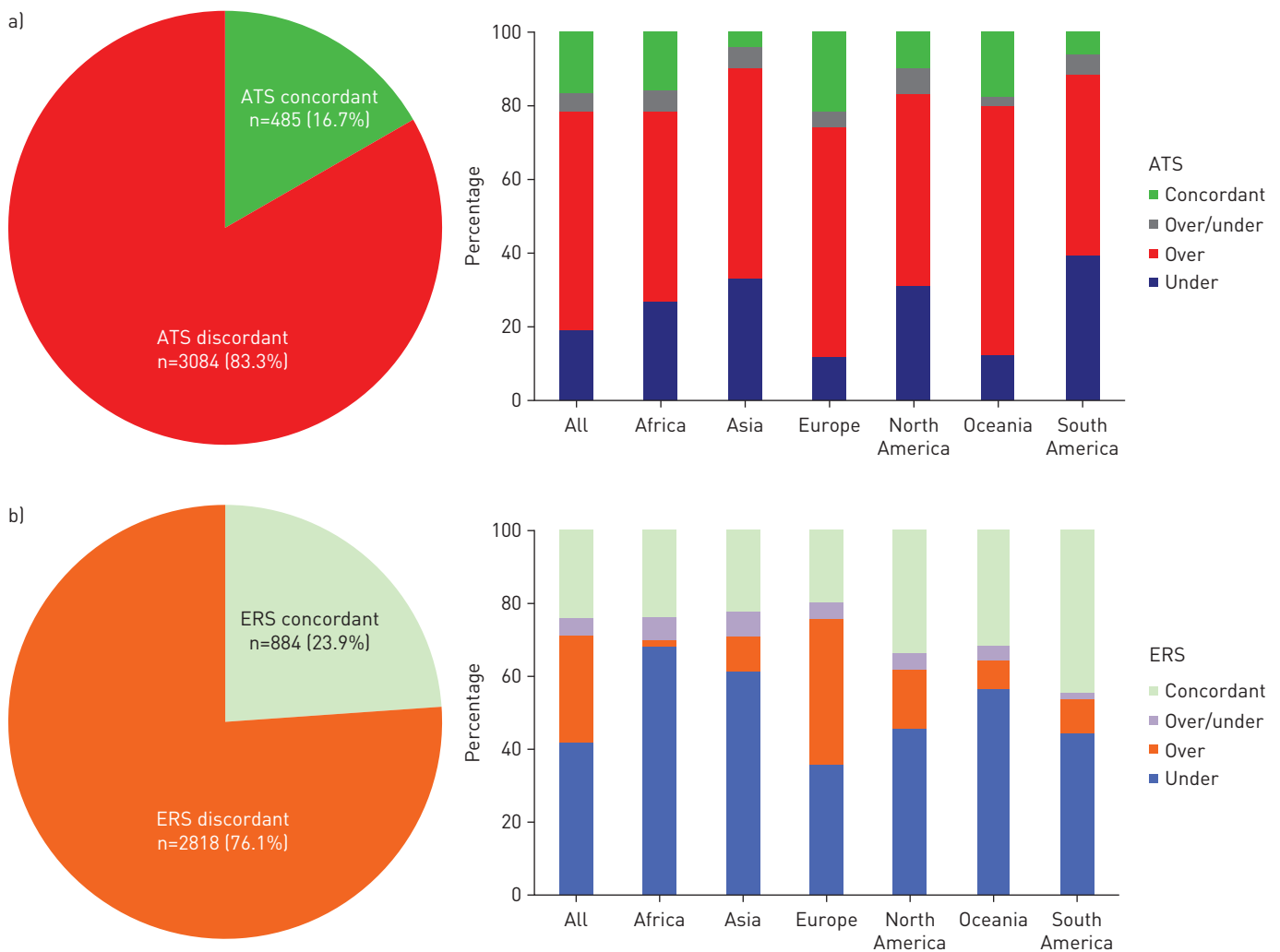


FIGURE 1 Discordance of diagnostic testing with the a) 2007 Infectious Diseases Society of America/American Thoracic Society (ATS) guidelines and b) 2011 European Respiratory Society (ERS) guidelines for community-acquired pneumonia by geographic area. Over: over-testing; under: under-testing; over/under: over-testing and under-testing.

Diagnostic testing was concordant with the IDSA/ATS and ERS recommendations in 16.7% and 23.9% of the patients, respectively. When the overall study population was analysed, over-testing and under-testing were reported in 59.3% and 19.1% of the IDSA/ATS-discordant patients, respectively (figure 1). Among IDSA/ATS-discordant patients, blood cultures performed without indications accounted for the majority of over-testing, while the lack of pneumococcal urinary antigen test was responsible for a significant percentage of under-testing. Over-testing and under-testing were documented in 29.3% and in 42.0% of the ERS-discordant patients, respectively (figure 1). Among ERS-discordant patients, pneumococcal and *Legionella* urinary antigen tests performed without an indication accounted for the majority of over-testing, while under-testing was mainly due to the lack of obtaining blood cultures when indicated. IDSA/ATS concordance was more common in Europe than in North America (21.5% versus 9.8%; $p < 0.01$), while ERS concordance was more common in North America than in Europe (33.5% versus 19.5%; $p < 0.01$).

