Get with the guidelines : management of chronic obstructive pulmonary disease in emergency departments in Europe and Australasia is sub-optimal

the AANZDEM and EuroDEM study groups

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Get With The Guidelines - Management Of COPD In EDs In Europe And Australasia is sub-optimal

Anne-Maree **KELLY**

Joseph Epstein Centre for Emergency Medicine Research, Western Health, St Albans 3021, Victoria, Australia and Department of Medicine, Melbourne Medical School – Western Precinct, The University of Melbourne, St. Albans, Vic, Australia, 3021.

Oene **VAN MEER**

Leiden University Medical Center, Leiden, the Netherlands.

Gerben **KEIJZERS**

Department of Emergency Medicine, Gold Coast Unviersty Hospital, Gold Coast, Australia, Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia and School of Medicine, Griffith University, Gold Coast, Australia.

Justina **MOTIEJUNAITE**

INSERM, U942, BIOmarkers in CArdioNeuroVAScular diseases, 75010, Paris, France; APHP, Saint Louis Lariboisière Hospitals, Department of Anesthesiology and Critical Care, 75010, Paris, France and Lithuanian University of Health Sciences Kaunas Clinics, Department of Cardiology, Kaunas, Lithuania.

Peter **JONES**

Department of Emergency Medicine, Auckland City Hosptial, Auckland 1172, New Zealand.

Richard **BODY**

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Emergency Department, Central Manchester University Hospitals NHS Foundation Trust, Oxford Road, Manchester and Cardiovascular Sciences Research Group, the University of Manchester, Manchester, England, UK.

Simon **CRAIG**

Emergency Department, Monash Medical Centre, Clayton, Victoria, Australia and School of Clinical Sciences at Monash Health, Monash University, Clayton, Australia.

Mehmet **KARAMERCAN**

Gazi University, Faculty of Medicine, Emergency Medicine Department, Ankara, Turkey and Istanbul Bagcilar Training and Research Hospital, Department of Emergency Medicine, Istanbul, Turkey.

Sharon **KLIM**

Joseph Epstein Centre for Emergency Medicine Research, Western Health, St Albans 3021, Victoria, Australia

Veli-Pekka **HARJOLA**

Emergency Medicine, University of Helsinki, Department of Emergency Medicine and Services, Helsinki University Hospital, Helsinki, Finland.

Franck **VERSCHUREN**

Université Catholique de Louvain, Cliniques Universitaires Saint-Luc, Department of Acute Medicine, Brussels, Belgium.

Anna **HOLDGATE**

Department of Emergency Medicine, Liverpool Hospital, Sydney, Australia and University of New South Wales (Southwest Clinical School), Sydney, Australia

Michael **CHRIST**

Department of Emergency Care, Luzerner Kantonsspital, Luzern, Switzerland and Paracelsus Medical University, Nuremberg, Germany.

Adela **GOLEA**

University of Medicine and Pharmacy, Emergency Department of the University County Emergency Hospital Cluj Napoca, Romania.

Colin A **GRAHAM**

Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR

Jean **CAPSEC**

Tours University Hospital, Emergency Medicine Department, 37044, Tours, France.

Cinzia **BARLETTA**

St. Eugenio Hospital, Department of Emergency Medicine, Rome, Italy.

Luis **GARCIA-CASTRILLO**

Servicio Urgencias Hospital Marqués de Valdecilla, Santander, Spain.

Win Sen **KUAN**

Emergency Medicine Department, National University Hospital, National University Health System, Singapore.

Said **LARIBI**

Tours University Hospital, Emergency Medicine Department, 37044, Tours, France and François-Rabelais University, School of Medicine, 37044, Tours, France.

on behalf of the AANZDEM and EuroDEM study groups

Corresponding author:

Anne-Maree Kelly MD FACEM FCCP

Joseph Epstein Centre for Emergency Medicine Research at Western Health

WHCRE, Sunshine Hospital, St Albans 3021 AUSTRALIA

Tel.: +61 418 592 361

Fax: +613 9318 4790

E-mail: anne-maree.kelly@wh.org.au

AUTHORSHIP STATEMENT:

AMK and SL had the concept for the study. All named authors contributed to study design, all named authors and study group members collected data, AMK and SL performed data analysis, AMK and SL wrote the first draft of the manuscript and all named authors contributed to its refinement and approved the final manuscript.

