

# Management of acute exacerbations of COPD in the ICU: an observational study from the OUTCOMEREA database, 1997-2018.

## Supplemental digital content.

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**eTable 1. Patient characteristics at admission to the ICU. Supplemental data.**

Periods	1997-2002	2003-2007	2008-2012	2013-2018
N	284	435	639	458
	Median [Q1; Q3] or N (Percentage)	Median [Q1; Q3] or N (Percentage)	Median [Q1; Q3] or N (Percentage)	Median [Q1; Q3] or N (Percentage)
<b>Characteristics of the AECOPD population</b>				
Non-pulmonary SOFA score Day-1	2 [1; 4]	1 [0; 3]	2 [0; 4]	2 [0; 4]
Non-pulmonary SOFA score Day-2	2 [0.5; 3.5]	1 [0; 3]	2 [1; 4]	1 [0; 4]
<b>Blood gases at admission to Intensive Care Unit</b>				
pH	7.32 [7.26; 7.38]	7.34 [7.27; 7.41]	7.32 [7.25; 7.4]	7.37 [7.3; 7.4]
PaCO <sub>2</sub> (mmHg)	61 [46.5; 76.5]	55.4 [43; 71.8]	54.1 [42.5; 72]	54.9 [42; 70]
PaO <sub>2</sub> (mmHg)	79.5 [59.2; 135.5]	76 [63; 110]	77.1 [62.2; 106.5]	72 [61; 92]
HCO <sub>3</sub> <sup>-</sup> (mmHg)	28 [25; 31]	28.5 [25; 33]	27 [23; 32.5]	29 [24; 35]
<b>Severity of airflow limitation (n=436)</b>				
FEV1 (% of expected value)	34.5 [27; 40.5]	41 [31; 50]	40 [30; 54]	39 [27; 54]
GOLD 1, number (%)	0 (0)	1 (1.1)	4 (2.2)	5 (3.7)
GOLD 2, number (%)	2 (7.1)	22 (24.2)	58 (31.7)	43 (32.1)
GOLD 3, number (%)	17 (60.7)	49 (53.8)	72 (39.3)	45 (33.6)
GOLD 4, number (%)	9 (32.1)	19 (20.9)	49 (26.8)	41 (30.6)
<b>Survival of patients with limitation of therapeutic effort in ICU</b>				
Overall mortality of patients with limitation of therapeutic effort in ICU, number (%)	43 (62.3)	39 (42.4)	82 (58.6)	37 (52.9)
Mortality in ICU of patients with limitation of therapeutic effort in ICU, number (%)	29 (72.5)	33 (58.9)	64 (67.4)	26 (56.5)
Mortality in hospital post-ICU of patients with limitation of therapeutic effort in ICU, number (%)	14 (48.3)	6 (16.7)	18 (40)	11 (45.8)
<b>Decision to limit of therapeutic effort</b>				
Limitation of therapeutic effort during stay in ICU, number (%)	59 (20.8)	61 (14)	131 (20.5)	59 (12.9)
Limitation of therapeutic effort on admission, number (%)	20 (7)	36 (8.3)	69 (10.8)	30 (6.5)

**Abbreviations:** SOFA Score, Sequential Organ Failure Assessment Score; ICU, Intensive Care Unit;

FEV1, forced expiratory volume in 1second; GOLD, Global Initiative for Chronic Obstructive Lung Disease.



**eTable 2. Ventilatory support.**

	Median [Q1; Q3] or N (Percentage)
<b>All types of ventilatory support in ICU, number (%)</b>	1474 (81.2)
<b>Non-Invasive Ventilation in ICU, number (%)</b>	1070 (58.9)
NIV in first intention, number (%)	878 (82.1)
NIV at admission, number (%)	855 (79.9)
Failure of NIV, number (%)	205 (19.2)
Decision to limit therapeutic effort, number (%)	187 (17.5)
Decision to limit therapeutic effort, at admission, number (%)	103 (9.6)
NIV duration (days)	3 [2; 5]
<i>Among patients with NIV in ICU and alive at discharge from ICU (n=961)</i>	
NIV at discharge, number (%)	393 (40.9)
<b>Invasive Mechanical Ventilation in ICU, number (%)</b>	772 (42.5)
IMV at admission, number (%)	649 (84.1)
IMV after failure of NIV, number (%)	176 (22.8)
Tracheostomy for IMV weaning, number (%)	56 (7.2)
IMV duration (days)	8 [4; 16]
<i>Among patients alive at weaning from IMV (n= 623)</i>	
IMV duration (days)	8 [4; 16]
NIV after weaning from IMV, number (%)	223 (35.8)

**Abbreviations:** ICU, Intensive Care Unit; NIV, Non-Invasive Ventilation; IMV, Invasive Mechanical Ventilation



**eTable 3. Non-invasive ventilation for AECOPD in the ICU.**

	Median [Q1; Q3] or N(Percentage)
<b>NIV in first intention</b>	878 (48.3)
NIV initiated at admission, number (%)	848 (96.6)
Failure of NIV, number (%)	205 (23.3)
Patients with decision to limit therapeutic effort, number (%)	151 (17.2)
Patients with decision to limit therapeutic effort, at admission, number (%)	87 (9.9)
<b>NIV as the unique ventilatory support used in ICU</b>	702 (38.7)
NIV at admission, number (%)	680 (96.9)
Failure of NIV, number (%)	29 (4.1)
Patients with decision to limit therapeutic effort, number (%)	104 (14.8)
Patients with decision to limit therapeutic effort, at admission, number (%)	74 (10.5)
<b>NIV duration</b>	
Patients with NIV in ICU (days) (n=1070)	3 [2; 5]
Ratio NIV duration / LOS in ICU for patients with NIV in ICU (%)	56.0
Patients with NIV, alive at discharge from ICU (days) (n=961)	3 [2; 5]
Ratio NIV duration / LOS in ICU for patients with NIV in ICU, alive at discharge from ICU (%)	56.6
Patients with NIV as the unique ventilatory support in ICU (days) (n=702)	3 [2; 5]
Ratio NIV duration / LOS in ICU for patients with NIV as the unique ventilatory support in ICU (%)	71.4
Patients with NIV as the unique ventilatory support in ICU, alive at discharge from ICU (days) (n=657)	3 [2; 5]
Ratio NIV duration / LOS in ICU for patients with NIV as unique ventilatory support in ICU, alive at discharge from ICU (%)	70.5