Discussion

This international, multicentre, point-prevalence study provides a high-quality, real-life picture of diagnostic testing in patients hospitalised with CAP. At least one microbiological test was performed in the vast majority of patients hospitalised with CAP and led to an aetiological diagnosis in one-third of patients tested. Geographic area and disease severity influenced testing frequency. Our study also highlights a significant discordance of real-life diagnostic testing compared to recommended testing in the 2007 IDSA/ATS and 2011 ERS guidelines for CAP management in adults. Several crucial points could be raised by our findings.

First, a pathogen was identified in one-third of adult inpatients with CAP. This pathogen-detection yield is similar to previously reported investigations [14–21] and consistent with the EPIC (Etiology of Pneumonia in the Community) study [1]. Despite extensive laboratory testing, the EPIC study identified a pathogen in 38% of 2259 patients hospitalised with CAP in the USA. The low pathogen-detection yield reported in this and other CAP studies highlights how limited our understanding is of CAP aetiologies among adult inpatients and how current empirical antimicrobial recommendations are based on weak evidence. Studies aimed at collecting as much data as possible to identify the aetiology using state-of-the-art diagnostic techniques and innovative pathogen-discovery approaches are urgently needed. Furthermore, aetiological studies should use novel analytical techniques in order to incorporate evidence from multiple specimens to account for the imperfect sensitivity and specificity of the diagnostic tests used [22]. Once a more accurate estimate of the aetiological distribution of CAP among adult inpatients is available, empirical antimicrobial recommendations should be updated.

Secondly, our study showed the existence of a strong association between pneumonia severity and performance of diagnostic testing, in accordance with IDSA/ATS and ERS recommendations. As a consequence, pneumonia severity was also associated with an increased probability of pathogen detection. Exploring the true determinants of pathogen detection would have required a systematic and universal testing strategy and, for this reason, it was out of the scope of this study.

Thirdly, our study confirmed the differing diagnostic yield of various diagnostic tests. Specifically, only 6.7% of blood cultures yielded a positive result, confirming the low sensitivity of blood cultures for revealing the aetiology of CAP, similar to the findings of other studies [16–23]. In contrast, BAL cultures were characterised by a high diagnostic yield (38.8%). While impractical and potentially associated with complications, BAL cultures represent an effective diagnostic tool for patients with severe infections, who may benefit the most from a targeted antimicrobial regimen. Indeed, a randomised trial by VAN DER EERDEN *et al.* [24] showed a statistically significant difference in mortality among ICU patients receiving empirical broad-spectrum antimicrobials (91%) versus patients receiving pathogen-directed antimicrobials (45%).

Fourthly, our analysis described a significant geographic variation in diagnostic testing strategies. We could speculate that the economical restraints of African health systems accounted for the reduced number of blood cultures and viral tests performed in this setting. Laboratory infrastructure to support diagnostic microbiological testing is limited in most African countries: bacteriological culture or molecular techniques that form the mainstay of CAP diagnostics in well-resourced settings are often lacking in Africa [25, 26]. In contrast, the seasonality and the epidemiological relevance of respiratory viruses, such as avian-origin influenza A and Middle East respiratory syndrome coronavirus, may have favoured the performance of viral testing in Asia [27, 28].

Fifthly, our study is among the first to evaluate the concordance of real-life diagnostic testing with international guidelines. To the best of our knowledge, only JENKINS *et al.* [12] made a similar attempt. They analysed the concordance of diagnostic testing practices retrospectively in a cohort of adult inpatients with CAP with the 2007 IDSA/ATS guidelines and reported over-testing with blood cultures. Our study

revealed that real-life diagnostic testing was not concordant with IDSA/ATS or ERS guidelines in the vast majority of the patients. Specifically, the discordance with the IDSA/ATS guidelines was mainly due to over-testing. This situation may be explained by the restrictive testing recommended by the IDSA/ATS guidelines. Of note, under-testing was also a cause of discordance with the IDSA/ATS guidelines and was more frequently encountered in North America than in Europe. Discordance with ERS guidelines was mainly due to under-testing, as a result of the extensive testing approach recommended by these guidelines. Over-testing was also identified as a cause of discordance with the ERS guidelines. This event was more frequently reported in Europe than in North America. We were intrigued by European clinicians' extensive ordering of diagnostic tests, even beyond what is recommended by the ERS guidelines. Insurance and healthcare system-related factors may have shaped the diagnostic approach both of European and North American clinicians. Nonetheless, the significant discrepancies between real-life diagnostic testing and IDSA/ATS/ERS recommended testing is worrisome and further studies aimed at assessing the clinical and economic implications of the testing approach proposed by the IDSA/ATS guidelines, the testing approach proposed by the ERS guidelines, and real-life diagnostic testing are needed.