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Get With The Guidelines - Management Of COPD In EDs In Europe And Australasia is sub-optimal

ABSTRACT

Objectives: Exacerbations of chronic obstructive pulmonary disease (COPD) are common in emergency departments (ED). Guidelines recommend administration of inhaled bronchodilators, systemic corticosteroids and antibiotics along with non-invasive ventilation (NIV) for patients with respiratory acidosis. We aimed to determine compliance with guideline

recommendations for patients with treated for COPD in ED in Europe (EUR) and South East Asia/Australasia (SEA) and to compare management and outcomes.

Methods: In each region, an observational prospective cohort study was performed that included patients presenting to EDs with the main complaint of dyspnoea during three 72-hour periods. This planned sub-study included those with an ED primary discharge diagnosis of COPD. Data were collected on demographics, clinical features, treatment, disposition and in-hospital mortality. We determined overall compliance with guideline recommendations and compared treatments and outcome between regions.

Results: 801 patients were included from 122 EDs (66 EUR and 46 SEA). Inhaled bronchodilators were administered to 80.3% of patients, systemic corticosteroids to 59.5%, antibiotics to 44% and 60.6% of patients with pH <7.3 received NIV. The proportion administered systemic corticosteroids was higher in SEA (EUR vs. SEA for all comparisons; 52% vs. 66%, p<0.001) as was administration of antibiotics (40% vs. 49%, p=0.02). Rates of NIV and mechanical ventilation were similar. Overall in-hospital mortality was 4.2% (SEA 3.9% vs. EUR 4.5%, p=0.77).

Conclusion: Compliance with guideline recommended treatments, in particular administration of corticosteroids and NIV, was sub-optimal in both regions. Improved compliance has the potential to improve patient outcome.

KEYWORDS:

Dyspnoea, emergency department, management, COPD, outcome

INTRODUCTION

Shortness of breath is one of the main reasons patients present to an emergency department (ED).[1]. Previously published research from the Asia-Pacific region reports that this symptom accounts for 5% of all ED presentations. Chronic obstructive pulmonary disease (COPD) was found to be the main ED diagnosis in 14% of these presentations. [2]

Recent guidelines [3,4] recommend a number of treatments in the acute phase of care in order to optimise outcomes. These include the use of controlled oxygen therapy, inhaled bronchodilators, systemic corticosteroids, antibiotics if there is clinical, laboratory or chest x-ray (CXR) evidence of bacterial infection, the taking of a CXR, blood gas analysis for cases classified as more than mild severity, and non-invasive ventilation (NIV) in patients with significant respiratory acidosis (pH<7.35). To date, evidence regarding compliance with these elements in EDs suggests gaps in compliance.[5-7] Most of these studies are single site or single region raising questions about generalisability.

The aim of this study was to determine overall compliance with guideline recommendations and to compare management and in-hospital outcomes between patients treated for ED-diagnosed COPD in Europe (EUR) and South East Asia/Australasia (SEA), in particular compliance with guideline recommendations [8].

MATERIALS AND METHODS

This is a combination of two international, multicentre, prospective, interrupted time series cohort studies, both occurring in 2014. They were designed to evaluate the epidemiology, treatment and in-hospital outcome of patients presenting to ED with shortness of breath as

the main complaint. The EuroDEM study was conducted in 66 European centres (Belgium 3, Finland 5, France 5, Germany 5, Italy 1, Netherlands 16, Romania 7, Spain 1, Turkey 7 and United Kingdom 16. The AANZDEM study was conducted in 46 Asia-Pacific/Australian centres (Australia 33, New Zealand 4, Singapore 3, Hong Kong 4 and Malaysia 2). The study sample was generated with consecutive patients attending EDs during three study periods of 72 hours each throughout one year. Detailed methodology for AANZDEM has been published previously.[9] The patient population of interest was consecutive adult patients presenting to the ED with acute dyspnoea as a main symptom. The studies were performed in accordance with the Declaration of Helsinki. Ethics committee approvals were obtained for all sites according to local requirements. If requested by the local ethics committee, patient consent for data collection was obtained. The population of interest for this sub-study were patients with an ED discharge diagnosis of COPD. [Figure 1].