**Abbreviations:** ICU, Intensive Care Unit; NIV, Non-Invasive Ventilation; LOS, Length of Stay.



**eTable 4. Evolution in characteristics of the population and outcomes by year.**

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017/2018
N	58	49	47	59	26	45	41	61	55	131	147	178	145	102	99	115	171	110	69	58	50
<b>POPULATION</b>																					
Age (years), median [Q1; Q3]	69.9 [64.0; 76.0]	71.3 [66.2; 79.7]	72.7 [64.0; 76.7]	71.0 [62.8; 77.3]	71.9 [66.4; 75.8]	68.7 [62.0; 79.9]	72.6 [67.2; 77.1]	74.9 [65.0; 79.1]	71.0 [62.9; 76.9]	71.4 [61.7; 79.6]	70.3 [57.9; 77.3]	73.0 [61.9; 79.1]	67.1 [59.4; 76.4]	70.4 [61.8; 78.8]	71.0 [61.1; 76.4]	71.8 [64.2; 79.4]	66.2 [60.7; 76.2]	68.7 [60.8; 78.3]	71.0 [62.6; 77.0]	66.0 [57.2; 74.3]	70.1 [61.7; 75.9]
Male, number (%)	34 (58.6)	33 (67.3)	27 (57.4)	38 (64.4)	14 (53.8)	26 (57.8)	23 (56.1)	40 (65.6)	37 (67.3)	89 (66.4)	95 (64.6)	113 (63.5)	96 (66.2)	62 (60.8)	65 (65.7)	73 (63.5)	119 (69.6)	68 (61.8)	42 (60.9)	41 (70.7)	32 (64.0)
Glasgow Score Scale at admission, Median [Q1; Q3]	15 [15; 15]	15 [15; 15]	15 [15; 15]	15 [15; 15]	14 [8; 15]	15 [14; 15]	15 [14; 15]	15 [13; 15]	15 [13; 15]	15 [13; 15]	15 [14; 15]	15 [12; 15]	15 [13; 15]	14 [9; 15]	15 [12; 15]	14 [12; 15]	15 [11; 15]	15 [14; 15]	15 [12; 15]	15 [14; 15]	15 [11; 15]
SAPS II, median [Q1; Q3]	36.5 [28; 46]	40 [31; 54]	41 [29; 48]	33 [26; 41]	36.5 [24; 55]	34 [28; 43]	35 [28; 43]	34 [29; 46]	32 [24; 45]	39 [29; 46]	34 [25; 44]	37.5 [30; 48]	36 [28; 49]	40 [32; 54]	37 [29; 52]	37 [29; 48]	37 [29; 50]	38 [26; 50]	43 [34; 54]	32.5 [26; 48]	39.5 [26; 47]
N Body mass index, n=1420	58	49	47	56	23	38	36	54	30	72	107	130	108	77	75	99	99	95	66	53	48
Body mass index (BMI) (kg/m2), Median [Q1; Q3]	22.5 [20.3; 28.3]	24.7 [21.5; 29.1]	24.9 [19.5; 28.5]	25.3 [22.9; 29.5]	25.4 [21.3; 32.7]	23.8 [20.3; 32.7]	23.2 [20.4; 27.5]	22.7 [19.1; 27.3]	26.2 [22.3; 31.2]	25.5 [22.9; 29.5]	26.3 [22.1; 31.2]	26.0 [21.7; 31.1]	24.6 [22.0; 28.3]	24.9 [21.3; 29.6]	25.1 [21.4; 30.2]	26.0 [21.9; 30.7]	24.9 [20.8; 31.5]	25.4 [21.0; 29.5]	23.6 [19.5; 28.9]	26.4 [22.6; 32.5]	26.2 [21.3; 31.4]
<b>CENTERS</b>																					
Participating enters by year, number	4	4	4	5	5	8	8	8	7	6	10	8	8	6	10	6	8	7	6	10	12
Inclusion by center (n=32 centers), median [Q1; Q3]	13.5 [6.5; 22.5]	12 [5; 19.5]	10 [1.5; 22]	5 [4; 18]	3 [3; 6]	4 [2; 7]	2.5 [2; 5.5]	2.5 [1; 9]	6 [1; 14]	19 [4; 22]	10.5 [1; 26]	17.5 [5.5; 37.5]	6.5 [4; 27.5]	6 [4; 35]	5.5 [3; 9]	16 [10; 22]	10.5 [5; 32.5]	6 [3; 35]	7.5 [1; 20]	3.5 [1; 7]	3 [2; 6]
<b>LENGTH OF STAY, MORTALITY AND LIMITATION OF THERAPEUTIC EFFORT</b>																					
ICU length of stay (days), median [Q1; Q3]	9 [6; 15]	9 [6; 27]	9 [6; 18]	6 [4; 12]	6.5 [4; 9]	8 [5; 14]	9 [6; 13]	7 [4; 11]	8 [5; 15]	5 [3; 9]	6 [3; 15]	6 [4; 12]	6 [4; 13]	6.5 [3; 12]	6 [3; 10]	6 [3; 14]	5 [3; 8]	4 [2; 7]	4 [3; 12]	4 [2; 6]	6 [3; 9]
Hospital length of stay (days), median [Q1; Q3]	20.5 [15; 52]	24 [15; 45]	27 [18; 45]	27.5 [14; 57]	20.5 [12; 35]	19 [14; 30]	20 [15; 41]	26 [14; 37.5]	22 [11.5; 29]	21 [11; 33]	22 [12; 39]	19 [11; 32.5]	19 [12; 34]	19 [9; 33]	15 [9; 24]	22.5 [13.5; 40]	14 [8; 23]	14 [8; 20]	14.5 [8; 25]	14.5 [8.5; 23]	14 [8; 19]
Overall mortality, number (%)	17 (29.3)	11 (22.4)	18 (38.3)	8 (13.6)	5 (19.2)	10 (22.2)	13 (31.7)	9 (14.7)	6 (10.9)	32 (24.4)	32 (21.8)	41 (23.0)	31 (21.4)	27 (26.5)	22 (22.2)	19 (16.5)	28 (16.4)	18 (16.4)	17 (24.6)	3 (5.2)	4 (8.0)
Mortality in ICU, number (%)	10 (17.2)	6 (12.2)	10 (21.3)	3 (5.1)	4 (15.4)	7 (15.6)	8 (19.5)	8 (13.1)	5 (9.1)	17 (13.0)	18 (12.2)	32 (18.0)	17 (11.7)	20 (19.6)	13 (13.1)	13 (11.3)	20 (11.7)	11 (10.0)	11 (15.9)	2 (3.4)	2 (4.0)
Mortality in hospital post-ICU, number (%)	7 (12.1)	5 (10.2)	8 (17.0)	5 (8.5)	1 (3.8)	3 (6.7)	5 (12.2)	1 (1.6)	1 (1.8)	15 (11.4)	14 (9.5)	9 (5.1)	14 (9.7)	7 (6.9)	9 (9.1)	6 (5.2)	8 (4.7)	7 (6.4)	6 (8.7)	1 (1.72)	2 (4.0)
Limitation of therapeutic effort, during stay in ICU, number (%)	11 (19.0)	10 (20.4)	13 (27.7)	7 (11.9)	5 (19.2)	13 (28.9)	8 (19.5)	14 (22.9)	2 (3.6)	18 (13.7)	19 (12.9)	29 (16.3)	31 (21.4)	30 (29.4)	22 (22.2)	19 (16.5)	17 (9.9)	13 (11.8)	20 (29.0)	4 (6.9)	5 (10.0)
Limitation of therapeutic effort at admission, number (%)	1 (1.7)	2 (4.1)	1 (2.1)	5 (8.5)	2 (7.7)	9 (20.0)	6 (14.6)	13 (21.3)	1 (1.8)	9 (6.9)	7 (4.8)	14 (7.9)	17 (11.7)	18 (17.6)	14 (14.1)	6 (5.2)	6 (3.5)	8 (7.3)	11 (15.9)	2 (3.4)	3 (6.0)
<b>BLOOD GASES AT ADMISSION TO ICU</b>																					
pH, median [Q1; Q3]	7.32 [7.29; 7.41]	7.29 [7.24; 7.35]	7.29 [7.21; 7.37]	7.35 [7.28; 7.41]	7.32 [7.29; 7.40]	7.33 [7.25; 7.37]	7.37 [7.28; 7.44]	7.32 [7.26; 7.39]	7.35 [7.28; 7.42]	7.34 [7.26; 7.41]	7.34 [7.26; 7.40]	7.31 [7.25; 7.38]	7.33 [7.25; 7.40]	7.34 [7.25; 7.41]	7.32 [7.21; 7.40]	7.31 [7.25; 7.38]	7.37 [7.29; 7.43]	7.37 [7.27; 7.43]	7.37 [7.30; 7.42]	7.39 [7.32; 7.45]	7.33 [7.26; 7.42]
PaCO <sub>2</sub> (mmHg), median [Q1; Q3]	62.5 [48; 77.0]	64.5 [55.0; 77.0]	61.0 [43.0; 78.0]	54.0 [45.0; 70.0]	59.1 [43.0; 80.0]	60.5 [45.8; 74.5]	48.0 [38.0; 63.0]	51.5 [43.0; 73.0]	56.0 [40.5; 69.0]	57.6 [43.0; 74.9]	55.9 [45.0; 71.0]	56.3 [45.0; 76.0]	54.0 [40.8; 69.6]	49.5 [40.1; 70.0]	54.4 [42.1; 76.3]	53.0 [43.0; 66.0]	57.0 [42.8; 70.5]	53.0 [39.0; 68.0]	51.0 [41.0; 63.0]	50.5 [41.5; 65.0]	58.5 [46.5; 75.0]



PaO <sub>2</sub> (mmHg), median [Q1; Q3]	72.0 [57.0;125.0]	75.0 [56.0; 115.0]	95.0 [69.0; 158.0]	75.0 [55.0; 134.0]	78.0 [61.0; 143.3]	86.5 [70.0; 135.5]	88.0 [66.0; 120.0]	75.0 [60.0; 102.8]	81.0 [64.0; 109.0]	73.0 [60.2; 100.0]	77.9 [65.5; 117.0]	76.9 [61.4; 106.0]	81.3 [60.6; 114.0]	78.0 [66.7; 105.2]	77.0 [63.4; 109.0]	74.0 [62.0; 101.0]	73.0 [64.0; 93.0]	70.0 [60.0; 91.0]	72.0 [58.0; 93.0]	75.5 [64.0; 88.5]	69.0 [56.0; 92.5]
HCO <sub>3</sub> <sup>-</sup> (mmHg), median [Q1; Q3]	28.0 [26.0; 30.0]	28.0 [26.0; 29.0]	27.0 [24.0; 29.0]	27.5 [24.0; 31.0]	31.0 [27.0; 38.0]	28.5 [24.0; 34.0]	27.0 [25.0; 31.0]	27.0 [22.5; 30.7]	29.0 [24.0; 34.0]	29.0 [25.7; 34.5]	29.0 [25.0; 33.0]	28.0 [24.0; 34.3]	27.0 [23.0; 31.0]	26.25 [23.0; 32.5]	27.0 [24.0; 33.0]	26.0 [22.0; 31.0]	30.0 [25.0; 37.0]	28.0 [23.0; 35.0]	27.0 [23.6; 33.0]	27.9 [24.0; 34.2]	32.0 [26.9; 36.0]

**Abbreviations:** BMI, Body Mass Index; ICU, Intensive Care Unit; SAPS II Score, Simplified Acute Physiology Score (SAPS) II.