Finally, this study has important strengths and limitations. To our knowledge, GLIMP is the first study to enrol a large and diverse group of adult patients hospitalised with CAP across six continents, providing a detailed, real-world picture of CAP diagnostic testing around the world. Our ability to assess the concordance of real-life diagnostic testing with IDSA/ATS and ERS guideline recommendations was affected by the lack of information about recent travel, failure of outpatient antibiotic therapy, presence of cavitary infiltrates, lymphopenia, and feasibility of sputum collection in the GLIMP database. Similarly, incomplete data regarding presence of pleural effusions and clinical and epidemiological determinants of *Legionella* infection limited the accuracy our findings, probably leading to an inflation of our over-testing estimates. Finally, due to its cross-sectional design, our study did not provide CAP outcome data.

In conclusion, our understanding of the aetiologies of CAP among hospitalised adults is scarce, limiting the accuracy of empirical antimicrobial regimens. Disease severity and geography are associated with differences in testing approaches. The wide discordance between IDSA/ATS/ERS recommendations and real-life testing strategies should prompt future studies to evaluate the clinical and economic implications of different testing approaches and investigate the reasons for these differences.

GLIMP investigators: We would like to thank the following study contributors for their valuable collaboration. Argentina: Patricia Karina Aruj, Dept of Internal Medicine, University Hospital Alfredo Lanari, Buenos Aires, Argentina; Silvia Attorri, Hospital Luis Lago Maggiore, Mendoza, Argentina; Enrique Barimboim, Hospital Central de Mendoza, Argentina; Juan Pablo Caeiro and María I. Garzón, Hospital Privado Universitario, Córdoba, Argentina; Victor Hugo Cambursano, V.H. Dr Cazaux A. Servicio de Neumología, Hospital Rawson, Córdoba, Argentina; Adrian Ceccato, Hospital Nacional Prof Alejandro Posadas, Argentina; Julio Chertcoff, Florencia Lascar and Fernando Di Tulio, Critical Care Unit and Respiratory Medicine, Buenos Aires British Hospital, Buenos Aires, Argentina; Ariel Cordon Diaz, Hospital General Alvear, Ciudad, Mendoza, Argentina; Lautaro de Vedia, Respiratory Intensive Care Unit, Hospital Muñoz, Buenos Aires, Argentina; Maria Cristina Ganaha, Infectious Diseases Ward, Hospital Interzonal General de Agudos "Vicente Lopez y Planes" from General Rodriguez, Buenos Aires, Argentina; Sandra Lambert, Hospital El Cruce – Alta Complejidad en Red, Argentina; Gustavo Lopardo, Hospital Bernardo Houssay, Vicente López, Argentina; Carlos M. Luna, Pulmonary Medicine Division, Dept of Medicine, Hospital de Clínicas, Universidad de Buenos Aires, Argentina; Alessio Gerardo Malberti, Hospital Nuestra Señora del Carmen, Argentina; Nora Morcillo and Silvina Tartara, Hospital Zonal Especializado de Agudos y Crónicos Dr Antonio A. Cetrangolo, Argentina; Claudia Pensotti, Infectious Diseases and Infection Control Dept, Buenos Aires, Clinica Privada Monte Grande, Argentina; Betiana Pereyra, Hospital San Roque, Córdoba, Argentina; Pablo Gustavo Scapellato, Infectious Diseases Dept, Hospital D.F. Santojanni, Argentina; Juan Pablo Stagnaro, HZGA Mi Pueblo, Florencia Varela, Argentina. Australia: Sonali Shah, Dept of General Medicine, Austin hospital, Heidelberg, Australia. Austria: Felix Lötsch and Florian Thalhammer, Division of Infectious Diseases and Tropical Medicine, Dept of Medicine I, Medical University of Vienna, Austria. Belgium: Kurt Anseeuw, ZNA Campus Stuivenberg, Antwerp, Belgium; Camille A. Francois, Anesthesia and Critical Care Dept, Erasme University Hospital, Brussels, Belgium; Eva Van Braeckel, Dept of Respiratory Medicine, Ghent University Hospital, Belgium; Jean Louis Vincent, Dept of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium. Benin: Marcel Zannou Djimon, Jules Bashi and Roger Dodo, Centre Hospitalier Universitaire HKM of Cotonou, Benin. Brazil: Simone Aranha Nouér, Federal University of Rio de Janeiro, Brazil. Bulgaria: Peter Chipev and Milena Encheva, Clinic of Pulmonary Diseases, Military Medical Academy, Sofia, Bulgaria; Darina Miteva, UMHAT "St Marina", Varna, Bulgaria; Diana Petkova, University Hospital Varna, Bulgaria. Cameroon: Adamou Dodo Balkissou, Yaounde Jamot Hospital, Yaounde, Cameroon; Eric Walter Pefura Yone, Département de Médecine Interne, University of Yaounde, Yaoundé, Cameroon; Bertrand Hugo Mbatchou Ngahane, Douala General Hospital, Douala, Cameroon. China: Ning Shen, Respiratory Medicine, Peking University Third Hospital, Beijing, China; Jin-fu Xu, Dept of Respiratory Medicine, Shanghai Pulmonary Hospital, Tongji University, China. Colombia: Carlos Andres Bustamante Rico and Ricardo Buitrago, Clinica Shaio, Bogota, Colombia; Fernando Jose Pereira Paternina, Las Americas Clinic, Medellin, Colombia. Congo: Jean-Marie Kayembe Ntumba, Cliniques Universitaires de Kinshasa, DR Congo. Croatia: Vesna Vldic Carevic, Interne Medicine, Dubrovnik, Croatia; Marko Jakopovic, Medical School, University of Zagreb, Dept for Respiratory Diseases Jordanovac, University Hospital Centre Zagreb, Zagreb, Croatia; Mateja Jankovic, University Hospital Center Zagreb, Dept for Respiratory Diseases, Zagreb, Croatia; Zinka Matkovic, University Hospital Dubrava, Zagreb, Croatia; Ivan Mitrecic, Karlovac general hospital, Karlovac, Croatia.

