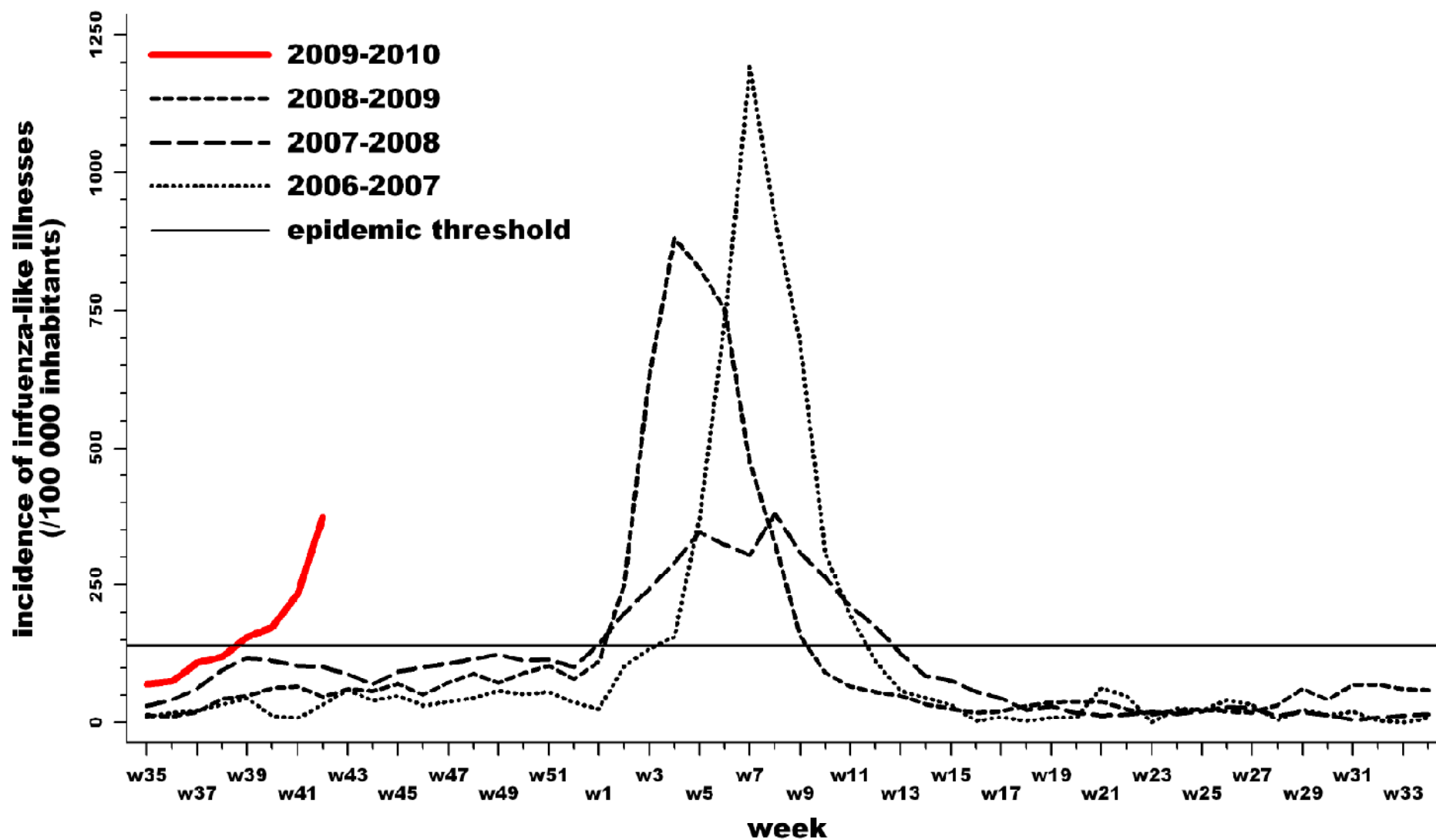
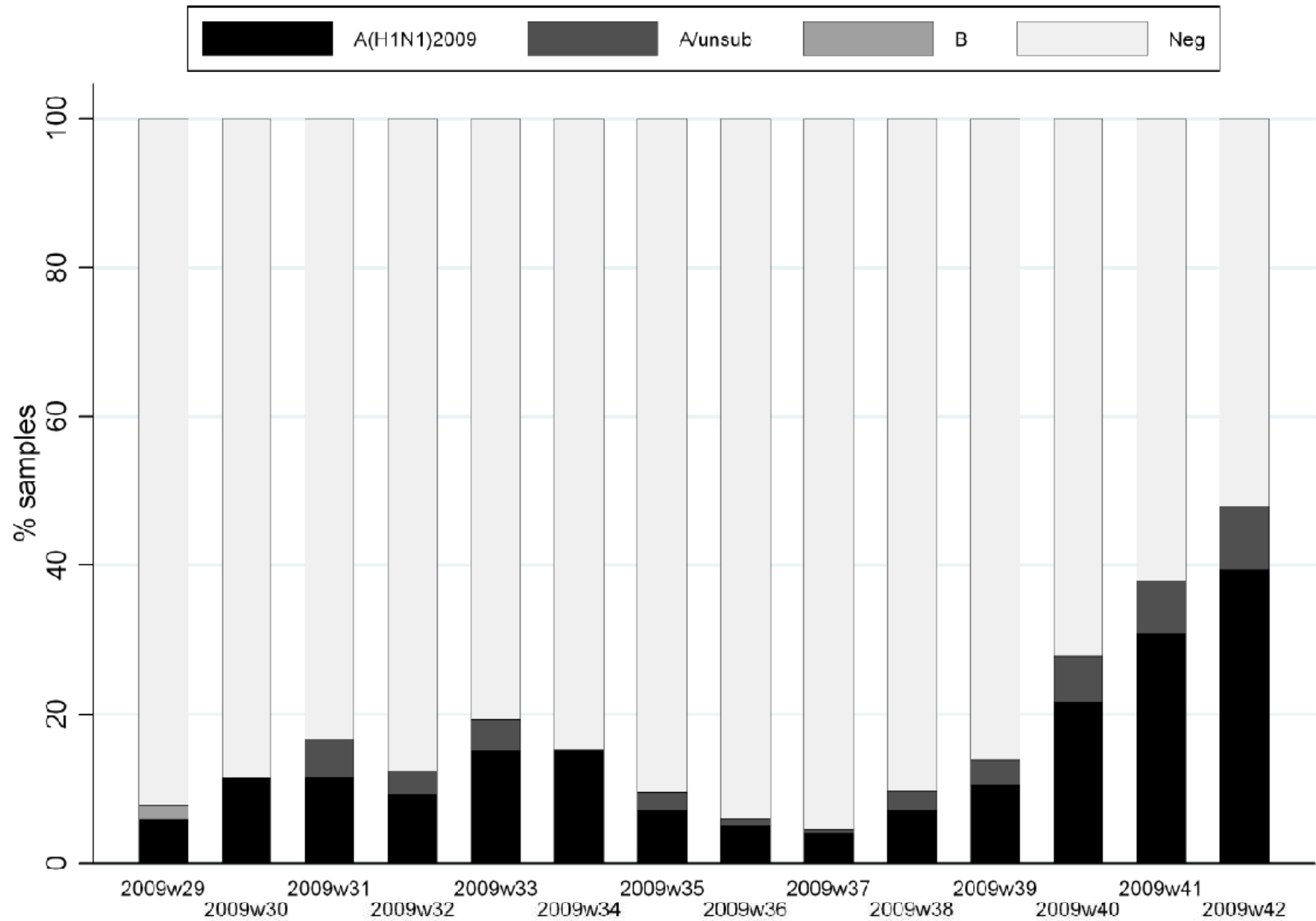