**eTable 5. Evolution of pharmacological therapy for AECOPD.**

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017/2018
N	58	49	47	59	26	45	41	61	55	131	147	178	145	102	99	115	171	110	69	58	50
CORTICOSTEROID THERAPY																					
Corticosteroid therapy in ICU, number (%)	33 (56.9)	18 (36.7)	19 (40.4)	32 (54.2)	9 (34.6)	19 (42.2)	23 (56.1)	30 (49.2)	21 (38.2)	36 (27.5)	72 (49.0)	89 (50.0)	72 (49.7)	57 (55.9)	47 (47.5)	56 (48.7)	68 (38.8)	34 (30.9)	19 (27.5)	10 (17.2)	21 (42.0)
Patients with corticosteroid therapy in ICU and length of stay in ICU ≥ 7 days (n= 432), number																					
Duration of corticosteroid therapy (days), median [Q1; Q3]	7 [5; 14]	9.5 [8; 17]	6 [3; 11]	8 [6; 10]	7 [7; 8]	8.5 [6; 13]	8 [7; 11]	7 [6; 12]	6.5 [3; 9.5]	13 [6; 15]	7.5 [5; 12]	7 [4; 12]	9.5 [5; 12]	8 [5; 12]	4.5 [3.5; 13.5]	9 [5; 14]	7 [5; 10]	6 [4; 9]	6 [4; 8]	6 [3; 9]	7 [4; 9.5]
Duration of corticosteroid therapy > 5 days, number (%)	15 (68.2)	9 (90.0)	8 (61.5)	9 (75.0)	5 (100.0)	8 (80.0)	15 (88.2)	15 (79.0)	9 (56.2)	13 (76.5)	34 (73.9)	31 (59.6)	24 (70.6)	24 (72.7)	8 (40.0)	22 (73.3)	25 (73.5)	9 (60.0)	7 (53.8)	1 (50.0)	8 (66.7)
ANTIBIOTIC THERAPY																					
Antibiotic therapy in ICU, number (%)	49 (84.5)	40 (81.6)	40 (85.1)	49 (83.0)	19 (73.1)	42 (93.3)	30 (73.2)	42 (68.8)	44 (80.0)	92 (70.2)	122 (83.0)	142 (79.8)	112 (77.2)	74 (72.5)	72 (72.7)	93 (80.9)	137 (80.1)	79 (71.8)	55 (79.7)	30 (51.7)	26 (52.0)
Patients with Antibiotic therapy in ICU and length of stay in ICU ≥ 7 days (n= 741)																					
Duration of antibiotic therapy (days), median [Q1; Q3] and length of stay in ICU ≥ 7 days (n= 741)	10 [7; 16]	16 [8; 25]	8 [7; 15]	9.5 [7; 19]	8.5 [6; 15.5]	10 [8; 18]	9 [7; 14]	9 [7; 14]	9 [6; 11]	8 [6; 14]	12 [8; 18]	9 [6; 15]	8 [6; 12]	10.5 [7; 18]	9 [7; 12]	9.5 [7; 17]	8 [6; 13]	7.5 [5; 11]	8 [7; 12]	8 [7; 12]	8 [7; 10]

**Abbreviations:** ICU, Intensive Care Unit.



**eTable 6. Evolution of ventilatory support used for AECOPD.**

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017/2018
N	58	49	47	59	26	45	41	61	55	131	147	178	145	102	99	115	171	110	69	58	50
<b>Ventilatory support</b>																					
All types of ventilatory support in ICU, number (%)	43 (74.1)	32 (65.3)	40 (85.1)	42 (71.2)	22 (84.6)	41 (91.1)	34 (82.9)	53 (86.9)	45 (81.8)	111 (84.8)	118 (80.3)	144 (80.9)	128 (88.3)	85 (83.3)	85 (85.9)	101 (87.8)	132 (77.2)	79 (71.8)	62 (89.9)	39 (67.2)	38 (76.0)
<b>NIV in ICU, number (%) (n=1070)</b>	25 (43.1)	19 (38.8)	24 (51.1)	29 (49.1)	11 (42.3)	31 (68.9)	23 (56.1)	32 (52.4)	28 (50.9)	90 (68.7)	90 (61.2)	104 (58.4)	86 (59.3)	61 (59.8)	66 (66.7)	74 (64.3)	99 (57.9)	71 (64.5)	49 (71.0)	28 (48.3)	30 (60.0)
NIV in first intention, number (%)	20 (80.0)	15 (79.0)	19 (79.2)	22 (75.9)	9 (81.8)	27 (87.1)	19 (82.6)	30 (93.7)	25 (89.3)	81 (90.0)	76 (84.4)	87 (83.6)	75 (87.2)	43 (70.5)	52 (78.8)	56 (75.7)	80 (80.8)	60 (84.5)	38 (77.5)	21 (75.0)	23 (76.7)
NIV at admission, number (%)	18 (72.0)	14 (73.7)	16 (66.7)	23 (79.3)	8 (72.7)	26 (83.9)	17 (73.9)	28 (87.5)	24 (85.7)	79 (87.8)	76 (84.4)	84 (80.8)	74 (86.0)	42 (68.8)	51 (77.3)	53 (71.6)	80 (80.8)	59 (83.1)	39 (79.6)	22 (78.6)	22 (73.3)
Failure of NIV, number (%)	9 (36.0)	3 (15.8)	8 (33.3)	5 (17.2)	2 (18.2)	12 (38.7)	6 (26.1)	7 (21.9)	2 (7.1)	19 (21.1)	25 (27.8)	22 (21.1)	14 (16.3)	6 (9.8)	9 (13.6)	15 (20.3)	14 (14.1)	13 (18.3)	11 (22.4)	1 (3.6)	2 (6.7)
Patients with decision of limitation of therapeutic effort, number (%)	3 (12.0)	2 (10.5)	7 (29.2)	3 (10.3)	2 (18.2)	12 (38.7)	5 (21.7)	9 (28.1)	0 (0)	13 (14.4)	13 (14.4)	17 (16.3)	14 (16.3)	18 (29.5)	15 (22.7)	14 (18.9)	10 (10.1)	10 (14.1)	13 (26.5)	2 (7.1)	5 (16.7)
Patients with decision of limitation of therapeutic effort at admission, number (%)	0 (0)	0 (0)	1 (4.2)	2 (6.9)	1 (9.1)	9 (29.0)	3 (13.0)	9 (28.1)	0 (0)	6 (6.7)	6 (6.7)	9 (8.6)	8 (9.3)	13 (21.3)	9 (13.6)	5 (6.8)	3 (3.0)	7 (9.9)	8 (16.3)	1 (3.6)	3 (10.0)
<b>NIV in first intention, number (%) (n=878)</b>	20 (34.5)	16 (30.6)	19 (40.4)	22 (37.3)	9 (34.6)	27 (60.0)	19 (46.3)	30 (49.2)	25 (45.4)	81 (61.8)	76 (51.7)	87 (48.9)	75 (51.7)	43 (42.1)	52 (52.5)	56 (48.7)	81 (46.8)	60 (54.5)	38 (55.1)	21 (36.2)	23 (46.0)
NIV at admission, number (%)	18 (90.0)	14 (93.3)	16 (84.2)	22 (100.0)	8 (88.9)	26 (96.3)	17 (89.5)	28 (93.3)	24 (96.0)	79 (97.5)	76 (100.0)	84 (96.5)	74 (98.7)	41 (95.3)	50 (96.1)	53 (94.6)	79 (98.7)	59 (98.3)	37 (97.4)	21 (100.0)	22 (95.7)
Failure of NIV, number (%)	9 (45.0)	3 (20.0)	8 (42.1)	5 (22.7)	2 (22.2)	12 (44.4)	6 (31.6)	7 (23.3)	2 (8.0)	19 (23.5)	25 (32.9)	22 (25.3)	14 (18.7)	6 (13.9)	9 (17.3)	15 (26.8)	14 (17.5)	13 (21.7)	11 (28.9)	1 (4.8)	2 (8.7)
Patients with decision of limitation of therapeutic effort, number (%)	3 (15.0)	1 (6.7)	6 (31.6)	2 (9.1)	1 (11.1)	8 (29.6)	2 (10.5)	9 (30.0)	0 (0)	12 (14.8)	11 (14.5)	14 (16.1)	12 (16.0)	11 (25.6)	12 (23.1)	10 (17.9)	9 (11.2)	10 (16.7)	12 (31.6)	1 (4.8)	5 (21.7)
Patients with decision of limitation of therapeutic effort at admission, number (%)	0 (0)	0 (0)	1 (5.3)	2 (9.1)	1 (11.1)	5 (18.5)	0 (0.0)	9 (30.0)	0 (0)	6 (7.4)	5 (6.6)	7 (8.0)	8 (10.7)	8 (18.6)	8 (15.4)	5 (8.9)	3 (3.7)	7 (11.7)	8 (21.0)	1 (4.8)	3 (13.0)
<b>NIV as the unique ventilatory support used in ICU, number (%) (n=702)</b>	11 (19.0)	12 (24.5)	12 (24.5)	17 (28.8)	7 (26.9)	15 (33.3)	13 (31.7)	25 (41.0)	23 (41.8)	66 (50.4)	54 (36.7)	69 (38.8)	63 (43.4)	40 (39.2)	44 (44.4)	43 (37.4)	68 (39.8)	48 (43.6)	30 (43.5)	21 (36.2)	21 (42.0)
NIV at admission, number (%)	10 (90.9)	12 (100.0)	11 (91.7)	17 (100.0)	6 (85.7)	14 (93.3)	11 (84.6)	24 (96.0)	22 (95.6)	66 (100.0)	54 (100.0)	66 (95.6)	62 (98.4)	38 (95.0)	42 (95.4)	41 (95.3)	67 (98.5)	47 (97.9)	29 (96.7)	21 (100.0)	20 (95.2)
Failure of NIV, number (%)	0 (0)	0 (0)	1 (8.3)	0 (0)	0 (0)	0 (0)	0 (0)	2 (8.0)	0 (0)	4 (6.1)	3 (5.6)	4 (5.8)	2 (3.2)	3 (7.5)	1 (2.3)	2 (4.6)	2 (2.9)	1 (2.1)	3 (10.0)	1 (4.8)	0 (0)
Patients with decision of limitation of therapeutic effort, number (%)	1 (9.1)	1 (8.3)	3 (25.0)	1 (5.9)	1 (14.3)	4 (26.7)	0 (0)	6 (24.0)	0 (0)	7 (10.6)	5 (9.3)	9 (13.0)	9 (14.3)	11 (27.5)	12 (27.3)	5 (11.6)	7 (10.3)	8 (16.7)	8 (26.7)	1 (4.8)	5 (23.8)
Patients with decision of limitation of therapeutic effort at admission, number (%)	0 (0)	0 (0)	1 (8.3)	1 (5.9)	1 (14.3)	4 (26.7)	0 (0)	6 (24.0)	0 (0)	5 (7.6)	2 (3.7)	7 (10.1)	6 (9.5)	8 (20.0)	8 (18.2)	4 (9.3)	3 (4.4)	7 (14.6)	7 (23.3)	1 (4.8)	3 (14.3)
<b>Length of use of NIV</b>																					
Patients with NIV in ICU (days) (n=1070), median [Q1; Q3]	5 [2; 6]	3 [2; 6]	2.5 [1; 6.5]	3 [2; 5]	5 [3; 7]	3 [2; 6]	5 [3; 7]	3 [2; 6.5]	5 [2; 8]	3 [2; 5]	3 [2; 5]	4 [2; 5]	3 [2; 5]	3 [2; 6]	3 [2; 4]	3 [1; 4]	2 [1; 5]	2 [1; 3]	2 [1; 3]	2 [1; 3]	2.5 [2; 6]
Ratio NIV duration / LOS in ICU for patients with NIV in ICU (%)	40.5	67.4	38.8	49.0	54.6	48.6	51.6	65.0	65.7	68.2	54.5	59.3	66.0	60.00	60.2	51.4	52.8	49.0	50.4	54.1	56.1
Patients with NIV, alive at discharge from ICU (days) (n=961), median [Q1; Q3]	5 [2; 7]	3 [2; 4]	3 [1; 7]	3.5 [2; 5]	5 [3; 7]	3.5 [2; 6]	4.5 [3; 6]	3 [2; 7]	5 [2; 8]	3 [2; 5]	3 [2; 5]	4 [2; 5.5]	3 [2; 5]	3.5 [2; 6]	3 [2; 5]	3 [1; 4]	3 [1; 5]	2 [1; 3]	2 [1; 3]	2 [1; 3]	2 [2; 6]
Ratio NIV duration / LOS in ICU for patients with NIV, alive at discharge from ICU (%)	39.7	34.3	37.7	50.4	54.6	52.3	53.1	65.8	65.7	70.4	57.2	59.6	66.2	61.7	61.6	51.7	53.0	48.5	47.3	52.4	55.3
Patients with NIV as the unique ventilatory support in ICU (days) (n=702), median [Q1; Q3]	5 [3; 7]	3.5 [2; 6]	3.5 [1; 7.5]	4 [2; 5]	3 [1; 5]	3 [2; 5]	5 [3; 6]	3 [2; 6]	6 [2; 10]	3 [2; 5]	3 [2; 5]	4 [2; 5]	3 [2; 5]	4 [2; 6]	2 [2; 3]	3 [2; 5]	3 [1; 5]	2 [1; 3]	2 [1; 3]	2 [1; 3]	4 [2; 6]
Ratio NIV duration / LOS in ICU for patients with NIV as the unique ventilatory support in ICU (%)	64.7	50.3	59.3	65.2	61.4	63.5	62.3	75.6	73.5	81.3	74.5	76.9	79.5	78.9	72.0	74.0	66.0	59.1	63.3	65.2	66.5
Patients with NIV as the unique ventilatory support in ICU, alive at discharge from ICU (days) (n=657), median [Q1; Q3]	5 [3; 7]	3.5 [2; 6]	3.5 [1; 8]	4 [2; 5]	3 [1; 5]	3 [2; 5]	5 [3; 6]	3 [2; 6]	6 [2; 10]	3 [2; 5]	3 [2; 5]	4 [2; 5]	3.5 [2; 5]	4 [2; 6]	2 [2; 3]	3 [2; 5]	3 [1; 5]	2 [1; 3]	2 [1; 3]	2 [1; 3]	3.5 [2; 6]
Ratio NIV duration / LOS in ICU for patients with NIV as unique ventilatory support in ICU, alive at discharge from ICU (%)	64.7	48.0	59.1	65.2	61.4	63.5	62.3	74.6	73.5	80.6	74.0	75.1	79.1	77.9	72.2	72.7	65.5	58.4	59.3	63.5	65.8
<b>NIV at discharge for patients alive at discharge from ICU</b>																					
For patients with NIV in ICU, number (%)	5 (21.7)	2 (11.1)	2 (10.5)	7 (25.0)	5 (45.4)	2 (7.7)	4 (22.2)	12 (44.4)	12 (42.9)	47 (58.7)	29 (37.2)	45 (51.1)	44 (52.4)	31 (62.0)	34 (56.7)	26 (38.9)	35 (38.9)	20 (30.3)	10 (22.7)	10 (37.0)	11 (37.9)
For patients with NIV as the unique ventilatory support in ICU, number (%)	3 (27.3)	1 (9.1)	2 (20.0)	5 (29.4)	3 (42.9)	2 (13.3)	2 (15.4)	12 (54.5)	11 (47.8)	39 (62.9)	23 (45.1)	37 (60.7)	36 (58.1)	22 (62.9)	23 (56.1)	19 (46.3)	29 (46.8)	15 (32.6)	7 (25.9)	8 (40.0)	6 (30.0)
<b>Invasive mechanical ventilation in ICU, number (%) (n=772)</b>	32 (55.2)	20 (40.8)	28 (59.6)	25 (42.4)	15 (57.7)	26 (57.8)	21 (51.2)	28 (45.9)	22 (40.0)	45 (34.3)	64 (43.5)	75 (42.1)	65 (44.8)	45 (44.1)	41 (41.4)	58 (50.4)	64 (37.4)	31 (28.2)	32 (46.4)	18 (31.0)	17 (34.0)