Denmark: Marie-Laure Bouchy Jacobsson, Emergency Dept, Nordsjællands Hospital, Hillerød, Denmark; Anette Bro Christensen, Dept of Anaesthesiology, Viborg Region Hospital, Denmark; Uffe Christian Heitmann Bødtger, Dept of Pulmonology, Naestved Hospital, Denmark; Christian Niels Meyer, Dept of Internal Medicine, Roskilde Hospital, Copenhagen University Hospital, Roskilde, Denmark; Andreas Vestergaard Jensen, Gertrud Baunbæk-Knudsen, Pelle Trier Petersen and Stine Andersen, Dept of Lung and Infectious Diseases, Nordsjællands Hospital, Hillerød, Denmark. Egypt: Ibrahim El-Said Abd El-Wahhab, Thoracic Medicine, Faculty of Medicine, Mansoura University, Egypt; Nesreen Elsayed Morsy, Pulmonary, Critical Care and Sleep Medicine, Faculty of Medicine, Mansoura University, Mansoura, Egypt; Hanaa Shafiek, Chest Diseases Dept, Faculty of Medicine, Alexandria University, Egypt; Eman Sobh, Chest Diseases Dept, Al-Azhar University, Cairo, Egypt. Ethiopia: Kedir Abdella Abdulsemed, Dept of Medical Laboratory Science and Pathology, College of Health Sciences, Mycobacteriology Research Centre, Institute of Biotechnology Research, Jimma University, Jimma, Ethiopia. France: Fabrice Bertrand, Critical Care Unit, Robert Ballanger Hospital, Aulnay sous Bois, France; Christian Brun-Buisson, Univ Hospital Henri Mondor, 94000 Créteil, France; Etienne de Montmollin, Intensive Care Unit, Hôpital Delafontaine, Centre hospitalier de Saint-Denis, Saint-Denis, France; Muriel Fartoukh, Unité de réanimation médico-chirurgicale, Pôle Thorax Voies aériennes, Hôpital Tenon, Groupe Hospitalier Est Parisien, France; Jonathan Messika, Publique-Hôpital de Paris, Service de Réanimation Médico-chirurgicale, Hôpital Louis Mourier, Colombes, France, and Université Paris Diderot, IAME, UMR 1137, Sorbonne Paris Cité, Paris, France; Pierre Tattevin, Infectious Diseases and ICU, Pontchaillou University Hospital, Rennes, France; Abdo Khoury, Dept of Emergency Medicine and Critical Care, University of Franche - Comté, Medical Center, France. Gambia: Bernard Ebruke, Medical Research Council Unit, Gambia. Germany: Michael Dreher, Dept of Cardiology, Pneumology, Vascular Medicine and Intensive Care Medicine, University Hospital Aachen, Aachen, Germany; Martin Kolditz, Division of Pulmonology, Medical Dept I, University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany; Matthias Meisinger, Klinikum Niederlausitz GmbH, Klinik für Innere Medizin und Intensivmedizin, Senftenberg, Germany; Mathias W. Pletz and Stefan Hagel, Center for Infectious Diseases and Infection Control, Jena University Hospital, Germany; Jan Rupp, Dept of Molecular and Infectious Diseases, University of Lübeck, Lübeck, Germany; Tom Schaberg, Zentrum für Pneumologie, Agaplesion Diakonieklinikum Rotenburg, Germany; Marc Spielmanns, Internal Medicine Dept, Pulmonary Rehabilitation and Dept of Health, School of Medicine, University Witten-Herdecke, St Remigius-Hospital, Leverkusen, Germany; Petra Creutz and Norton Suttorp, Dept of Infectious Disease and Respiratory Medicine, Charité - University Medicine, Berlin, Germany. Ghana: Beatrice Siaw-Lartey, Komfo-Anokye Teaching Hospital, Kumasi, Ghana. Greece: Katerina Dimakou, 5th Respiratory Medicine Dept, "SOTIRIA" Chest Hospital, Athens, Greece; Dimosthenis Papapetrou, Medical Group of Athens (Paleo Faliro Clinic), Athens, Greece; Evdoxia Tsigou and Dimitrios Ampazis, Agioi Anargiroi Hospital, Kifissia, Athens, Greece; Evangelos Kaimakamis, Intensive Care Unit, "G. Papanikolaou" General Hospital of Thessaloniki, Greece; Mina Gaga, 7th Respiratory Medicine Dept and Asthma Center, Athens Chest Hospital, Greece. India: Mohit Bhatia, S.S. Hospital IMS BHU Varanasi, India; Raja Dhar, Fortis Hospitals, Kolkata, India; George D'Souza, Dept of Pulmonary Medicine, St John's Medical College Hospital, Bangalore, India; Rajiv Garg, Dept of Respiratory Medicine, King George's Medical University UP, Lucknow, India; Parvaiz A. Koul, Dept of Internal and Pulmonary Medicine, SheriKashmir Institute of Medical Sciences, Srinagar, India; P.A. Mahesh and B.S. Jayaraj, Dept of Pulmonary Medicine, JSS Medical College, JSS University, Mysore, India; Kiran