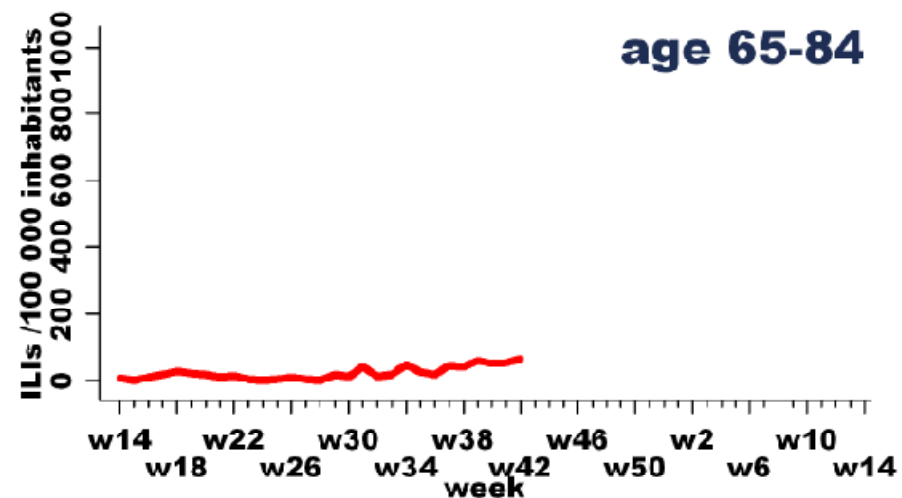
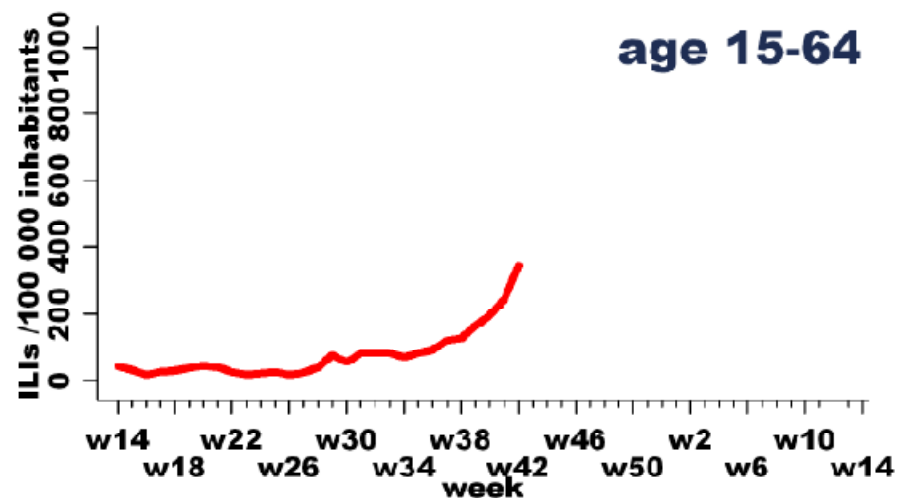
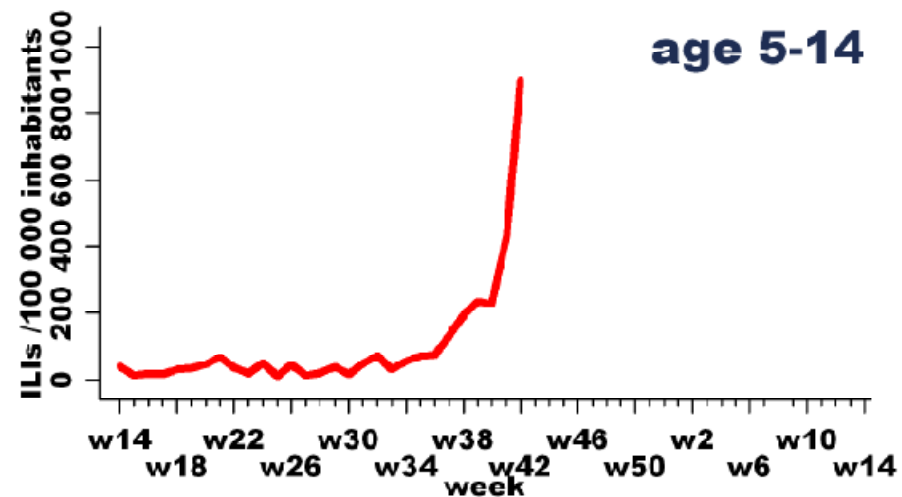
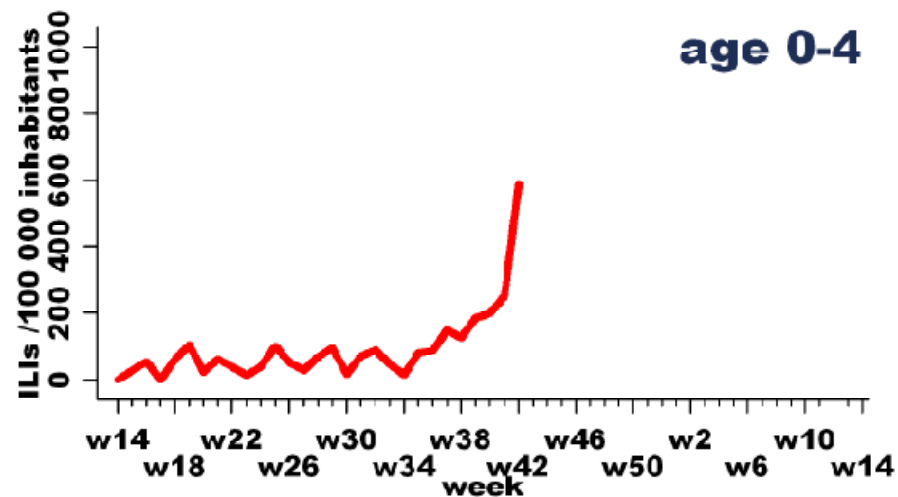
H1N1: SPECIFICITIES IN CRITICALLY ILL PATIENTS

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Last update week 42 (OCT 12-18)

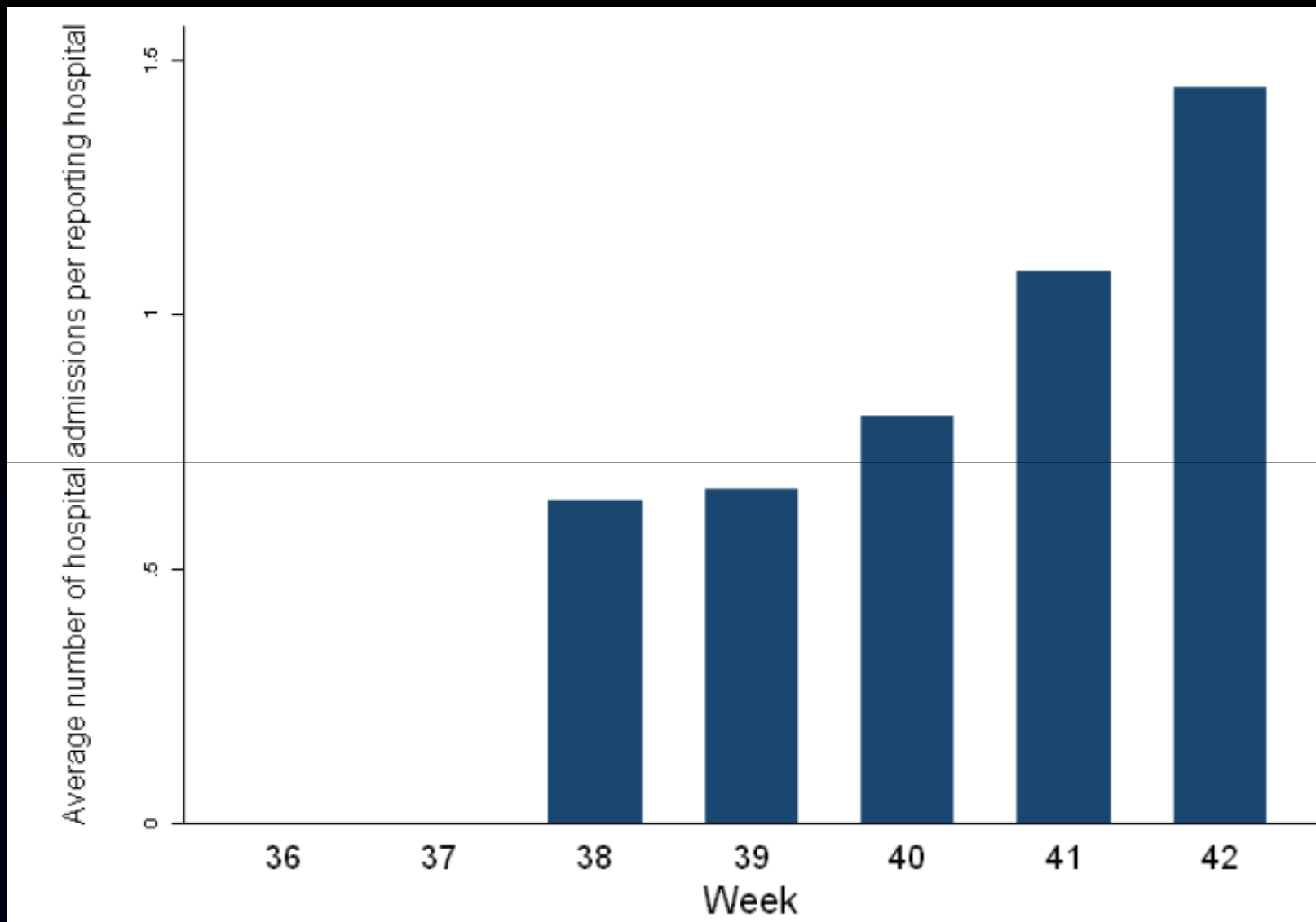




Last update week 42 (OCT 12-18)

Weekly admission for SARI (in reporting hospitals)

ISP



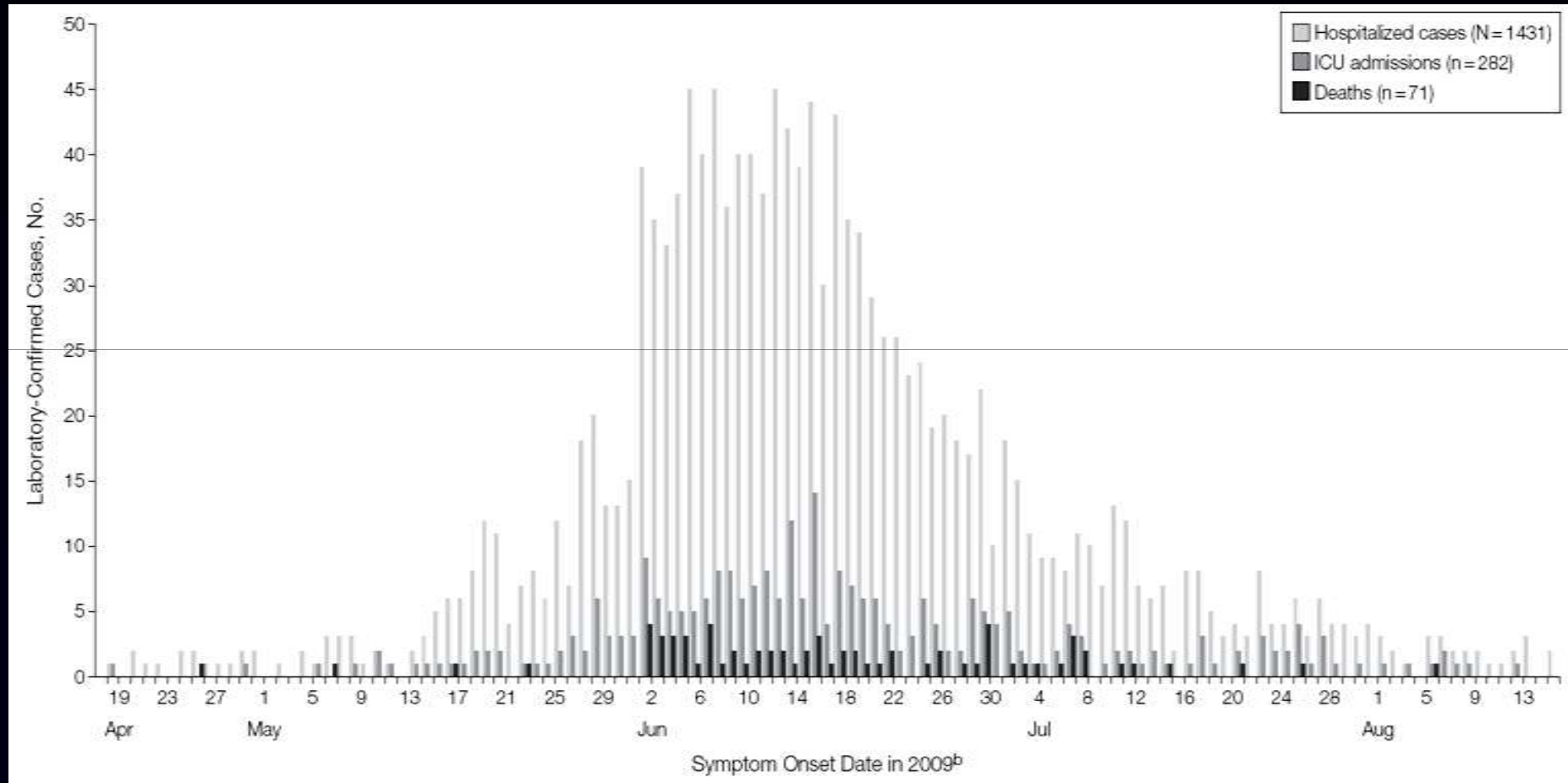
Last update week 42 (OCT 12-18)