A specifically designed data collection form was developed independently by each steering committee. Data was collected by local site investigators and submitted to central databases in each region as de-identified data. Data collected included patient characteristics, comorbidities, mode of arrival, usual medications, prehospital treatment as documented in ED clinical records, initial assessment (clinical assessment and vital signs), investigations performed (laboratory tests, electrocardiogram, imaging, etc.) and results, treatment in the ED, final ED diagnosis, in-hospital outcome including disposition, in-hospital mortality and final hospital diagnosis. There were some minor differences in data points e.g. EUR did not collect data on imaging. Local data collectors were not blinded to objectives of the parent studies although they were unaware that specific comparative sub-analyses by condition would be undertaken.

The outcomes of interest were compliance with guideline recommended treatment and comparison of treatment and outcome (disposition and in-hospital mortality) between EUR and SEA. Published COPD guidelines were used as the reference standard for treatment.[3,4]. We assumed that patients attending an ED for care had at least a moderate exacerbation of COPD. Results are presented as frequencies or as medians with interquartile range (IQR). The Chi-square test or Fisher's exact test (as appropriate) were used to compare categories. Continuous variables were compared using the Mann Whitney test (nonparametric). Statistical significance was defined as $p < 0.05$. Statistical analysis was performed using SAS version 9.1 software (SAS Institute, Cary, NC, USA) and Analyse-It™ (https://analyse-it.com/).

RESULTS

Eight hundred and one patients had a final ED diagnosis of COPD and formed the study population; 415 SEA and 386 EUR. In SEA, 44 sites contributed cases with a median number of cases/site of 8.5 (IQR 5-14, range 1-22). In EUR, 59 sites contributed cases with a median number of cases/site of 5 (IQR 2-9, range 1-25). Variability in the number of cases/site was expected due to differences in ED size and caseload.

Median age was 72 and 58% of patients were male. Median duration of symptoms was 3 days (IQR 1-7). The cohorts were mostly comparable for comorbidities with 90.4% having a past history of COPD, 18% a past history of heart failure and 24% a past history of coronary artery disease.(Table 1) Of note, there was a significant difference in reported (current) smoking rates – SEA 23.8% versus 40.8% EUR ($p<0.001$).

Regarding regular medications, the EUR cohort had lower use of inhaled beta-agonists (63.5% versus 74.4%, p<0.001) and higher use of diuretics (31.3% versus 21.5%, p<0.001). Home oxygen usage rates were similar.(Table 1) Clinical features at presentation were similar, including the proportion with clinically significant acidosis (overall 8.2%).(Table 2)

The proportion of patients who received the defined evidence-based treatments was sub-optimal – inhaled bronchodilators 80.3% and systemic corticosteroids 59.5%. The proportion of patients receiving systemic corticosteroids was lower in EUR than SEA (52.6% versus 65.9%, p<0.001) as was administration of antibiotics (40.2% versus 48.5%, p=0.003). NIV and mechanical ventilation rates were similar.(Table 3)

While the proportion of patients requiring intensive care unit admission was similar (5.5%), the proportion of patients discharged home from ED was significantly higher in EUR compared to SEA (33.9% versus 19.3%, p<0.001). Overall in-hospital mortality was 4.2%, (SEA 3.9% versus EUR 4.5%, p=0.77)

DISCUSSION

This study has provided a rare opportunity to explore the epidemiology, treatment and outcome of patients presenting to ED with a final ED diagnosis of COPD, to determine compliance with guideline recommended treatment and to compare management and in-hospital outcomes across two major regions. Our findings suggest that compliance with guideline recommended treatment is sub-optimal in both regions and that ED could do more to improve quality of care for this patient group.