Vishnu Narayan, Pulmonary Medicine, Government Medical College Kozhikode, Kerala, India; Hirennappa B. Udnur and Shashi Bhaskara Krishnamurthy, Columbia Asia Hospital, Hebbal, Bengaluru, Karnataka, India; Surya Kant, Dept of Respiratory Medicine, King George's Medical University, Chowk, Lucknow, Uttar Pradesh, India; Rajesh Swarnakar, Getwell Hospital and Research Institute, Dhantoli, Nagpur, India; Sneha Limaye and Sundeep Salvi, on behalf of the Respiratory Research Network of India (RRNI) from the Chest Research Foundation in Pune, India. Iran: Keihan Golshani, Isfahan University of Medical Sciences; Iran. Ireland: Vera M. Keatings, Letterkenny General Hospital, Co Donegal, Ireland; Ignacio Martin-Loeches, Multidisciplinary Intensive Care Research Organization (MICRO), St James's University Hospital, Trinity Centre for Health Sciences Dublin, Ireland. Israel: Yasmin Maor, Infectious Disease Unit, Affiliated to Tel Aviv University, Wolfson Medical Center, Holon, Israel; Jacob Strahilevitz, Dept of Clinical Microbiology and Infectious Diseases, Hadassah-Hebrew University, Jerusalem, Israel. Italy: Salvatore Battaglia, University of Palermo, Pneumologia DiBiMIS, Palermo, Italy; Maria Carrabba, Internal Medicine Dept, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; Piero Ceriana, Pulmonary Rehabilitation, IRCCS Fondazione Maugeri, Pavia, Italy; Marco Confalonieri, Dept of Pulmonology, University Hospital, Trieste, Italy; Antonella d'Arminio Monforte, Dept of Health Sciences, Clinic of Infectious Disease, San Paolo Hospital, University of Milan, Italy; Bruno Del Prato, Interventional Pneumology, Hospital Antonio Cardarelli, Naples, Italy; Marino De Rosa, UOC Pneumologia P.O. San Filippo Neri ASL RM E Roma, Italy; Riccardo Fantini, Respiratory Diseases clinic, Policlinico di Modena, Modena, Italy; Giuseppe Fiorentino, UOC Fisiopatologia e Riabilitazione Respiratoria AO Ospedali dei Colli PO Monaldi, Italy; Maria Antonia Gammino, Pulmonary Medicine Unit, San Martino Hospital, ASL 5 Oristano, Sardegna, Italy; Francesco Menzella, Dept of Cardiac-Thoracic-Vascular and Intensive Care Medicine, Pneumology Unit, IRCCS- Arcispedale Santa Maria Nuova, Reggio Emilia, Italy; Giuseppe Milani, Azienda Ospedaliera Sant Anna di Como, Presidio Ospedale S. Anna Nuovo, Unità Operativa di Pneumologia, Como, Italy; Stefano Nava, Alma Mater University of Bologna, DIMES, Respiratory and Critical Care Unit Sant'Orsola Malpighi Hospital, Italy; Gerardo Palmiero, Respiratory Unit, Versilia Hospital, Azienda USL 12 Viareggio, Lido di Camaiore, Lucca, Italy; Roberta Petrino and Barbra Gabrielli, Emergency Medicine Unit, S. Andrea Hospital, Vercelli, Italy; Paolo Rossi, Internal Medicine Dept, Azienda Ospedaliero-Universitaria S. Maria della Misericordia, Udine, Italy; Claudio Sorino, Pulmonology Unit, A.O. Sant Anna di Como, Italy; Gundi Steinhilber, Spedali Civili Brescia, U.O. Pneumologia e Fisiopatologia Respiratoria, Brescia, Italy; Alessandro Zanforlin, ULSS 18 Rovigo, Ospedale San Luca, Trecenta, Italy; Fabio Franzetti, Manuela Carugati, Manuela Morosi and Elisa Monge, Dept of Biomedical and Clinical Sciences, Division of Infectious Diseases, Luigi Sacco Hospital, Università degli Studi di Milano, Milan, Italy; Mauro Carone, Fondazione Salvatore Maugeri, IRCCS, Cassano Murge, Italy; Vincenzo Patella, Allergology and Clinical Immunology Unit, Dept of Medical Sciences, Battipaglia Hospital, Battipaglia, Salerno, Italy; Simone Scarlata, Geriatrics, Unit of Respiratory Pathophysiology and Thoracic Endoscopy, Campus Bio Medico University and Teaching Hospital, Rome, Italy; Andrea Comel, UO Pneumologia, Ospedale Pederzoli, Peschiera del Garda, Italy. Japan: Kiyoyasu Kurahashi, Yokohama City University Medical Center, Japan. Lebanon: Zeina Aoun Bacha, Medicine School, St Joseph University, Beyrouth, Lebanon. Mexico: Daniel Barajas Ugalde, National Institute of Respiratory Diseases, Mexico; Omar Ceballos Zuñiga, Hospital General de Mexicali, Mexicali, Baja California, Mexico; José F. Villegas, Hospital Universitario, Monterrey, Mexico. Montenegro: Milic Medenica, Hospital for Lung Diseases - Brezovik, Niksic, Montenegro. The