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THE EPIDEMY

H1N1 in Canadian ICUs

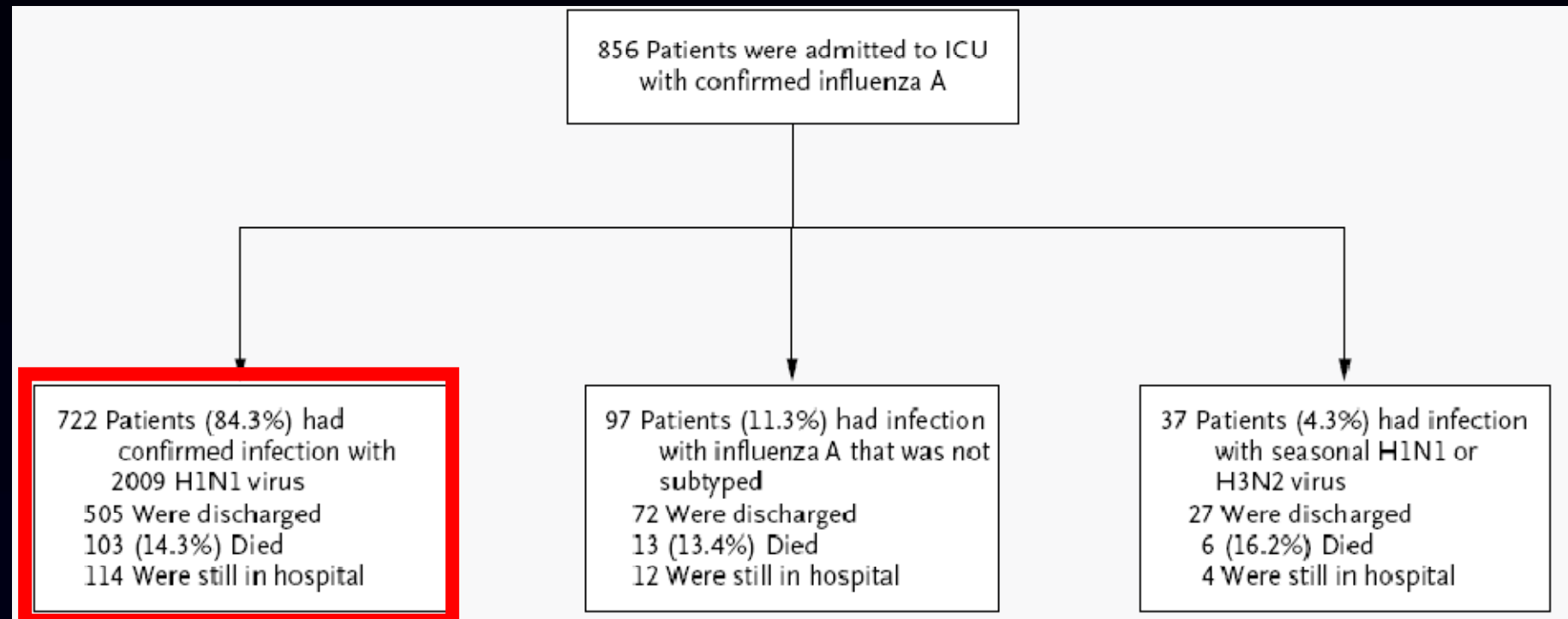
**Kumar et al
CCCTG
JAMA 302:1496;2009**



1-2 weeks

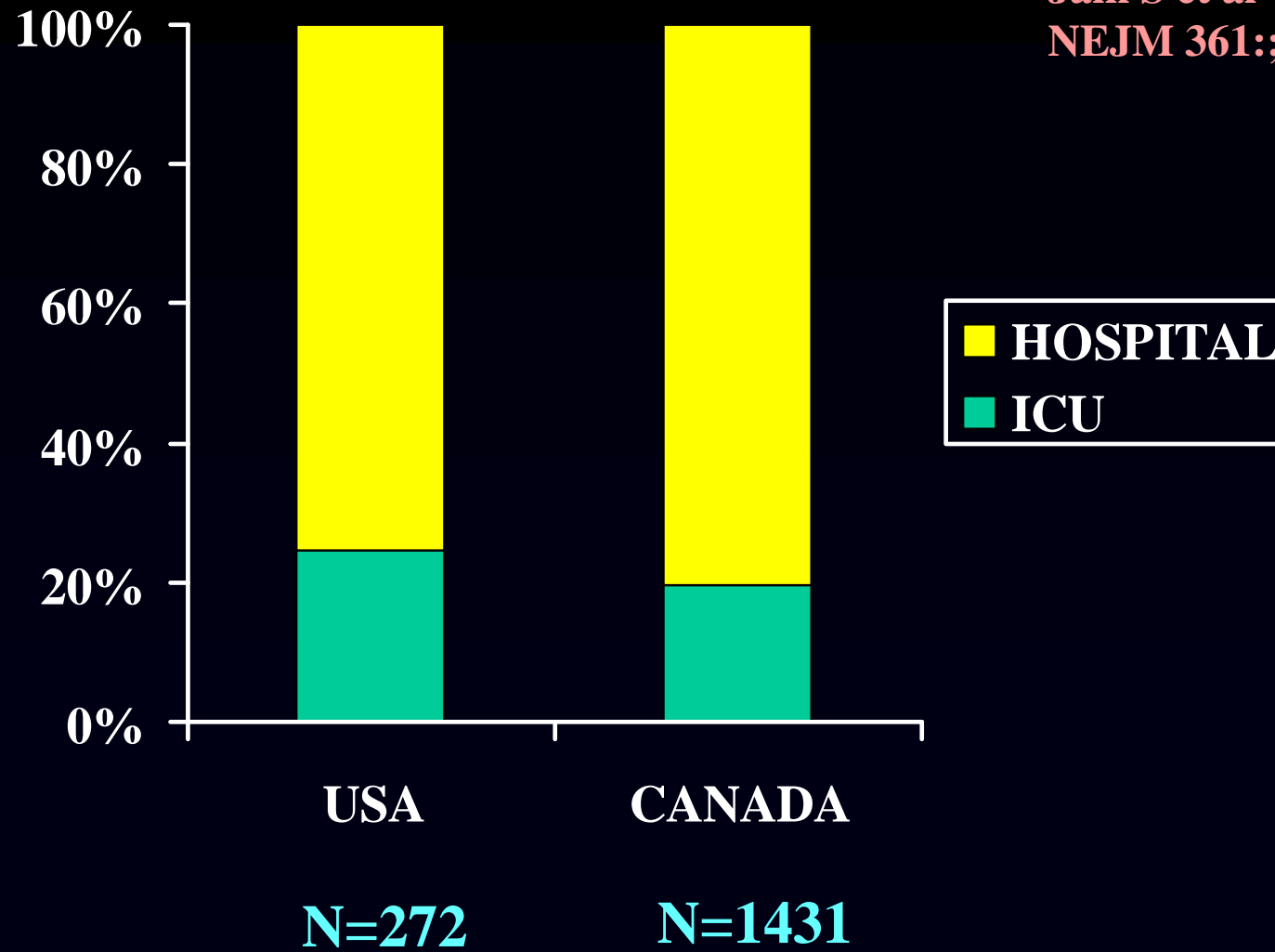
8 weeks

H1N1 is the dominant virus



**Kumar et al (CCCTG)
JAMA 302:1496;2009**

**Jain S et al
NEJM 361:;2009**



WHO WERE THESE PATIENTS ?

H1N1 in US

Jain S et al
NEJM 361:;2009

Non ICU (n=205)

ICU (n=67)

Median age (range) [†]	19 years (21 days-80 years)	29 years (13 months-86 years)
Number (%) < 18 years old	98 (48%)	24 (36%)
Median days from illness onset to admission (range) ^{†, ‡}	3 (0 to 18) (n=199)	4 (0 to 15) (n=63)
Median length of stay after illness onset (days, range) ^{†, ‡}	3 (1 to 23) (n=204)	8 (1 to 49) (n=64)
Median days from illness onset to discharge or death (range) ^{†, ‡}	6 (1 to 30) (n=201)	12 (3 to 61) (n=64)

H1N1 in US

Jain S et al
NEJM 361:;2009

Non ICU (n=205)

ICU (n=67)

Acute respiratory distress syndrome [†]	1/192 (1)	24/53 (45)
Diagnosed with sepsis at admission [†]	2/186 (1)	21/53 (40)
Invasive mechanical ventilation [†]	0/195 (0)	42/65 (65)
Treated with antivirals [†]	144/203 (71)	56/65 (86)
Within 2 days of illness onset [†]	62/139 (45)	13/56 (23)
Treated with antibiotics [†]	134/195 (74)	62/65 (95)
Treated with steroids [†]	57/183 (31)	29/56 (52)
Among those treated with antivirals, days from illness onset to initiation of antivirals [†]	3 days (range, 0 to 29 days) (n=139)	5 days (range, 0 to 24 days) (n=56)
Morbidly Obese [†]	17/72 (24)	9/28 (32)
Influenza vaccination during 2008-2009 season [†]	61/123 (50)	12/42 (29)