IMV duration (days), median [Q1; Q3]	9 [5; 17.5]	14.5 [7; 25.5]	12 [6; 18.5]	10 [5; 16]	4 [2; 10]	8.5 [4; 18]	10 [5; 12]	7 [4; 14.5]	10 [6; 20]	6 [3; 13]	11 [5; 20]	8 [4; 21]	10 [5; 15]	10 [6; 22]	7 [4; 14]	10 [4; 20]	5.5 [2; 12]	6 [2; 11]	7.5 [3; 12.5]	4.5 [2; 7]	7 [3; 8]
IMV at admission, number (%)	22 (68.7)	16 (80.0)	24 (85.7)	20 (80.0)	14 (93.3)	22 (84.6)	17 (80.9)	26 (92.9)	19 (86.4)	33 (73.3)	46 (71.9)	60 (80.0)	56 (85.1)	43 (95.6)	38 (92.7)	49 (84.5)	57 (89.1)	29 (93.5)	25 (78.1)	18 (100.0)	15 (88.2)
Patients with IMV after failure of NIV, number (%)	9 (28.1)	3 (15.0)	7 (25.0)	5 (20.0)	2 (13.3)	12 (46.1)	6 (28.6)	5 (17.9)	2 (9.1)	15 (33.3)	22 (34.4)	18 (24.0)	12 (18.5)	3 (6.7)	8 (19.5)	13 (22.4)	12 (18.7)	12 (38.7)	8 (25.0)	0 (0.0)	2 (11.8)
Patients underwent tracheostomy, number (%)	7 (21.9)	4 (20.0)	4 (14.3)	3 (12.0)	2 (13.3)	2 (7.7)	0 (0.0)	1 (3.6)	3 (13.6)	2 (4.4)	3 (4.7)	6 (8.0)	6 (9.2)	4 (8.9)	1 (2.4)	4 (6.9)	3 (4.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)
Among patients alive at weaning from IMV (n= 623), number (%)	23 (71.9)	18 (90.0)	21 (75.0)	22 (88.0)	13 (86.7)	24 (92.3)	17 (80.9)	24 (85.7)	17 (77.3)	36 (80.0)	53 (82.8)	55 (73.3)	52 (80.0)	34 (75.6)	33 (80.5)	49 (84.5)	51 (79.7)	23 (74.2)	25 (78.1)	17 (94.4)	16 (94.1)
IMV duration (days), median [Q1; Q3]	8 [5; 20]	14.5 [9; 24]	12 [7; 19]	9.5 [5; 16]	4 [3; 10]	8.5 [4; 17.5]	11 [4; 14]	7 [4; 14.5]	9 [6; 16]	6.5 [3; 12.5]	9 [4; 16]	7 [4; 15]	10 [5; 14.5]	9 [6; 16]	8 [4; 14]	10 [4; 19]	4 [2; 12]	6 [2; 8]	7 [3; 12]	5 [2; 7]	6 [3; 8]
NIV after weaning of IMV, number (%)	4 (17.4)	4 (22.2)	6 (28.6)	8 (36.4)	3 (23.1)	9 (37.5)	3 (17.6)	3 (12.5)	3 (17.6)	14 (38.9)	18 (34.00)	19 (34.5)	14 (26.9)	17 (50.0)	15 (45.4)	19 (38.8)	22 (43.1)	14 (60.9)	14 (56.0)	6 (35.3)	8 (50.0)

**Abbreviations:** ICU, Intensive Care Unit; NIV, Non-Invasive Ventilation; IMV, Invasive Mechanical Ventilation; LOS, Lengths of Stay.