Netherlands: E.M.W. van de Garde, Dept Clinical Pharmacy, St Antonius Hospital, Utrecht/Nieuwegein, The Netherlands. Nepal: Deebya Raj Mihsra, Internal Medicine, BP Koirala Institute of Health Sciences, Nepal; Poojan Shrestha, Oxford University Clinical Research Unit, Patan Hospital, Nepal. New Zealand: Elliott Ridgeon, Medical Research Institute of New Zealand. Nigeria: Babatunde Ishola Awokola, Dept of Family Medicine and Primary Care, Lily Hospitals Limited, Warri, Nigeria; Ogonna N.O. Nwankwo, University of Calabar Teaching Hospital, Calabar, Nigeria; Adefuye Bolanle Olufunlola, Olabisi Onabanjo University teaching hospital, Sagamu, Ogun State, Nigeria; Segbolu Olumide, Dept of Medicine (Pulmonary Unit), University College Hospital, Ibadan, Nigeria; Kingsley N. Ukwaja, Dept of Medicine, Federal Teaching Hospital Abakaliki, Ebonyi State, Nigeria. Pakistan: Muhammad Irfan, Section of Pulmonary and Critical Care Medicine, Dept of Medicine, Aga Khan University, Karachi, Pakistan. Poland: Lukasz Minarowski, Dept of Lung Diseases and Tuberculosis, Medical University of Bialystok, Poland; Skoczyński Szymon, Dept of Pneumology, School of Medicine in Katowice, Medical University of Silesia, Katowice, Institute of Occupational Medicine and Environmental Health, Sosnowiec, Poland. Portugal: Felipe Froes, Hospital Pulido Valente – CHLN, Lisbon, Portugal; Pedro Leuschner, Centro Hospitalar do Porto, Porto, Portugal; Mariana Meireles, Cláudia Ferrão, Pedro Leuschner and João Neves, Serviço de Medicina, Centro Hospitalar do Porto, Largo Prof Abel Salazar, Porto, Portugal; Sofia B Ravara, Faculty of Health Sciences, University of Beira Interior; Cova da Beira Hospital Center, Covilhã, Portugal. Republic of Moldova: Victoria Brocovschii, Dept of Pneumology and Allergology, State University of Medicine and Pharmacy “Nicolae Testemitanu” Republic of Moldova; Chesov Ion, Clinic of Anesthesia and Intensive Care “Valeriu Ghreng”, Institute of Emergency Medicine, State University of Medicine and Pharmacy “Nicolae Testemitanu”, Chisinau, Republic of Moldova; Doina Rusu, SMFU “N. Testemitanu”, Chisinau, Republic of Moldova; Cristina Toma, Dept of Pneumology and Allergology, State University of Medicine and Pharmacy “Nicolae Testemitanu”, Chisinau, Republic of Moldova. Romania: Daniela Chirita, Hospital Sfântul Stefan, Bucharest, Romania; Carmen Mihaela Dorobat, Universitatea de Medicină și Farmacie “Gr. T. Popa” Iași Facultatea de Medicină Stomatologică, Spitalul Clinic de Boli Infecțioase “Sfânta Parascheva”, Iași, Romania. Russia: Alexei Birkun, Dept of Anesthesiology, Critical Care and Emergency Medicine, Medical Academy named after S.I. Georgievsky, Russian Federation; Anna Kaluzhenina, Volgograd State Medical University, Russia. Saudi Arabia: Abdullah Almotairi, King Fahad medical City (KFMC), Riyadh, KSA; Zakeya Abdulbaqi Ali Bukhary, College of Medicine, Taibah University, Medina, KSA; Jameela Edathodu, Al Faisal University, King Faisal Specialist Hospital, Riyadh, KSA; Amal Fathy, Pulmonary and respiratory critical care Medicine, Mansoura University Egypt, Affiliate at Taibah University, KSA; Abdullah Mushira Abdulaziz Enani and Nazik Eltayeb Mohamed, Infectious Diseases Section, Medical Specialties Dept, King Fahad Medical City, Riyadh, KSA; Jawed Ulhadi Memon, Pulmonology Division, Dept of Internal Medicine, King Fahad Hospital, Hofuf, Al Ahasa, KSA; Abdelhaleem Bella, Dammam University-Saudi Arabia and King Fahad Hospital, KSA. Serbia: Nada Bogdanović, Pulmonary Dept of KHC Dr Dragiša Mišović, Belgrade, Serbia; Branislava Milenkovic, Clinic for Pulmonary Diseases, Clinical Centre of Serbia, Faculty of Medicine, University of Belgrade, Belgrade, Serbia; Dragica Pesut, University of Belgrade School of Medicine, Teaching Hospital of Pulmonology, Clinical Centre of Serbia, Belgrade, Serbia. South Africa: Charles Feldman, Division of Pulmonology, Dept of Internal Medicine, Charlotte Maxeke Johannesburg Academic Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa. South Korea: Ho Kee Yum, Inje Univ Seoul Paik Hospital, South Korea. Spain: Luis Borderias, Respiratory and Sleep