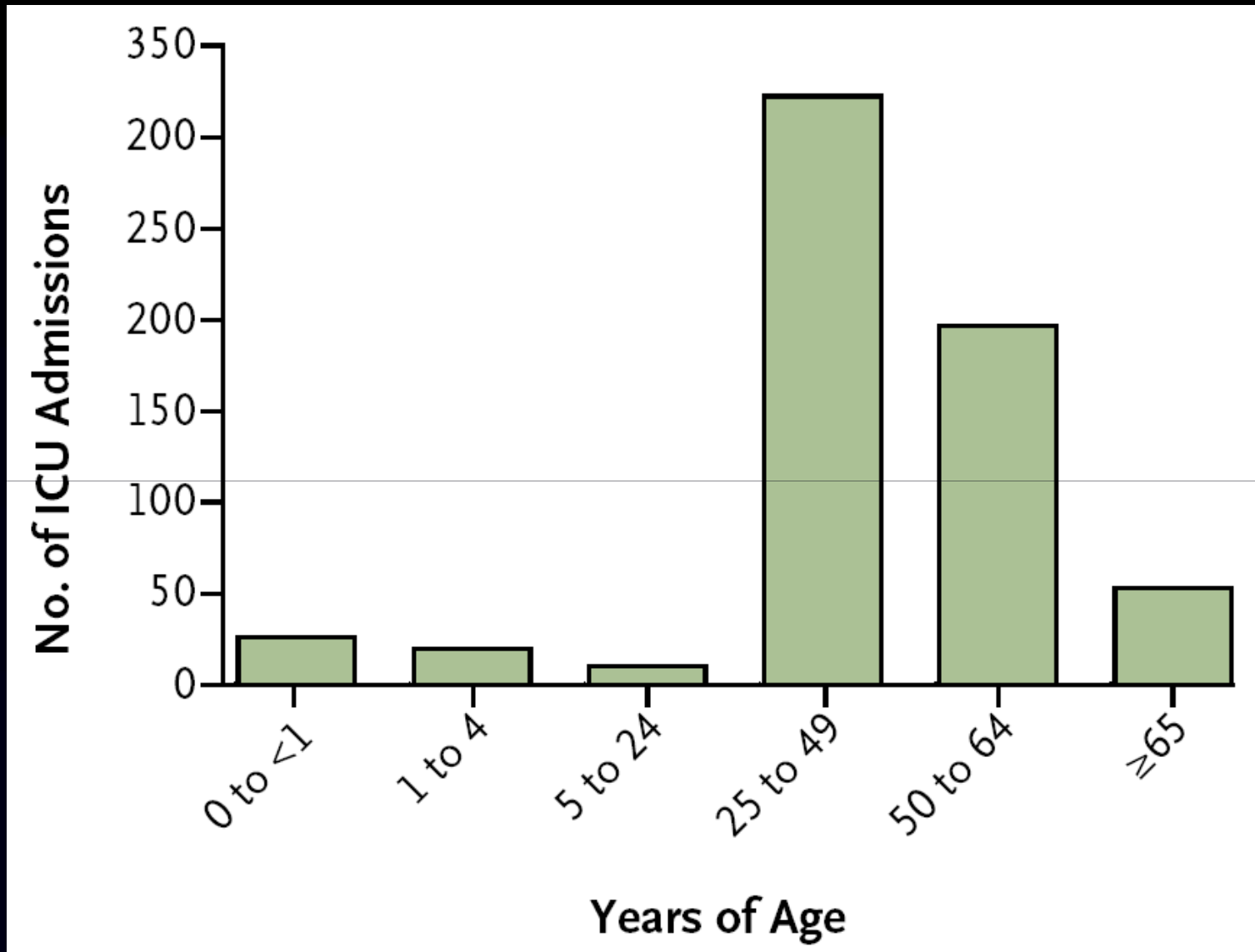
H1N1 in Canadian ICUs

Kumar et al
CCCTG
JAMA 302:1496;2009

	No. (%) of Patients (N = 168) ^a
Age, mean (SD), y	32.3 (21.4)
≥18 (adults)	118 (70.2)
<18 (children and adolescents)	50 (29.8)
Female sex	113 (67.3)
Health care worker	9 (5.4)
Influenza vaccination in 2008 or 2009	10 (6.0)
Test score, mean (SD)	
APACHE II (age ≥18 y)	19.7 (8.7)
PRISM III (age <18 y)	9.1 (9.8)
Nosocomial acquisition	16 (9.5)
Race	
White	67 (39.9)
First nations, Inuit, Métis, or aboriginal	43 (25.6)
Black	14 (8.3)
Other ^b	16 (9.5)
Unknown	28 (16.7)