**eTable 7. Evolution of characteristics of the population and outcomes.**

	Variation per year	Standard Error	p-value
<b>Characteristics of the population</b>			
Variation in age (year/year)	-0.09	0.06	0.12
Variation in sex (% of males/year)	0.004	1.12	0.99
Variation in BMI (%/year)	0.32	0.13	0.02
Variation in SAPS II Score (%/year)	0.61	0.22	<.01
Variation in SOFA Score Day-1 (%/year)	0.82	0.36	0.02
<b>COPD characteristics (n=1069)</b>			
Long-term oxygen therapy, number (%)	-4.29	1.92	0.03
Non-Invasive Ventilation at home, number (%)	5.73	3.37	0.09
Very severe COPD (Long-term oxygen therapy and/or GOLD 4), number (%)	-3.37	1.88	0.07
<b>Length of ICU stay</b>			
Variation in LOS in ICU (% /year)	-3.21	0.46	<.01
Variation in LOS in ICU among patients alive at discharge from ICU (%/year)	-3.2	0.46	<.01
Variation in LOS in Hospital (%/year)	-2.6	0.51	<.01
Variation in LOS in Hospital among patients alive at discharge from hospital (%/year)	-2.45	0.54	<.01
<b>Mortality</b>			
Variation in overall hospital mortality (%/year)	-5.81	1.66	<.01
Variation in mortality in ICU (%/year)	-4.09	1.92	0.03
Variation in mortality in hospital post-ICU (%/year)	-4.21	1.76	0.02
Mortality D-28, number (%)	-2	1.52	0.18
Mortality D-90, number (%) (n=1287)	-4.98	2.17	0.02

**Notes:** Variations in length of stay and variation in mortality were adjusted on age, sex, BMI, SAPS Score, decision of limitation of therapeutic effort and severity status of COPD.

**Abbreviations:** BMI, Body Mass Index; SAPS II Score, Simplified Acute Physiology Score II; SOFA Score, Sequential Organ Failure Assessment Score; COPD, Chronic Obstructive Pulmonary Disease; ICU, Intensive Care Unit; LOS, Length of Stay; ICU, Intensive Care Unit.



**eTable 8. Trends in pharmacological therapy.**

	Variation per year	Standard Error	p-value
<b>Corticosteroid Therapy</b>			
Variation in prescription of corticosteroids (%/year)	-4.75	1.18	<.01
Variation in prescription of corticosteroids > 5 days among patients with ICU length of stay $\geq$ 7 days (%/year) (n=432)	-6.01	2.52	0.02
<b>Antibiotic Therapy</b>			
Variation in prescription of antibiotics (%/year)	-5.78	1.37	<.01
Variation in duration of antibiotic therapy among patients with ICU stays in ICU $\geq$ 7 days and given antibiotics (%/year) (n=741)	-1.10	0.43	0.01

**Notes:** Variation in prescription of corticosteroids, in prescription of corticosteroids > 5 days, prescription of antibiotics, in use of NIV at admission to ICU, in failure of NIV, in use of IMV, in use of weaning tracheostomy, in duration on IMV and use of NIV after weaning from IMV were adjusted on age, sex, BMI, SAPS Score, decision to limit therapeutic effort and severity status of COPD.

Variation in duration of antibiotic therapy among patients with ICU stay  $\geq$  7 days and given antibiotics were adjusted on age, sex, BMI, SAPS Score, decision to limit therapeutic effort, severity status of COPD and length of stay in the ICU.

**Abbreviations:** BMI, Body Mass Index; ICU, Intensive Care Unit; NIV, Non-Invasive Ventilation; IMV, Invasive Mechanical Ventilation; LOS, Length of Stay; SAPS II Score, Simplified Acute Physiology Score II. COPD, Chronic Obstructive Pulmonary Disease.



**eTable 9. Trends in ventilation therapy.**

	Variation per year	Standard Error	p-value
Variation in use of all types of ventilation (%/year)	2.61	1.53	0.09
<b>Non-Invasive Ventilation</b>			
Variation in use of NIV (%/year)	5.15	1.16	<.01
<b>Patients with NIV during hospitalization in ICU (n=1070)</b>			
Variation in use of NIV in first-intention in ICU (%/year)	0.45	1.99	0.82
Variation in use of NIV at admission to ICU (%/year)	1.69	1.94	0.38
Variation in failure of NIV (%/year)	-6.21	1.75	<.01
Variation in NIV duration in ICU (%/year)	-2.07	0.56	<.01
<i>Among patients treated with NIV in ICU and alive at ICU discharge (n=961)</i>			
Variation in NIV at discharge from ICU (%/year)	2.05	1.92	0.29
<b>Invasive Mechanical Ventilation</b>			
Variation in use of IMV (%/year)	-3.71	1.34	0.01
<b>Patients with IMV during hospitalization in ICU (n=772)</b>			
Variation in use of tracheostomy (%/year)	-10.2	2.72	<.01
<i>Among patients alive at weaning from IMV (n= 623)</i>			
Variation in IMV duration (%/year)	-3.13	0.93	<.01
Variation of use of NIV after weaning from IMV (%/year)	8.14	2.18	<.01

**Notes:** Variation in use of all types of ventilation, in use of NIV in ICU, in use of NIV in first-intention in ICU, in use of NIV at admission to ICU, in failure of NIV, in use of IMV, in use of weaning tracheostomy, on duration on IMV and use of NIV after weaning from IMV were adjusted on age, sex, BMI, SAPS Score, decision to limit therapeutic effort and severity status of COPD.

Variation in length of use of NIV in ICU among patients with NIV was adjusted on age, sex, BMI, SAPS Score, decision to limit therapeutic effort, severity status of COPD and LOS in ICU.

Variation in use of NIV at discharge from patients with NIV in ICU and alive at discharge from ICU was adjusted on age, sex, BMI, SAPS Score, decision to limit therapeutic effort, severity status of COPD and diagnosis of obstructive sleep apnea.

**Abbreviations:** BMI, Body Mass Index; ICU, Intensive Care Unit; NIV, Non-Invasive Ventilation; IMV, Invasive Mechanical Ventilation; LOS, Length of Stay; SAPS II Score, Simplified Acute Physiology Score II. COPD, Chronic Obstructive Pulmonary Disease.



**eTable 10. Patients with NIV failure by period**

Periods	1997-2002	2003-2007	2008-2012	2013-2018
Patients with Non-Invasive Ventilation in ICU, number	139	263	391	277
NIV failure, number (%)	39 (28.1)	59 (22.4)	66 (16.9)	41 (14.8)
Death in hospital after NIV failure, number (% of NIV failure)	12 (30.8)	31 (52.5)	29 (44.0)	16 (39.0)
Death in ICU after NIV failure, number (% of NIV failure)	9 (23.1)	26 (44.1)	26 (39.4)	13 (31.7)