Unit, Hospital San Jorge, Huesca, Spain; Noel Manuel Bordon Garcia, Barcelona Policlínica and Moises Broggi Hospital at Sant Joan Despí, Spain; Hugo Cabello Alarcón, Sant Hospital Seu de Urgell, Catalonia, Spain; Catia Cilloniz and Antoni Torres, Dept of Pneumology, Institut Clinic del Tòrax, Hospital Clinic of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Spain; Vicens Diaz-Brito and Xavier Casas, Infectious Diseases Unit and Pneumology Service, Parc Sanitari Sant Joan de Deu, Sant Boi, Barcelona, Spain; Alicia Encabo González, Hospital Complex of Pontevedra, Spain; Maria Luisa Fernández-Almira, Medicina Interna, Hospital Universitario Central de Asturias, Spain; Miguel Gallego, Dept of Respiratory Medicine, Hospital de Sabadell, Institut Universitari Parc Taulí-UAB, Sabadell, CIBER de Enfermedades Respiratorias, CIBERES, Bunyola, Spain; Inmaculada Gaspar-García, Dept of Respiratory Medicine, Hospital Costa del Sol, Marbella, Málaga, Spain; Juan González del Castillo, Emergency Dept, Hospital Universitario Clínico San Carlos, Madrid, Spain; Patricia Javaloyes Victoria, Hospital General Universitario de Alicante, Alicante, Spain; Elena Laserna Martínez, Hospital Mollet, Barcelona, Spain; Rosa Malo de Molina, University Hospital Puerta de Hierro Majadahonda, Madrid; Pedro J. Marcos, Servicio de Neumología, Complejo Hospitalario Universitario de A Coruña (CHUAC), INIBIC, Sergas, Universidade de A Coruña (UDC), Spain; Rosario Menéndez, Pneumology Service, University and Polytechnic Hospital La Fe, Valencia, Spain; Ana Pando-Sandoval, Hospital Universitario Central de Asturias, Area de Gestión Clínica de Pulmon, Servicio de Neumología, Oviedo, Spain; Cristina Prat Aymerich, Alicia Lacoma de la Torre and Ignasi García-Olivé, Microbiology Dept and Pneumology Dept, Hospital Universitari Germans Trias i Pujol, Institut d'Investigació Germans Trias i Pujol, Badalona, Universitat Autònoma de Barcelona, CIBER Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Spain; Jordi Rello and Silvia Moyano, Critical Care Dept, Hospital Vall d'Hebron, Barcelona, Spain; Francisco Sanz, Servicio de Neumología, Consorci Hospital General Universitari de Valencia, Valencia, Spain; Oriol Sibila and Ana Rodrigo-Troyano, Servei de Pneumologia, Hospital de la Santa Creu i Sant Pau, IIB-Sant Pau, Barcelona, Spain; Jordi Solé-Violán, Hospital Universitario de Gran Canaria Dr Negrín, Las Palmas de Gran Canaria, Spain; Ane Uranga, Pulmology Dept, Hospital of Galdakao-Usansolo, Spain; Job F.M. van Boven, Hospital Universitari Son Espases, Palma de Mallorca, Spain; Ester Vendrell Torra and Jordi Almirall Pujol, Intensive Care Medicine, Hospital de Mataró, Spain. Togo: Arnauld Attannon Fiogbe, Pulmonology and Infectious Diseases Service/University Hospital of Sylvanus Olympio, Lomé, Togo. Tunisia: Ferdaous Yangui, Dept of Pneumology, Hospital of Internal Forces Security (IFS), Marsa, Tunis, Tunisia. Turkey: Semra Bilaceroglu, Izmir Dr Suat Seren Training and Research Hospital for Thoracic Medicine and Surgery, Izmir, Turkey; Levent Dalar, Pulmonary Medicine, Istanbul Bilim University, Istanbul, Turkey; Ufuk Yilmaz, Suat Seren Chest Disease and Surgery Training and Research Hospital, Izmir, Turkey. Ukraine: Artemii Bogomolov, Vinnitsa National Pirogov Memorial Medical University, Vinnitsa Regional Antituberculosis Hospital, Vinnitsa, Ukraine. United Arab Emirates: Naheed Elahi, Dubai Hospital, UAE. UK: Devesh J. Dhasmana, Victoria Hospital, Kirkcaldy, NHS Fife, UK; Andrew Feneley, Rhiannon Ions, Julie Skeemer and Gerrit Woltmann, University Hospitals of Leicester NHS Trust and University of Leicester, Leicester, UK; Carole Hancock, Royal Respiratory Research Team, Royal Liverpool University Hospital, Liverpool, UK; Adam T. Hill, Royal Infirmary and University of Edinburgh, UK; Banu Rudran, The Royal London Hospital, Barts Health Trust, London, UK; Silvia Ruiz-Buitrago and Marion Campbell, Hairmyres Hospital, Eaglesham Road, East Kilbride, UK; Paul Whitaker, Dept of Respiratory Medicine, St James's Hospital, Leeds, UK; Alexander Youzguin, Southport and Ormskirk Hospitals NHS Trust, UK; Anika