H1N1 in Australia and New Zealand

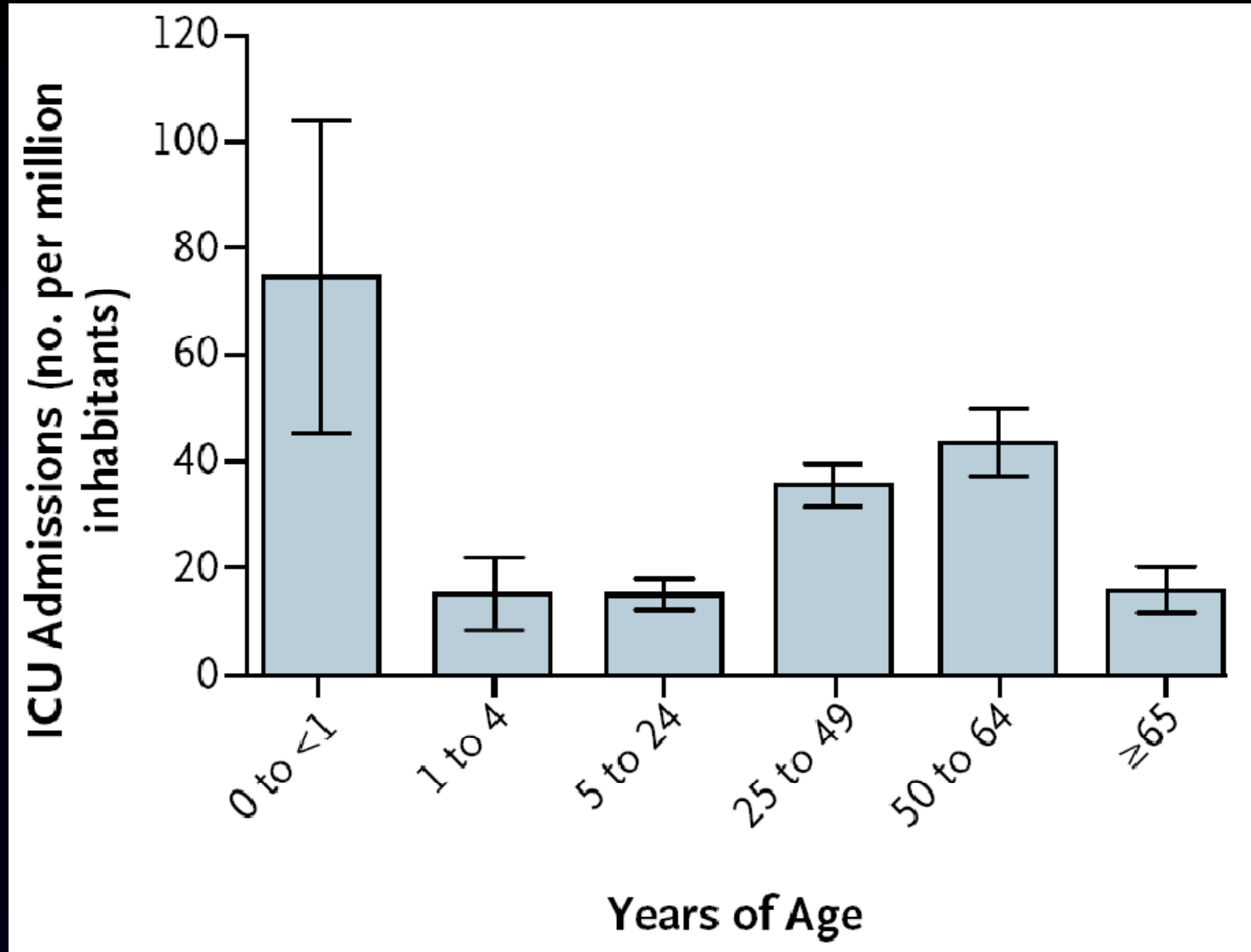
ANZIC
NEJM 361;2009



N=722

H1N1 in Australia and New Zealand

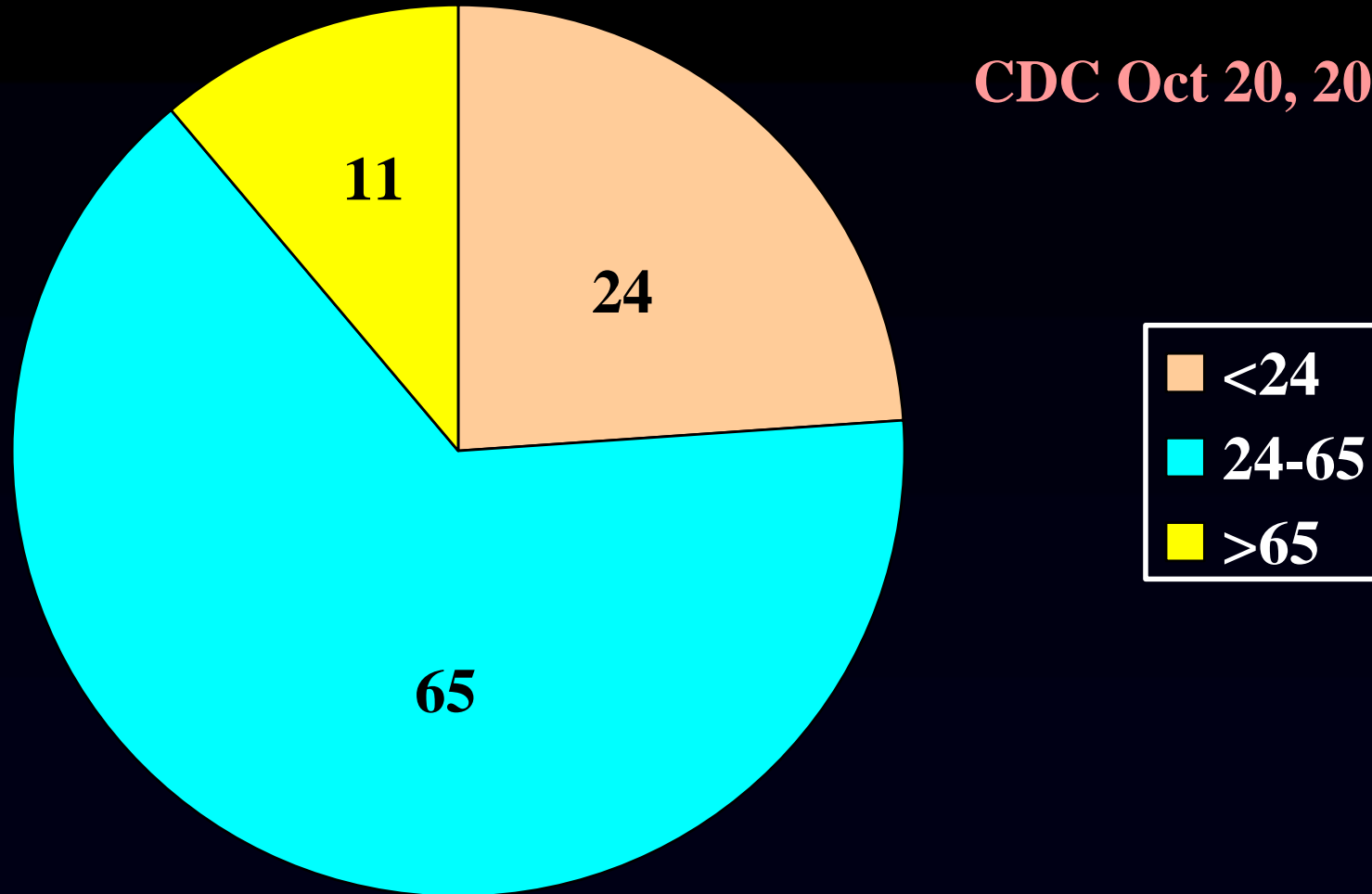
ANZIC
NEJM 361;2009



N=722

Proportion of death according to age (seasonal flu 90%>65 YO)

CDC Oct 20, 2009



H1N1 in Canadian ICUs

Kumar et al
CCCTG
JAMA 302:1496;2009

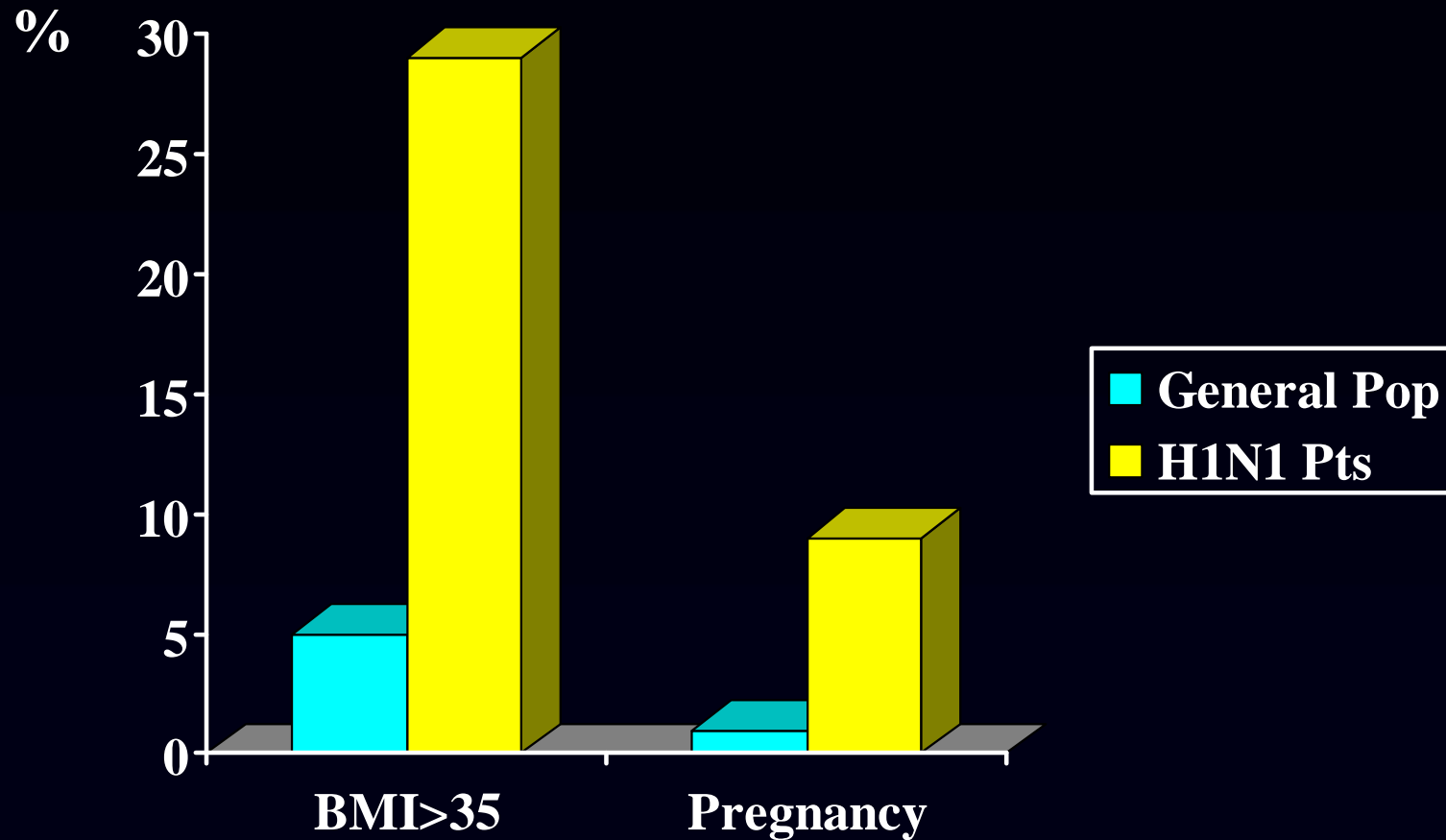
	No. (%) of Patients (N = 168) ^a
No. of comorbidities, median (IQR)	2 (1-4)
Any comorbidity	165 (98.2)
Major comorbidity ^b	51 (30.4)
Chronic lung disease ^c	69 (41.1)
Asthma	38 (22.6)
COPD	16 (9.5)
Bronchopulmonary dysplasia	3 (1.8)
Other	31 (18.5)
Obesity ^d	56 (33.3)
Hypertension	41 (24.4)
Ever smoker	38 (22.6)
Type 1 or 2 diabetes	35 (20.8)
Immune suppression ^c	33 (19.6)
Corticosteroid use	26 (15.5)
Chemotherapy	6 (3.6)
HIV/AIDS	2 (1.2)
Other	14 (8.3)

Neurological disease ^c	26 (15.5)
Cerebrovascular disease	8 (4.8)
Seizures	13 (7.7)
Cerebral palsy	16 (9.5)
Other	6 (3.6)
Cardiac disease ^c	25 (14.9)
Ischemic heart	11 (6.5)
Congestive heart failure	12 (7.1)
Valvular heart	5 (3.0)
Congenital heart	5 (3.0)
Arrhythmia	6 (3.6)
Pregnancy	13 (7.7)
Gastrointestinal tract disease	11 (6.5)
Chronic renal insufficiency ^e	12 (7.1)
Substance abuse	10 (6.0)
Autoimmune disease	8 (4.8)
Malignancy	6 (3.6)
Hematologic	5 (3.0)
Metastatic solid cancer	1 (0.6)
Scoliosis	6 (3.6)
Peripheral vascular disease	5 (3.0)
Cirrhosis	1 (0.6)

Characteristic	Value
Age — yr	
Median	40
IQR	26–54
Female sex — no./total no. (%)	376/722 (52.1)
Pregnant — no./total no. (%)	66/722 (9.1)
Adults with BMI >35 — no./total no. (%)‡	172/601 (28.6)
Diabetes — no./total no. (%)	112/700 (16.0)
Asthma or chronic pulmonary disease — no./total no. (%)	231/707 (32.7)
Chronic heart failure — no./total no. (%)	74/703 (10.5)
Coexisting condition — no./total no. (%)§	192/687 (27.9)
No known predisposing factors — no./total no. (%)	229/722 (31.7)
Time from first symptoms to hospital admission — days¶	
Median	4
IQR	2–7
Influenza syndrome — no./total no. (%)	
Viral pneumonitis or ARDS	336/689 (48.8)
Secondary bacterial pneumonia	140/689 (20.3)
Exacerbation of airflow limitation	95/689 (13.9)
Intercurrent illness or other illness	118/689 (17.1)

H1N1 in Australia and New Zealand

ANZIC
NEJM 361:;2009



N=722

SEVERITY

H1N1 in Canadian ICUs

Kumar et al
CCCTG
JAMA 302:1496;2009

	Day 1 (N = 168)	Day 3 (n = 156)	Day 7 (n = 125)	Day 14 (n = 82)
SOFA score, mean (SD) ^a	6.8 (3.6)	6.6 (4.2)	6.1 (4.3)	5.7 (4.2)
Ratio of PaO ₂ to FiO ₂ , mean (SD), mm Hg	147 (128)	168 (86)	172 (101)	190 (122)
Lowest SBP, mean (SD), mm Hg	95 (24)	104 (28)	107 (27)	112 (27)
Inotropes or vasopressors, No. (%)	55 (32.7)	58 (37.2)	31 (24.8)	14 (17.1)
Heart rate, mean (SD), /min	119 (28)	106 (26)	106 (29)	106 (25)
Creatinine, median (IQR), mg/dL	0.73 (0.50-1.15)	0.74 (0.52-1.19)	0.74 (0.55-1.28)	0.80 (0.57-1.72)
Platelet count, mean (SD), ×10 ³ /μL	189 (87)	187 (93)	283 (171)	404 (228)
Bilirubin, median (IQR), mg/dL	0.41 (0.23-0.79)	0.44 (0.23-1.05)	0.50 (0.29-1.02)	0.47 (0.36-0.94)
White blood cell count, mean (SD), ×10 ⁹ /L	9.4 (10.0)	9.1 (7.0)	11.3 (5.3)	13.4 (7.4)
AST, median (IQR), U/L	64 (37-126)	70.5 (42-163)	49 (31-96)	43 (29-65)
ALT, median (IQR), U/L	35 (21-68)	35 (25-69)	44.5 (24-74)	30 (20-61)
Creatine kinase, median (IQR), U/L	243 (99-922)	580 (203-1728)	228 (76-1046)	48 (22-91)
INR, mean (SD)	1.22 (0.27)	1.18 (0.29)	1.18 (0.27)	1.18 (0.18)