While the use of inhaled beta agonists was similar, it is lower than expected. The proportion of patients receiving systemic corticosteroids was considerably below expected levels. COPD guidelines recommend systemic corticosteroid for non-mild exacerbations of COPD as they reduce severity and shorten recovery.[8,10] Overall, almost 40% of patients did not receive them, with EUR compliance being significantly lower than SEA. Previous research suggests that the proportion of patients with COPD who have clinical, investigatory or radiological evidence of infection is 65-70%.[11] That only 43.3% of patients received antibiotics falls well below what would be expected on the basis of that data. That said, the features used to define evidence of potential bacterial infection in that paper are liberal and some could apply to viral and well as bacterial infection. For this reason we are unable to comment further on whether the reported rate of antibiotic use was appropriate. The proportion of patients with acidosis who received treatment with NIV was also lower than expected, despite level 1 evidence that it improves outcome. [12] We did not collect reasons for non-use of NIV. Based on our experience and knowledge of the sector, possible explanations include lack of awareness of the evidence, lack of availability of the required equipment in ED and lack of appropriately trained staff to safety undertake this therapy in ED. Other contributors may have been that the patient declined NIV or under-estimation of severity by treating clinicians.

The results of our study do not compare favourably with a published European audit of management of COPD admissions.[13] That study reported that 91% of patients received short-acting bronchodilators, 82% received systemic corticosteroids and 91% of eligible patients received antibiotics; all much higher than this study. Our study found a higher use of

NIV in patients with respiratory acidosis (61% vs. 51%). The comparisons should be considered cautiously however as that study was of patients admitted to hospital rather than presenting to ED – a quite different clinical practice environment. It seems logical that evidence-based care should be initiated as early as possible in a patient's journey. The evidence suggests there may be a disjunct between ward-based pathways and ED pathways for this patient group; a gap that should be closed. The European audit [13] also reported variation in guideline compliance between countries and hospitals. In our study, the aggregation of data into regions may obscure site-to-site or country-to-country variation within regions. Numbers at individual sites within our study were too small for comparative analysis. That said, we believe that lessons from regions form an important step in understanding widespread gaps in guideline compliance. They inform individual health services and hopefully encourage them to audit their own practice and implement quality improvement activities with an emphasis on the identified gaps.

Our study did not explore treatment decision-making. Contributing factors to non-compliance with guideline recommendations may include lack of awareness of the evidence, the cognitive overload associated with ED practice, time constraints in ED, distraction and competing patient priorities as several patients may be being processed by a doctor at any given time and the historically high turnover of ED staff making it difficult to ensure that all staff are educated in evidence-based recommendations and recent changes. One approach suggested to address deficits in care is the introduction of a COPD proforma or checklist. Using this approach, Sen et al demonstrated improvements in categorization of respiratory failure, administration of controlled oxygen therapy and appropriate referral for NIV.[14] Similarly, McCarthy et al showed that a proforma improved compliance with defined

treatments.[15] This approach may be effective because it makes doctors aware of, or reminds them about, guideline-based care. Since the healthcare world is moving towards paperless systems, the use of clinical informatics systems such as computer-assisted decision support will probably be required. Such systems have been proven to improve patient safety and have been recommended by the US Agency for Healthcare Research and Quality. [16]

The marginally higher EUR in-hospital mortality may simply be a reflection that there was higher tolerance for ED discharge of patients with moderate exacerbations of COPD in EUR. It may also have been influenced by higher smoking rates and higher proportion of patients with heart disease. We cannot confirm this.

The disparities in admission rate (SEA being much higher) are striking. There may be a number of reasons for this. When deciding whether hospital admission is required, a range of factors are taken into account including patient factors (for example health literacy and ability to self-manage), illness severity, social factors, use of disease specific ED short stay unit pathways and access to appropriate follow-up care (such as primary care or specialist clinics, disease-specific outreach services, etc.). We are unable to comment which of these might have contributed to the observed disparity. The difference does raise the possibility that there were unnecessary admissions in the SEA cohort, which may be an area worthy of more research.