**Abbreviations:** ICU, Intensive Care Unit; NIV, Non-Invasive Ventilation.

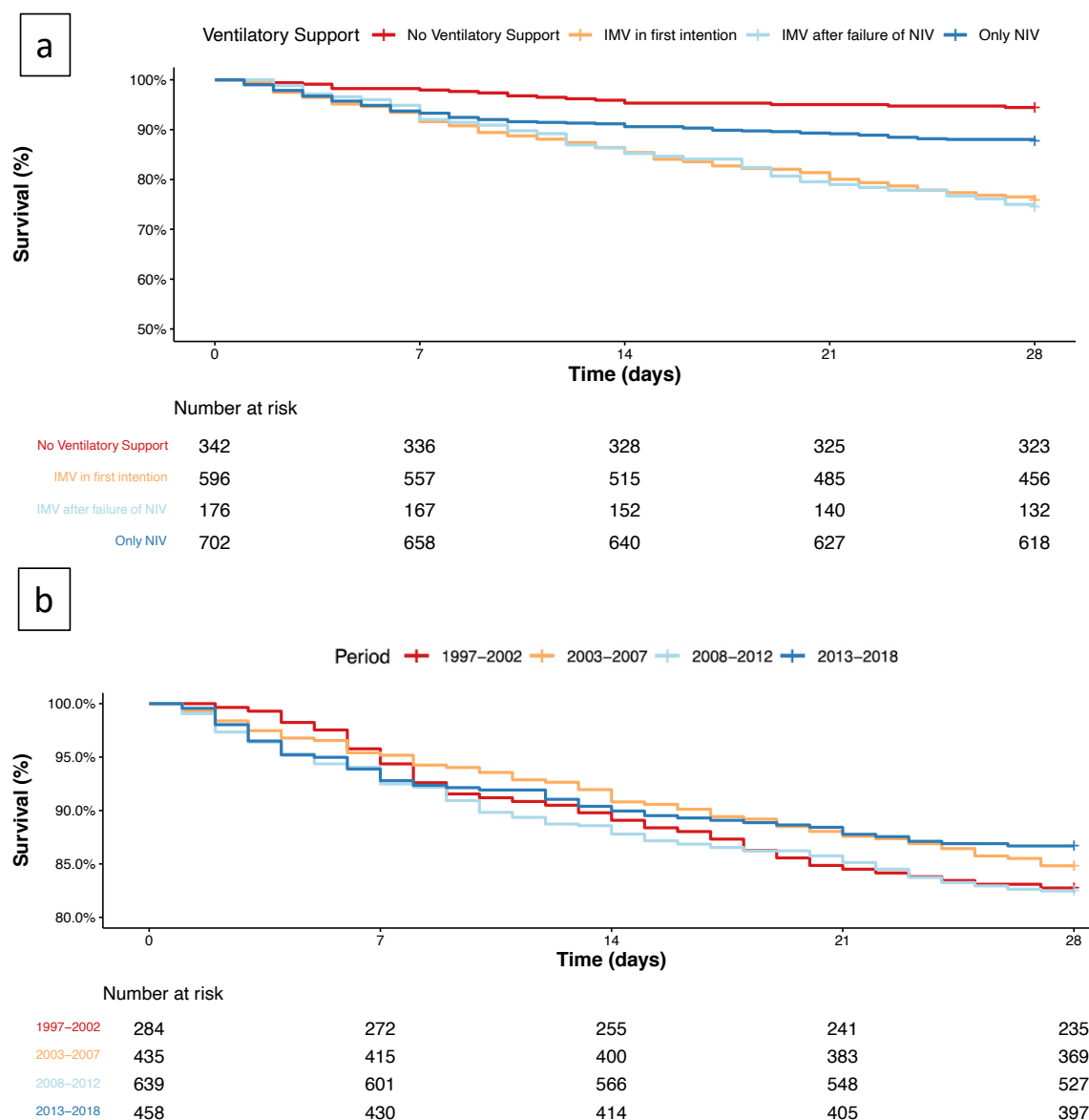
**eTable 11. Evolution in mortality of the population with NIV failure**

	Variation per year	Standard Error	p-value
Variation in overall mortality after NIV failure (%/year)	-4.88	4.33	0.26
Variation in mortality in ICU after NIV failure (%/year)	-3.43	4.38	0.43

**Notes:** Variation in overall mortality after NIV failure and Variation in mortality in ICU after NIV failure are adjusted on age, sex, BMI, SAPS Score, decision to limit therapeutic effort, severity status of COPD and LOS in ICU.

**Abbreviations:** ICU, Intensive Care Unit; NIV, Non-Invasive Ventilation.



**eFigure 1. Survival at day-28****a. Survival at day-28 according to type of ventilatory support**

**Notes:** Log rank test used for survival statistical analysis. No ventilatory support vs. IMV in first intention:  $p < 0.01$ ; No ventilatory support vs. IMV after failure of NIV:  $p < 0.01$ ; No ventilatory support vs. Only NIV:  $p < 0.01$ ; IMV in first intention vs. IMV after failure of NIV:  $p = 0.75$ ; IMV in first intention vs. Only NIV:  $p < 0.01$ ; IMV after failure of NIV vs. Only NIV:  $p < 0.01$ .

Hospital-acquired pneumonia (defined as a diagnosis of pneumonia after more than 24 hours in intensive care) was proportionally more common in patients who received IMV (Incidence of hospital-acquired pneumonia was 3 (0.9%) for no ventilatory support group, 133 (22.3%) for IMV in first intention group, 43 (24.4%) for IMV after failure of NIV group and 4 (0.6%) for Only NIV group. ( $p < .01$ ,  $\chi^2$  test)).

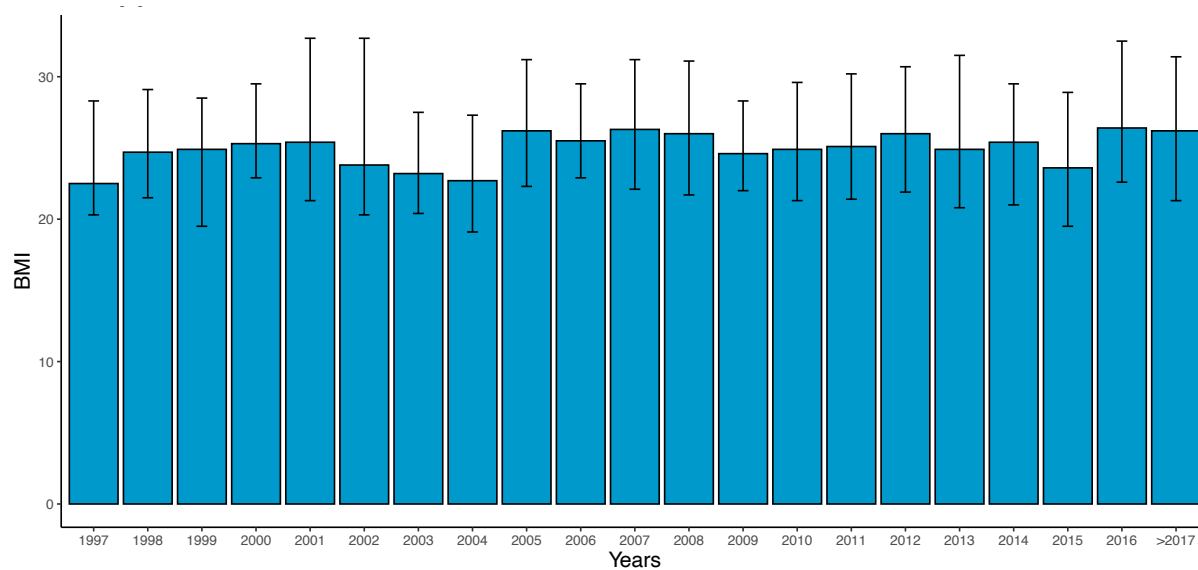
**Abbreviations:** NIV, Non-Invasive Ventilation; IMV, Invasive Mechanical Ventilation.

**b. Survival at day-28 by period**

**Notes:** Log rank test used for survival statistical analysis. Period 1 vs. Period 2:  $p = 0.45$ ; Period 1 vs. Period 3:  $p = 0.87$ ; Period 1 vs. Period 4:  $p = 0.17$ ; Period 2 vs. Period 3:  $p = 0.28$ ; Period 2 vs. Period 4:  $p = 0.49$ ; Period 3 vs. Period 4:  $p = 0.24$ . The variation in mortality 28 days after admission is -2%/year ( $p = 0.18$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort and severity status of COPD.



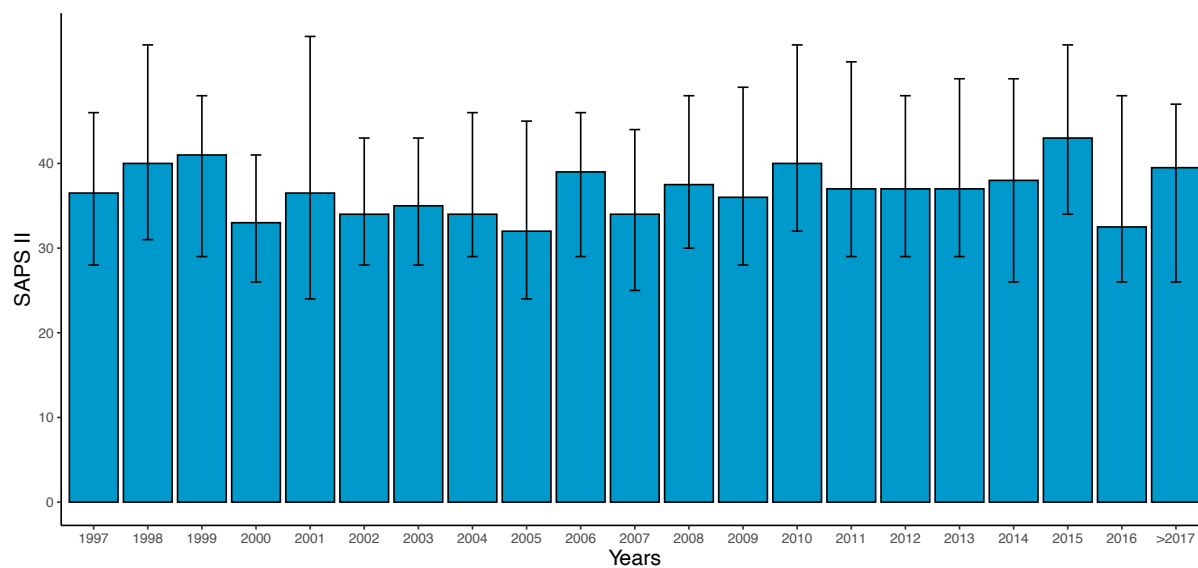
**eFigure 2. BMI of patients with AECOPD in the ICU by year.**



**Notes:** Representation of median and interquartile [Q1; Q3] of BMI in ICU by years. The variation of BMI in the ICU is +0.32%/year ( $p=0.01$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort and severity status of COPD.