H1N1 in Australia and New Zealand

ANZIC
NEJM 361:;2009

	N with data available (% of the total study population of 722)
Vasopressor drugs	498 (69.0%)
Renal replacement therapy	506 (70.1%)
Steroid therapy	494 (68.4%)

N=722

H1N1 in Canadian ICUs

**Kumar et al
CCCTG
JAMA 302:1496;2009**

	No. (%) of Patients [95% CI] (N = 168) ^b
Time from ICU admission to death	
Day 14	18 (10.7) [6.6-16.6]
Day 28	24 (14.3) [9.5-20.7]
Day 90	29 (17.3) [12.0-24.0]
Time course of illness, d	Median (IQR)
Symptoms to hospital admission	4 (2-7)
Hospitalization to ICU admission	1 (0-2)
Hospitalization to death	14 (6-20)
ICU length of stay, d	Median (IQR) [95% CI]
Survivors	12 (5-22) [9-14]
Nonsurvivors	10 (4-19) [5-14]
Duration of ventilation, d	
Survivors	12 (6-20) [9-14]
Nonsurvivors	12 (4-20) [5-15]

**Kumar et al (CCCTG)
JAMA 302:1496;2009**

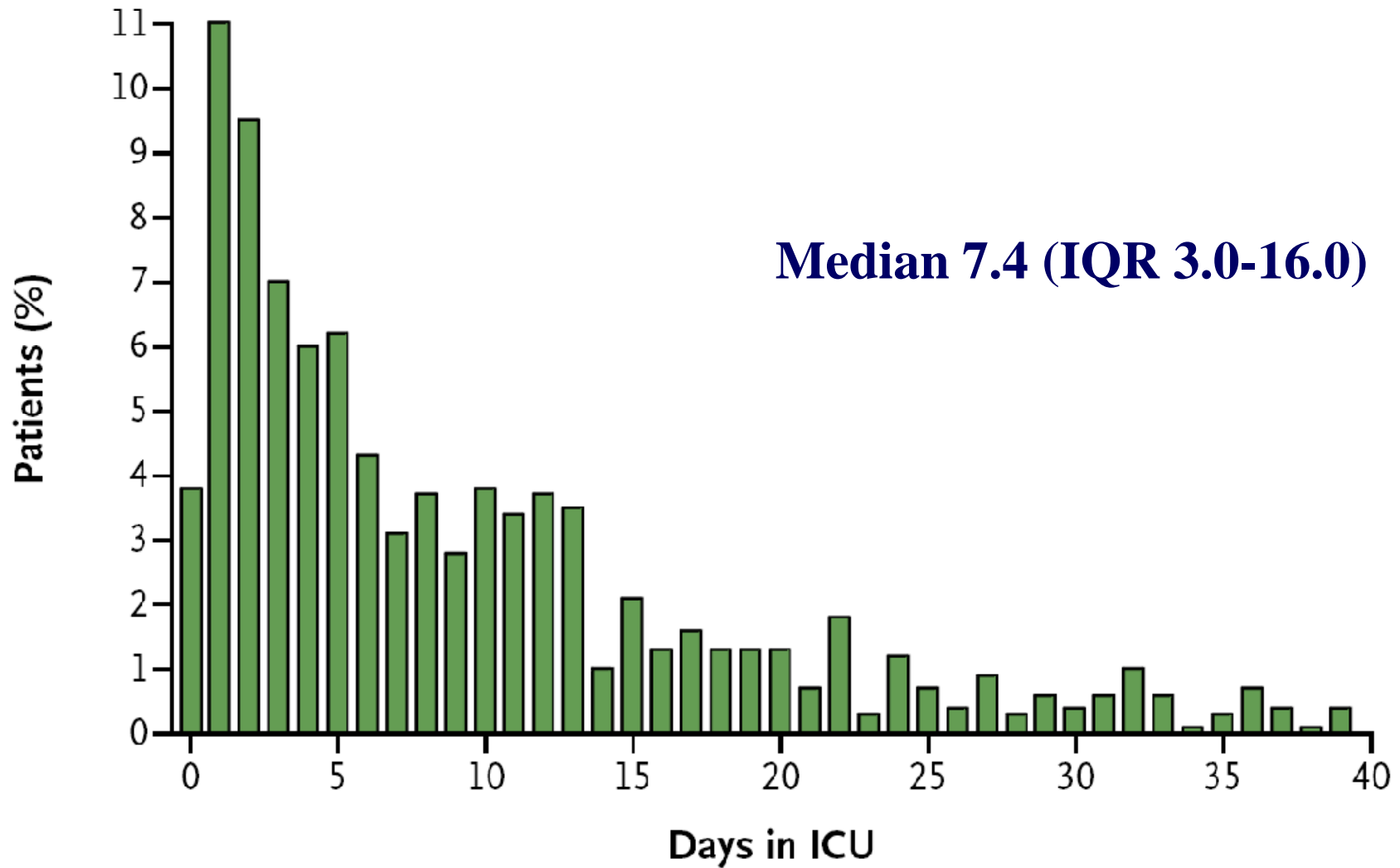
	No. (%) of Patients [95% CI] (N = 168) ^b
Time from ICU admission to death	
Day 14	18 (10.7) [6.6-16.6]
Day 28	24 (14.3) [9.5-20.7]
Day 90	29 (17.3) [12.0-24.0]
Time course of illness, d	Median (IQR)
Symptoms to hospital admission	4 (2-7)
Hospitalization to ICU admission	1 (0-2)
Hospitalization to death	14 (6-20)
ICU length of stay, d	Median (IQR) [95% CI]
Survivors	12 (5-22) [9-14]
Nonsurvivors	10 (4-19) [5-14]
Duration of ventilation, d	
Survivors	12 (6-20) [9-14]
Nonsurvivors	12 (4-20) [5-15]

**Dominguez-Cherit et al
JAMA 302:1536;2009**

Mortality	No. (%) of Patients [95% CI] (N = 58)
From ICU admission	
Day 14	19 (33) [21.4-46.5]
Day 28	23 (40) [27.3-53.4]
Day 60	24 (41) [28.9-55.0]
Time course of illness, d	Median (IQR)
Symptoms to hospital admission	6 (4-8)
Hospitalization to ICU admission	1 (0-3)
Hospitalization to death	10 (4-14)
ICU length of stay, d	Median (IQR) [95% CI]
Survivors	13.5 (6-24) [8-22]
Nonsurvivors	7.0 (2-13) [4-13]
Duration of ventilation, d	Median (IQR) [95% CI]
Survivors	15.0 (8-26) [9-24]
Nonsurvivors	7.5 (3-13.5) [5-13]
Location of death (n = 24)	No. (%)
ICU	20 (83)
Emergency department ^a	4 (17)