The higher proportion of current smokers in the EUR cohort is noteworthy. It suggests that there is opportunity to improve long term outcomes by targeting smoking cessation. Many

areas in SEA have been aggressive in bureaucratic attempts to encourage smoking cessation such as taxing cigarettes, requiring plain unattractive packaging, requiring health warnings (and sometimes photos of complications) on cigarette packets, banning smoking in restaurants and some public areas and requiring cigarettes to be stored out of sight in retail outlets [17]. Measures such as these may also be generalizable to Europe.

Our study confirms that shortness of breath is a high risk presenting complaint for in-hospital mortality. We report in-hospital mortality of 4.2% which is similar to previously reported mortality rates in COPD exacerbations.[18-20].

The finding that only about a third of patients are current or recent smokers is interesting and COPD is uncommon in non-smokers. The design of our study did not allow us to collect detailed data regarding patients' smoking pack-year history. This is likely to have shown that the majority of patients had a significant history of smoking even if not smoking recently.

Our study has some limitations that should be considered when interpreting our results. There was no central committee for the adjudication of final diagnosis. It was based on final ED diagnosis, representing the 'real world' of emergency medicine practice. This is to an extent is offset by a large sample size suggesting generalisation of findings. Local data collectors were provided with detailed data collection information (including a data dictionary) therefore minimising bias. We did not distinguish between acute exacerbations, therapeutic failure and relapse. In Emergency Medicine practice, distinguishing these is not clinically relevant. We did not formally assess severity. That said, vitals signs observations and the proportion of patients with significant acidosis were not statistically different between the

groups. The nature of ED practice means that some data that lung specialists rely on to confirm the diagnosis of COPD and severity of illness is not available. For example, dyspnoea scores and spirometry are rarely used in ED. It is possible that compliance with guideline recommended treatments in the EuroDEM sample has been under-estimated. Some patients who presented to hospital via ambulance in the EuroDEM may have had treatments initiated by paramedics/physicians in the ambulance which were not captured by data collection processes. It is a potential limitation that only about 90% of patients had a previous known diagnosis of COPD. Again, this reflects the 'real world' situation of emergency care. Further, a significant proportion of the remainder reported a past history of asthma, possibly reflecting difficulty distinguishing between these, especially in mid-late age. To test the bias this might have introduced we repeated the analysis for the patients with previous COPD only and the results were not substantially different (Supplementary tables 1b-3b). There is a small amount of missing data that may have influenced results with the amount of missing data is higher in the European sample than the SEA sample. While it is unlikely that data is missing completely at random, it is very small relative to the sample size. There is the potential risk of inclusion and registration bias. Given the nature of this study it is not possible to qualify the risk of this bias. Finally, the sites contributing data were not selected at random. Rather than chose to participate voluntarily. Therefore it is possible that they are not representative of their regions. This however is a weakness shared with many similar audit of care studies and is hard to avoid.

CONCLUSION

Compliance with guideline recommended treatments, in particular administration of corticosteroids and NIV, was sub-optimal in both regions. Improved compliance has the potential to improve patient outcome.

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FIGURE LEGEND

Figure 1: Sample derivation

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EuroDEM study group

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EuroDEM Steering Committee:

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EuroDEM Study Group (includes all hospitals that provided data):

- France: Patrick Plaisance, Ghanima Al Dandachi (CHU Lariboisière, Paris), Maxime Maignan (CHU Grenoble), Dominique Pateron, Christelle Hermand (CHU Saint Antoine, Paris), Cindy Tessier (CHU de Dijon), Pierre-Marie Roy (CHU d'Angers), Lucie Bucco (CH de Chalon sur Saône), Nicolas Duytsche (CH de Macon).
- Spain: Pablo Garmilla (Hospital Universitario Marques Valdecilla).
- Italy: Cinzia Barletta (St Eugenio Hospital, Rome), Giorgio Carbone (Gradenico Hospital, Turin), Roberto Cosentini (Polyclinic Hospital, Milan).
- Romania: Sorana Truță (Emergency Department of the County Emergency Hospital, Târgu Mureș), Natalia Hrihorișan (Emergency Department of the County Emergency Hospital, Oradea), Diana Cimpoeșu (University of Medicine and Pharmacy, Emergency Department of the University County Emergency Hospital, Iași), Luciana Rotaru (University of Medicine and Pharmacy, Emergency Department of the University County Emergency Hospital, Craiova), Alina Petrică (Emergency Department of the County Emergency Hospital, Timișoara), Mariana Cojocaru (Emergency Department of the Emergency Hospital Elias București), Silvia Nica (Emergency Department of the University Emergency Hospital București), Rodica