Singanayagam, Imperial College Healthcare NHS Trust, London, UK. USA: Karen S. Allen, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; Veronica Brito, Texas A&M Health Science Center, Division of Pulmonary, Critical Care and Sleep Medicine, Baylor Scott & White Health, TX, USA; Jessica Dietz, Fargo VA Health Care System, Fargo, ND, USA; Claire E. Dysart and Susan M. Kellie, Clement J. Zablocki VA Medical Center, Milwaukee, WI, USA, Division of Infectious Diseases, University of New Mexico School of Medicine, Raymond G. Murphy VA Medical Center, Albuquerque, NM, USA; Ricardo A. Franco-Sadud and Garnet Meier, Division of Hospital Medicine, Cook County Hospital, Chicago, IL, USA; Thomas L. Holland and Stephen P. Bergin, Dept of Medicine, Duke University Medical Center and School of Medicine, Duke Clinical Research Institute, Durham, NC, USA; Faye Kheir, Dept of Pulmonary Diseases, Critical Care and Environmental Medicine, Tulane University Health Sciences Center, New Orleans, LA, USA; Mark Landmeier, Division of Pulmonary and Critical Care Medicine, Northwestern Memorial Hospital, Chicago, IL, USA; Manuel Lois, John Peter Smith Hospital, Fort Worth, TX, USA; Girish B. Nair, Interstitial Lung Disease Program and Pulmonary Rehabilitation, SUNY Stony Brook Winthrop University Hospital, Mineola, NY, USA; Hemali Patel, Dept of Medicine, Division of General Internal Medicine, Hospital Medicine Group, University of Colorado, CO, USA; Katherine Reyes, Henry Ford Hospital, Detroit, IL, USA; William Rodriguez-Cintron, Pulmonary/Critical Care Medicine, VA Caribbean Healthcare System, USA; Shigeki Saito, Tulane University, New Orleans, LA, USA; Nilam J. Soni, Julio Noda, Cecilia I. Hinojosa, Stephanie M. Levine, Luis F. Angel and Antonio Anzueto, Divisions of Hospital Medicine and Pulmonary/Critical Care Medicine, South Texas Veterans Health Care System, University of Texas Health Science Center San Antonio, San Antonio, TX, USA; K. Scott Whitlow, John Hipskind, Kunal Sukhija and Vicken Totten, Kaweah Delta Health Care District, Dept of Emergency Medicine, Visalia, CA, USA; Richard G. Wunderink and Ray D. Shah, Northwestern University Feinberg School of Medicine, Chicago, IL, USA. Zambia: Kondwelani John Mateyo, Dept of Internal Medicine, University Teaching Hospital, Lusaka, Zambia. Other investigators: Lorena Noriega, Ezequiel Alvarado, Mohamed Aman and Lucia Labra.

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