H1N1 in Australia and New Zealand

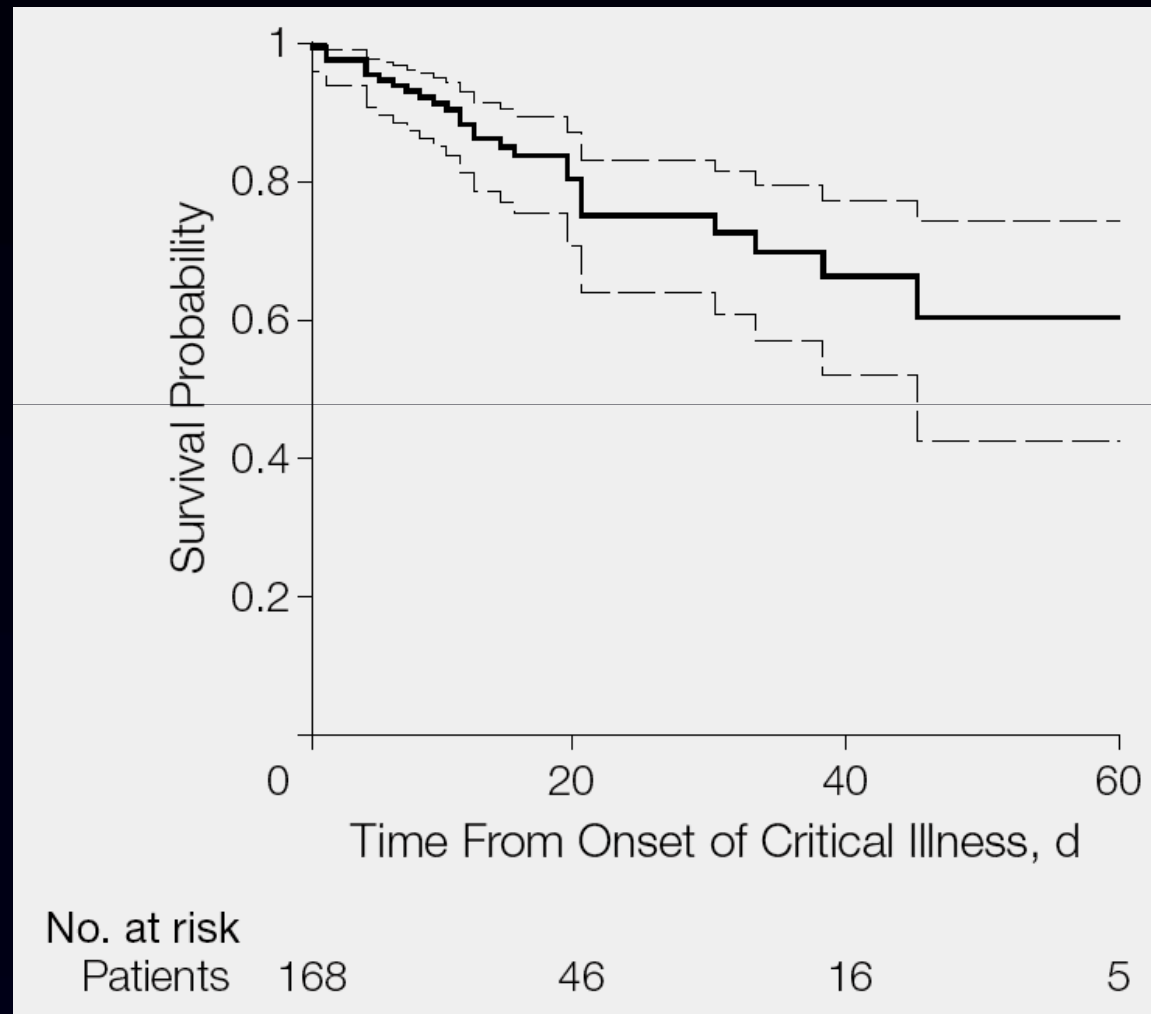
ANZIC
NEJM 361;2009



N=722

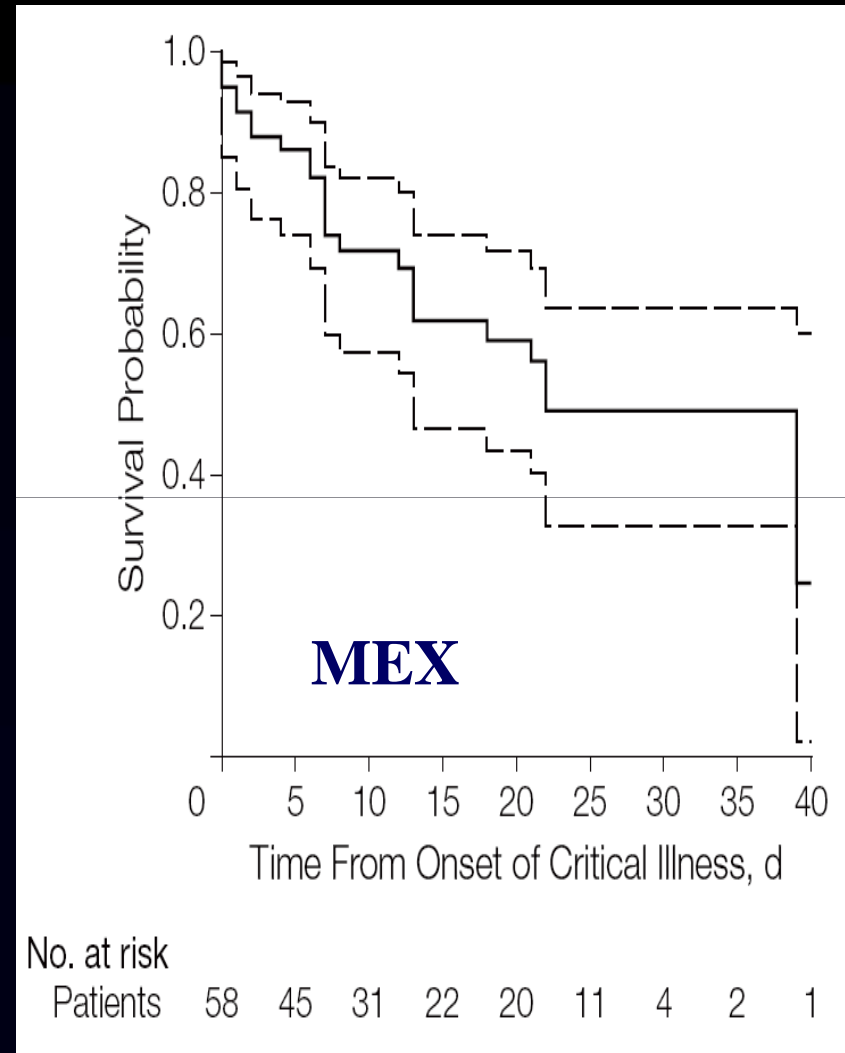
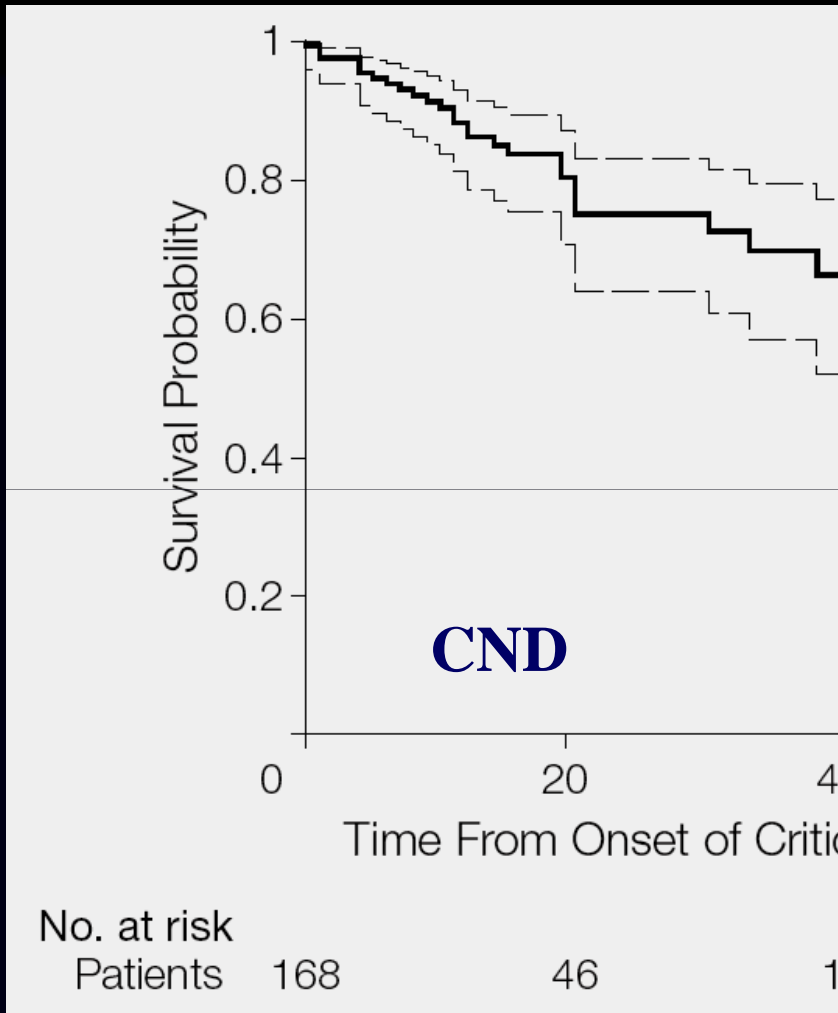
H1N1 in Canadian ICUs