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- Germany: Michael Christ, Felicitas Geier, Yvonne Smolarsky (Department of Emergency and Critical Care Medicine, Paracelsus Medical University, Nuremberg), Sabine Blaschke (Department of Emergency Care Medicine, University of Goettingen), Clemens Kill, Andreas Jerrentrup (Department of Emergency Care Medicine, University of Marburg), Christian Hohenstein (Department of Emergency Care Medicine ,University of Jena), Felix Rockmann, Tanja Brünnler (Department of Emergency Care Medicine, Krankenhaus Barmherzige Brüder, Regensburg).
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- Finland: Hanna Suurmunne, Liisa Kokkonen (Päijät-Häme Social and Health Care Group, Lahti), Jukka Tolonen, Juha Valli (Helsinki and Uusimaa Hospital District, Hyvinkää), Minna Kiljunen (North Karelia Central Hospital and Honkalampi Centre, Joensuu), Jukka Tolonen (Helsinki University Hospital, Helsinki), Sanna Kaye (City of Helsinki Department of Social Services and Health Care, Helsinki), Jukka Tolonen,

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Table 1: Patient characteristics

	Total	AANZDEM	Missing data	EuroDEM	Missing data	p value
N (%)	801	415 (51.8%)		386 (48.2%)		
Age (years), (median [IQR)	72 [64-80]	73 [65-81]	0	71 [63-78]	3	<0.001
Male (N, %)	466 (58.3%)	249 (60.0%)	0	217 (57%)	2	0.3
Duration of symptoms (days), (median [IQR])	3 [1-7]	3 [1-7]	17	3 [2-6]	66	0.84
Co-morbidities (N, %)						
Prior history of COPD	720 (90.8%)	375 (90.6%)	1	345 (91%)	7	0.92
Smoker	254 (32.8%)	98 (23.8%)	3	156 (43.1%)	24	<0.001
Chronic heart failure	142 (18.4%)	73 (17.7%)	3	69 (19.2%)	26	0.79
Diabetes mellitus	162 (20.9%)	78 (19.0%)	4	84 (23%)	21	0.2
Hypertension	398 (51%)	215 (52.2%)	3	183 (49.6%)	17	0.52
Coronary artery disease	182 (23.8%)	102 (24.8%)	3	80 (22.7%)	33	0.55
Atrial fibrillation / flutter	99 (12.7%)	55 (13.3%)	3	44 (12%)	18	0.63
Chronic renal disease	73 (9.3%)	47 (11.4%)	3	24 (6.4%)	11	0.02
Active malignancy	40 (5.1%)	22 (5.4%)	4	18 (4.9%)	16	0.88

Asthma	112 (14.2%)	54 (13.1%)	2	58 (15.4%)	10	0.43
Prior pulmonary embolism	37 (4.7%)	17 (4.1%)	3	20 (5.4%)	18	0.813
Chronic medication use (N,%)						
Inhaled beta-2 agonists	553 (69.1%)	308 (74.4%)	1	245 (63.5%)	0	0.001
Inhaled corticosteroids	455 (56.9%)	211 (51%)	1	244 (63.2%)	0	<0.001
Oral steroids	140 (17.5%)	68 (16.5%)	2	72 (18.7%)	0	0.47
Home oxygen	117 (14.7%)	57 (13.8%)	3	60 (15.5%)	0	0.56
Diuretics	210 (26.3%)	89 (21.5%)	2	121 (31.3%)	0	0.002
Mode of arrival (N, %)						
By ambulance	490 (62.5%)	260 (64.5%)	12	230 (60.4%)	5	0.24