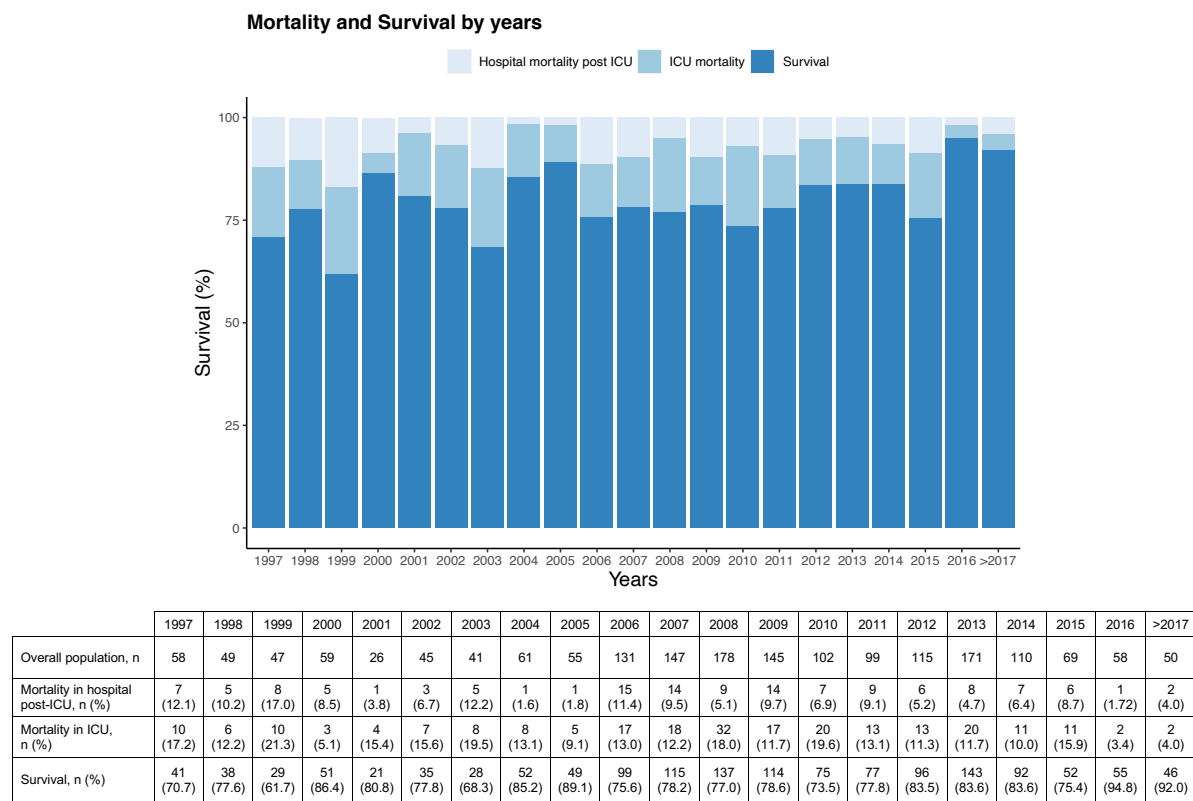


**eFigure 3. SAPS II of patients with AECOPD in the ICU by year.**



**Notes:** Representation of median and interquartile [Q1; Q3] of SAPS II in ICU by years. The variation in SAPS II in ICU was +0.61%/year ( $p < .01$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort and severity status of COPD.

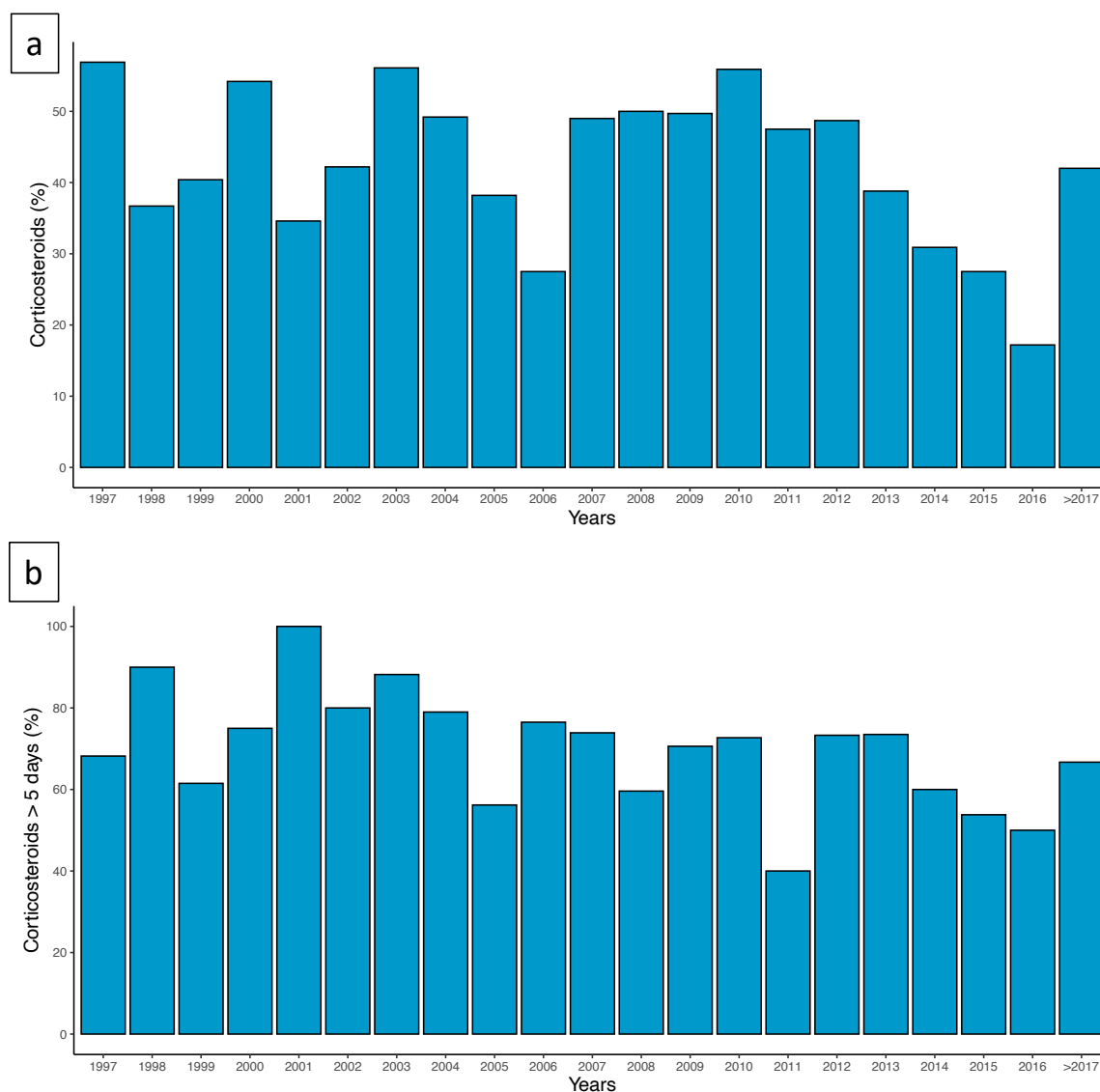


**eFigure 4. Mortality of patients with AECOPD in the ICU by year.**

**Notes:** The variation in ICU mortality is -4.09%/year ( $p=0.03$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort and severity status of COPD. The variation of post-ICU hospital mortality is -4.21%/year ( $p=0.02$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort and severity status of COPD.