COPD: chronic obstructive pulmonary disease; IQR: interquartile range

Table 2: Clinical features at admission

***** Excludes patients arriving on oxygen

	Total	AANZDEM	Missing data	EuroDEM	Missing data	p value
Vital signs at admission						
SBP (mmHg), (median [IQR)	140 [120-156]	139 [120-157]	13	140 [120-155]	6	0.72
SBP<100mmHg (N, %)	22 (2.8%)	9 (2.2%)		13 (3.4%)		0.4
Heart rate (bpm), (median [IQR)	62 [82-110]	99 [84-112]	12	95 [80-109]	8	0.008
Heart rate >120 bpm (N, %)	105 (13.4%)	61 (15.1%)		43 (11.4%)		0.15
Respiratory rate (cycles/min), (median [IQR)	24 [20-28]	25 [22-30]	18	24 [20-28]	69	<0.001
Respiratory rate >30 cycles/min (N, %)	123 (17.3%)	74 (18.6%)		49 (15.5%)		0.31
SpO_2 <90% on air* (N, %)	182 (27.2%)	87 (30.2%)	127	95 (25%)	6	0.19
Temperature <35 or >38° C (N, %)	55 (7.3%)	32 (8.2%)	23	23 (6.4%)	29	0.46
pH (N, %)						
Blood gas taken	504 (62.9%)	229 (51.2%)	-	275 (71.2%)	-	<0.001
pH <7.3 (N, %)	66 (8.2%)	38 (9.2%)	-	28 (7.3%)	-	0.4

IQR: interquartile range; SBP: systolic blood pressure, SpO_2: arterial blood oxygen saturation.

Table 3: Management at the ED and outcomes

	Total	AANZDEM	Missing data	EuroDEM	Missing data	p value
Treatment in the ED (N, %)						
Oxygen therapy			4		7	<0.001
Low flow O2 (nasal prongs or Venturi system)	421 (53.3%)	237 (57.2%)		184 (45.5%)		
High flow face mask	119 (15.1%)	33 (8%)		86 (22.7%)		
None	170 (21.5%)	99 (24.1%)		71 (18.7%)		
NIV combined	81 (10.2%)	46 (11.1%)	0	35 (9.2%)	7	0.46
NIV if pH<7.3	40 (60.6%)	22 (57.9%)	0	18 (64.3%)	0	0.79
Mechanical ventilation	6 (0.8%)	4 (1.0%)	0	2 (0.5%)	7	0.76
Inhaled Beta-2 agonists	636 (79.4%)	332 (80.4%)	2	294 (78.4%)	11	0.55
Inhaled anticholinergic	423 (54.1%)	226 (54.7%)	2	197 (53.4%)	17	1
Inhaled bronchodilator (Beta- 2 agonist, anticholinergic or both)	633 (80.3%)	332 (80.4%)	2	301 (80.2%)	11	1
Corticosteroids (IV or oral)	463 (59.5%)	271 (65.3%)	2	192 (52.6%)	21	<0.001
Antibiotics	347 (44%)	200 (48.5%)	3	147 (40.2%)	20	0.02
Discharge from the ED (N, %)						

Home	211 (26.4%)	80 (19.3%)	0	131 (34%)	1	p<0.001#
Ward (including transfer for admission)	543 (67.9%)	306 (73.7%)	0	237 (61.6%)	1	
Intensive care unit	44 (5.5%)	28 (6.7%)	0	16 (4.2%)	1	
Death in ED	2 (0.2%)	1 (0.1%)	0	1 (0.3%)	1	
In hospital outcome (N, %)						
Mortality	32 (4.2%)	16 (3.9%)	0	16 (4.5%)	33	0.77

ED: emergency department, CPAP: continuous positive airway pressure, BiPAP: bilevel positive airway pressure, NIV: non-invasive ventilation, IV: intravenous. * Fisher's exact test # Omnibus chi square