**Abbreviation:** ICU, Intensive Care Unit.



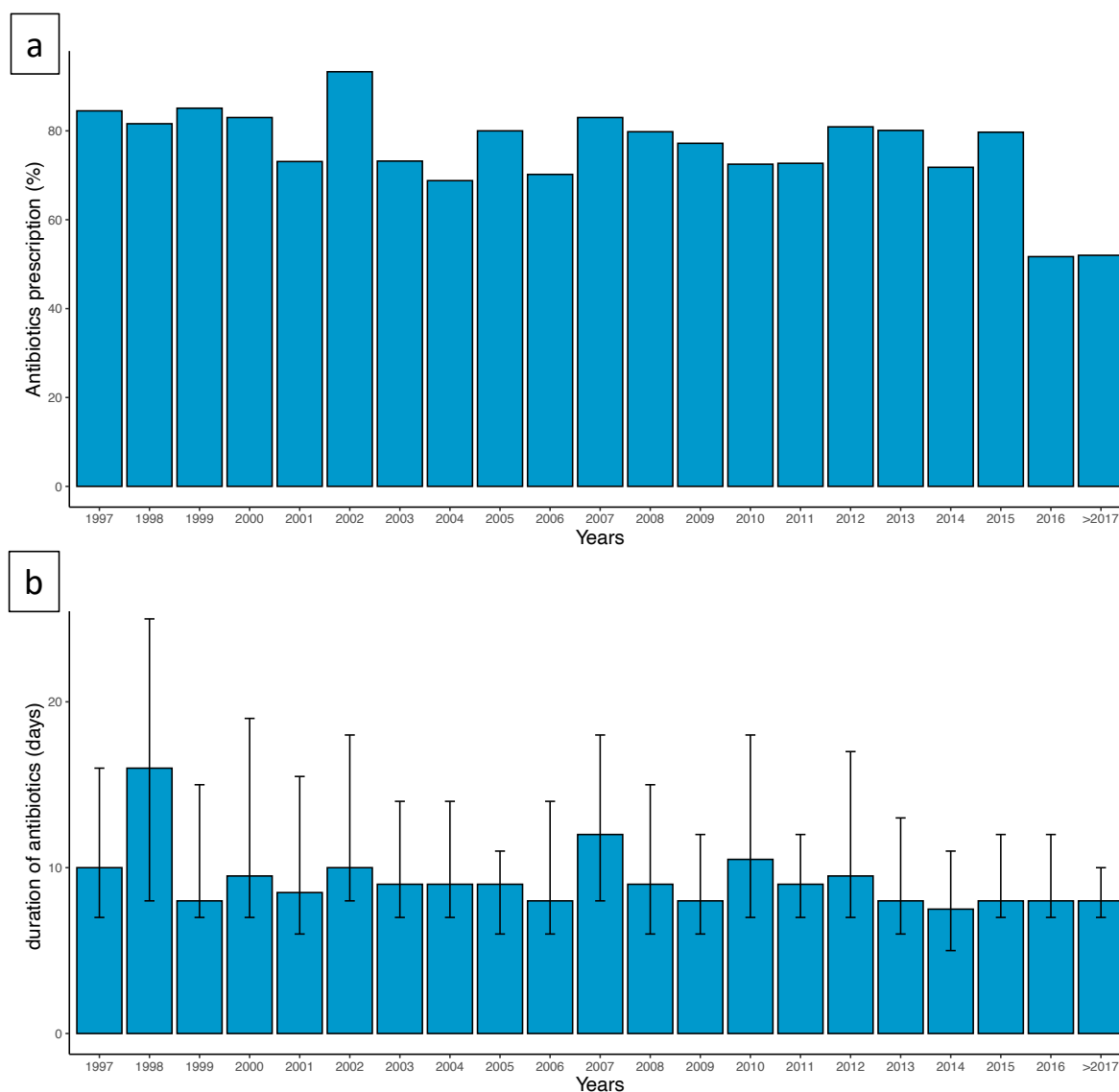
**eFigure 5. Corticosteroids for AECOPD in the ICU by year.****a. Corticosteroid prescriptions for acute exacerbations of COPD in the ICU by year.**

**Notes:** The variation in Corticosteroid prescriptions was  $-4.75\%/year$  ( $p < .01$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort and severity status of COPD.

**b. Corticosteroids prescription > 5 days among patients with ICU length of stay  $\geq 7$  days for acute exacerbations of COPD in the ICU by year.**

**Notes:** The variation in Corticosteroid prescription for > 5 days among patients with ICU length of stay  $\geq 7$  days was  $-6.01\%/year$  ( $p = 0.02$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort and severity status of COPD.



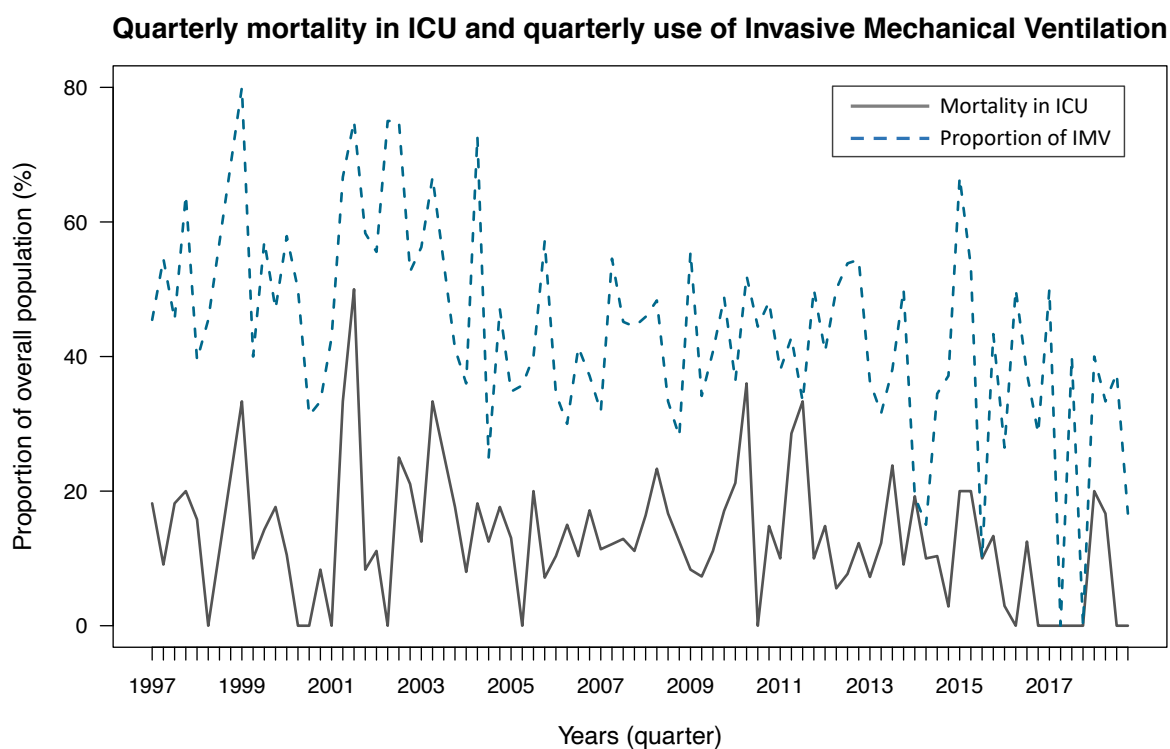
**eFigure 6. Antibiotic prescriptions for AECOPD in the ICU by year.****a. Antibiotic prescriptions for acute exacerbations of COPD in the ICU by year.**

**Notes:** The variation in antibiotic prescriptions was -5.78%/year ( $p < .01$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort and severity status of COPD.

**b. Duration of antibiotic therapy among patients with ICU stays ≥ 7 days and given antibiotics for acute exacerbations of COPD in the ICU by year.**

**Notes:** The variation in duration of antibiotic therapy among patients with ICU stays ≥ 7 days and given antibiotics was -1.1%/year ( $p = 0.01$ ) with an analysis using a mixed model and adjusted on age, BMI, SPAS II Score, decision to limit therapeutic effort, severity status of COPD and length of stay in the ICU in addition to the other adjustments previously specified



**eFigure 7. Mortality and invasive mechanical ventilation**

**Notes:** The quarters when no patient was included are not shown (Q3 1998, Q4 1998, Q3 2003). The time series analysis showed a positive correlation between use of IMV and mortality ( $p < 0.01$ ).

**Abbreviations:** ICU, Intensive Care Unit; NIV, Non-Invasive Ventilation; IMV, Invasive Mechanical Ventilation.



**Definitions of NIV and IMV as first-intention, NIV and IMV at admission, NIV failure and limitation of therapeutic effort are given below:**

NIV as first-intention was defined as the use of NIV as the unique ventilatory support or NIV before the use of IMV.

IMV as first-intention was defined as the use of the IMV without the prior use NIV.

NIV at admission and IMV at admission were defined as the use of one or other of these ventilatory supports during the first day of the patient's ICU stay.

NIV failure was defined as use of IMV after NIV in first-intention or by death despite ongoing non-invasive ventilation in patients receiving only NIV as ventilatory support.

The decision to limit therapeutic effort was defined as a decision by the medical team during hospitalization in the ICU to reduce the invasiveness of therapeutic interventions or to stop therapeutic interventions.

Decision to limit therapeutic effort at admission was defined as a decision to limit therapeutic effort during the first day in the ICU.



### **Statistical analysis. Dynamic regression model - ARIMA model.**

The relationship between quarterly mortality in the ICU and the use of corticosteroids, antibiotics and IMV were assessed using a dynamic regression model. No patients had been included during certain quarters in some years (Q3 1998, Q4 1998, Q3 2003), probably due to inclusion in the cohort and follow-up having only just started and the seasonality of AECOPD (more frequent in the winter). These quarters in which no patient was included were censored for this analysis. In our study, this method consisted of modeling mortality in the ICUs using an ARIMA model and adding use of corticosteroids, antibiotics or invasive mechanical ventilation as explanatory variables through a specific function (called a 'transfer function'). The ARIMA model [1] was designed to model a series over time by identifying the correlation with the past values of the same variable (AR stands for autoregressive) and abrupt changes in the recent past (MA stands for moving average). The model-building process involved three steps: (i) an ARIMA model was fitted to the ICU mortality series, to the use of corticosteroids series, to the use of antibiotics series and to the use of IMV series; (ii) the cross-correlations of the series were estimated to identify any significant and relevant association over time; and (iii) these series were entered in the ICU mortality model using the transfer function in ARIMA (1,1,1). In our case, there was no lag for the occurrence of the potential effect of corticosteroids, antibiotics and IMV on mortality in the ICU. Series stationarity was checked graphically and confirmed by data differencing or transformation. The model yielding the lowest Akaike information criterion was chosen as the best model. Goodness-of-fit was assessed throughout model fitting process using a white noise test of residuals and cross-correlation check of residuals.

1. Nelson BK. Statistical methodology: V. Time series analysis using autoregressive integrated moving average (ARIMA) models. Acad. Emerg. Med. Off. J. Soc. Acad. Emerg. Med. 1998; 5: 739–744.



## **Appendix**

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