Kumar et al
CCCTG
JAMA 302:1496;2009



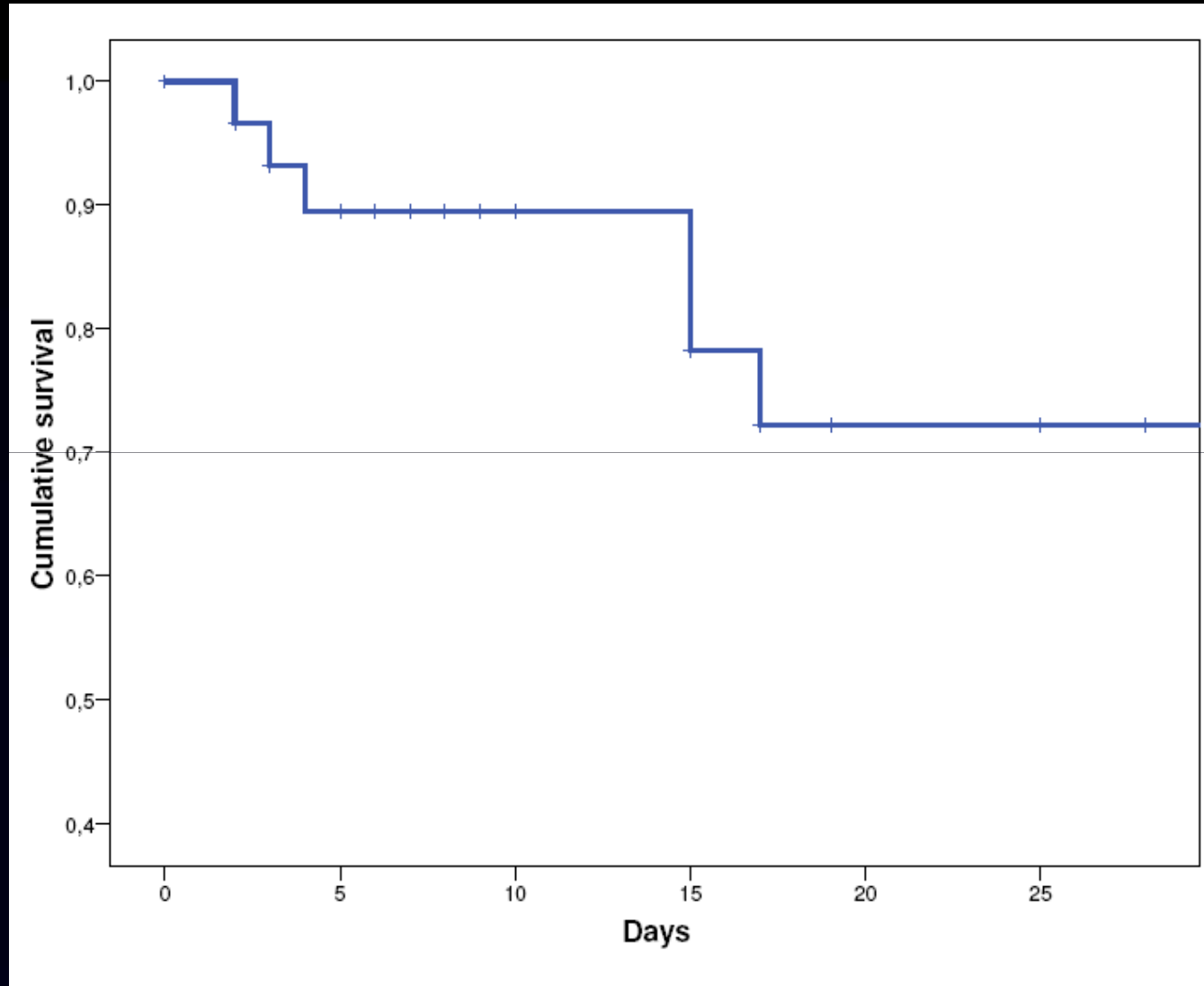
H1N1 in Canada and Mexico

Dominguez-Cherit et al
JAMA 302:1536;2009



H1N1 in Spanish ICUs

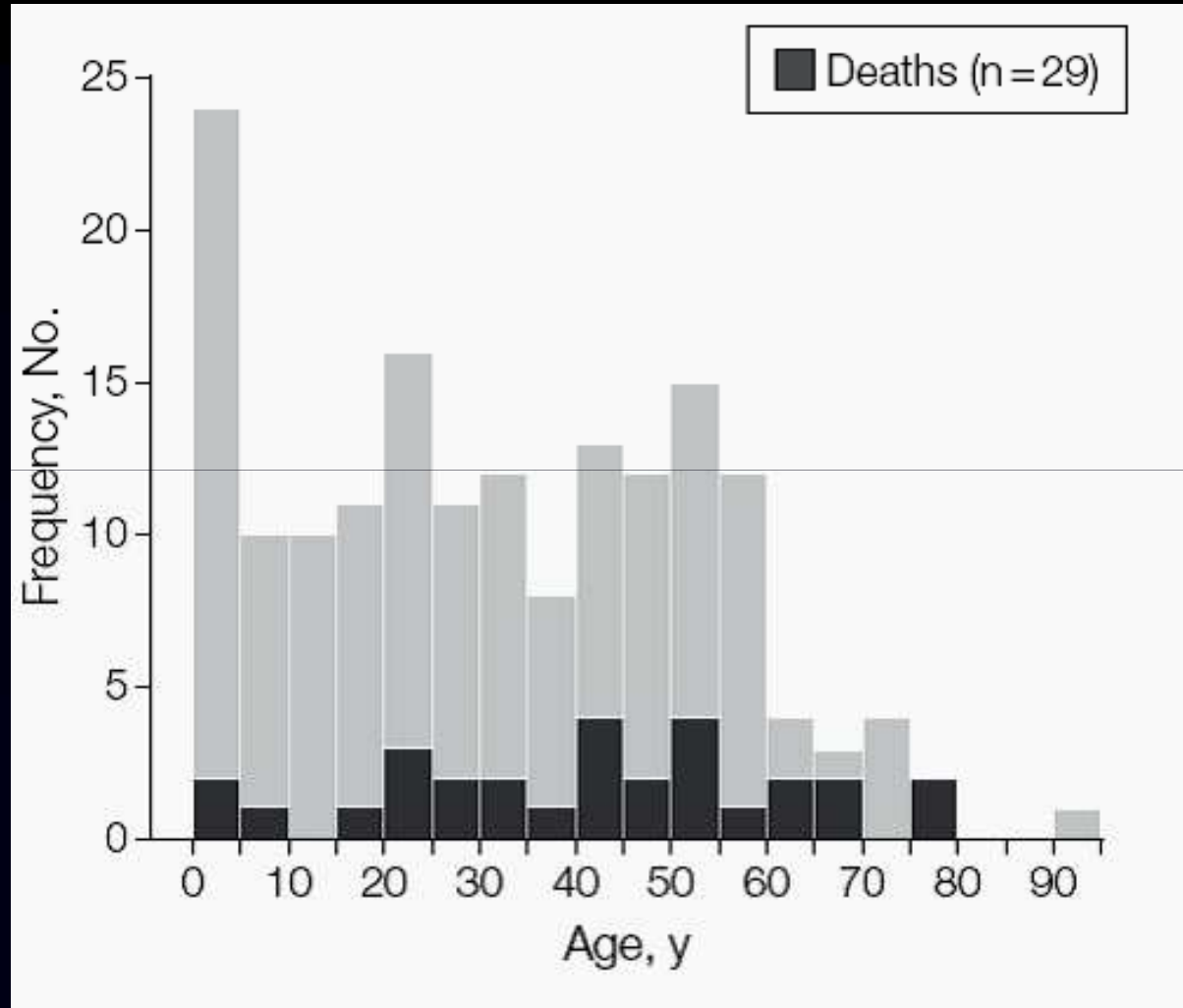
Rello J et al
Crit Care 13:R148;2009



N=32 (5 weeks period)

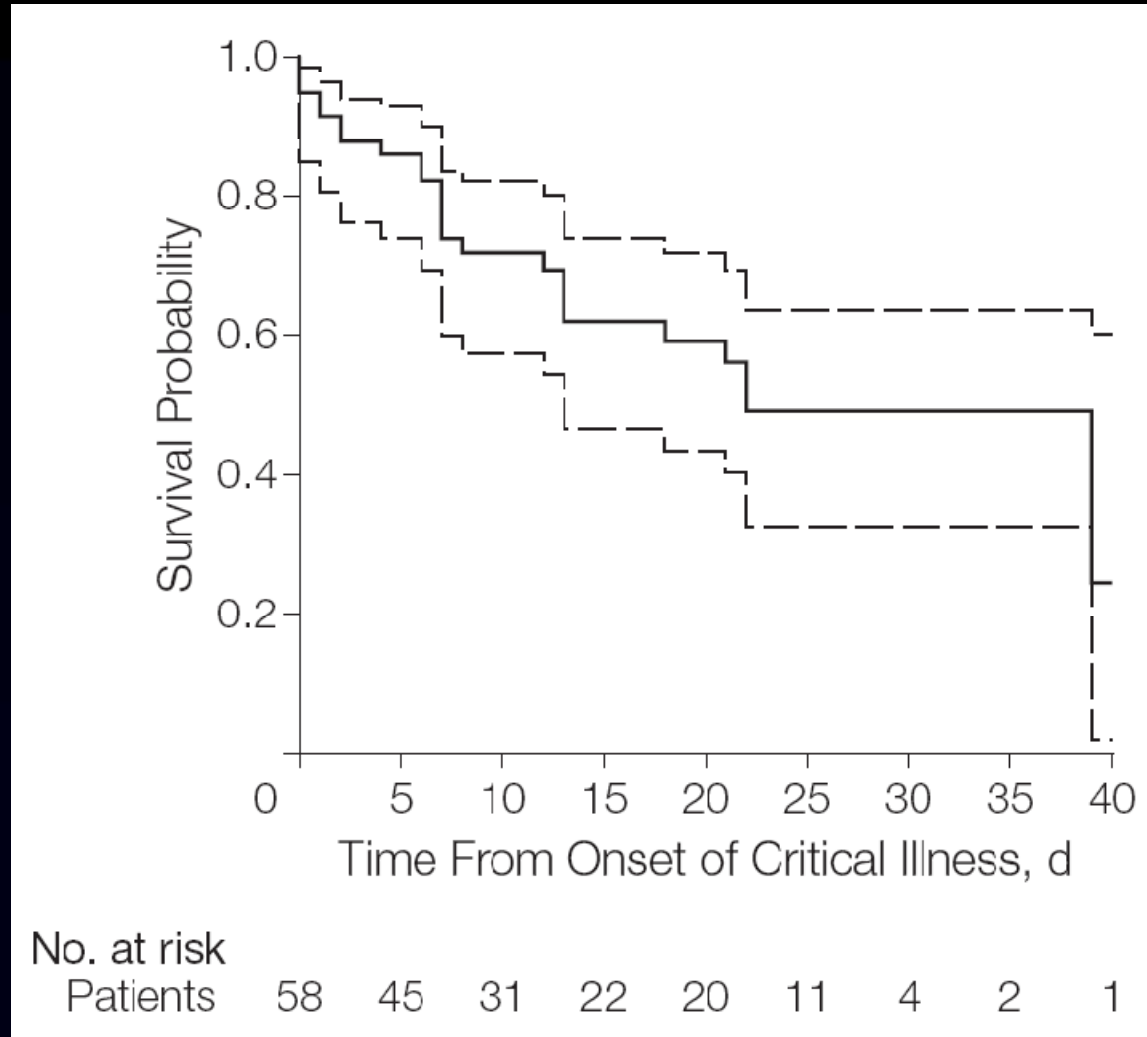
H1N1 in Canadian ICUs

Kumar et al
CCCTG
JAMA 302:1496;2009



H1N1 in Mexico (6 ICUs)

Dominguez-Cherit et al
JAMA 302:1536;2009



N = 58

**CHARACTERISTICS OF THE MOST
SEVERE PATIENTS ?**

H1N1 in Canadian ICUs

Kumar et al
 CCCTG
 JAMA 302:1496;2009

	Survivors (n = 139)	Nonsurvivors (n = 29)	P Value
Age, mean (SD), y	30 (21)	42 (21)	.007
Female sex, No. (%)	92 (66)	21 (72)	.52
Comorbidities			
Ever smoker, No. (%)	32 (23)	6 (21)	.96
BMI, median (IQR) ^a	29 (24-39)	31 (28-41)	.33
Time course of illness, median (IQR), d			
Symptoms to hospital admission	4 (2-7)	5 (3-7)	.21
Hospitalization to ICU admission	0 (0-2)	1 (0-3)	.29
Characteristics at ICU admission			
APACHE II score, mean (SD)	18 (8)	26 (8)	<.001
Ratio of PaO ₂ to FiO ₂ , median (IQR), mm Hg	124 (80-181)	85 (67-166)	.10
Initial mean arterial pressure, median (IQR), mm Hg	65 (58-77)	68 (58-83)	.31
Ventilation at ICU admission, mean (SD)			
Tidal volume for ideal body weight, mL/kg	9.2 (2.4)	8.6 (2.7)	.36
Plateau pressure, cm H ₂ O	25.6 (9.3)	28.0 (10.6)	.70
Set PEEP, cm H ₂ O	9.6 (3.8)	10.5 (4.7)	.36
Organ dysfunction, median (IQR) ^b			
SOFA score on day 1, mean (SD)	6.4 (3.4)	8.4 (3.5)	.01
Creatinine, mg/dL	0.71 (0.46-1.01)	0.97 (0.58-2.33)	.005
AST, U/L	60 (37-125)	71.5 (40-207)	.58
White blood cell count, ×10 ⁹ /L	6.7 (3.8-12.1)	6.9 (3.7-9.5)	.63
Platelet count, mean (SD), ×10 ³ /μL	195 (88)	161 (77)	.05
Bilirubin, mg/dL	0.41 (0.23-0.76)	0.52 (0.29-0.93)	.39
Creatine kinase, U/L	255 (104-1117)	221 (42-455)	.45

H1N1 in Spanish ICUs

Rello J et al
 Crit Care 13:R148;2009

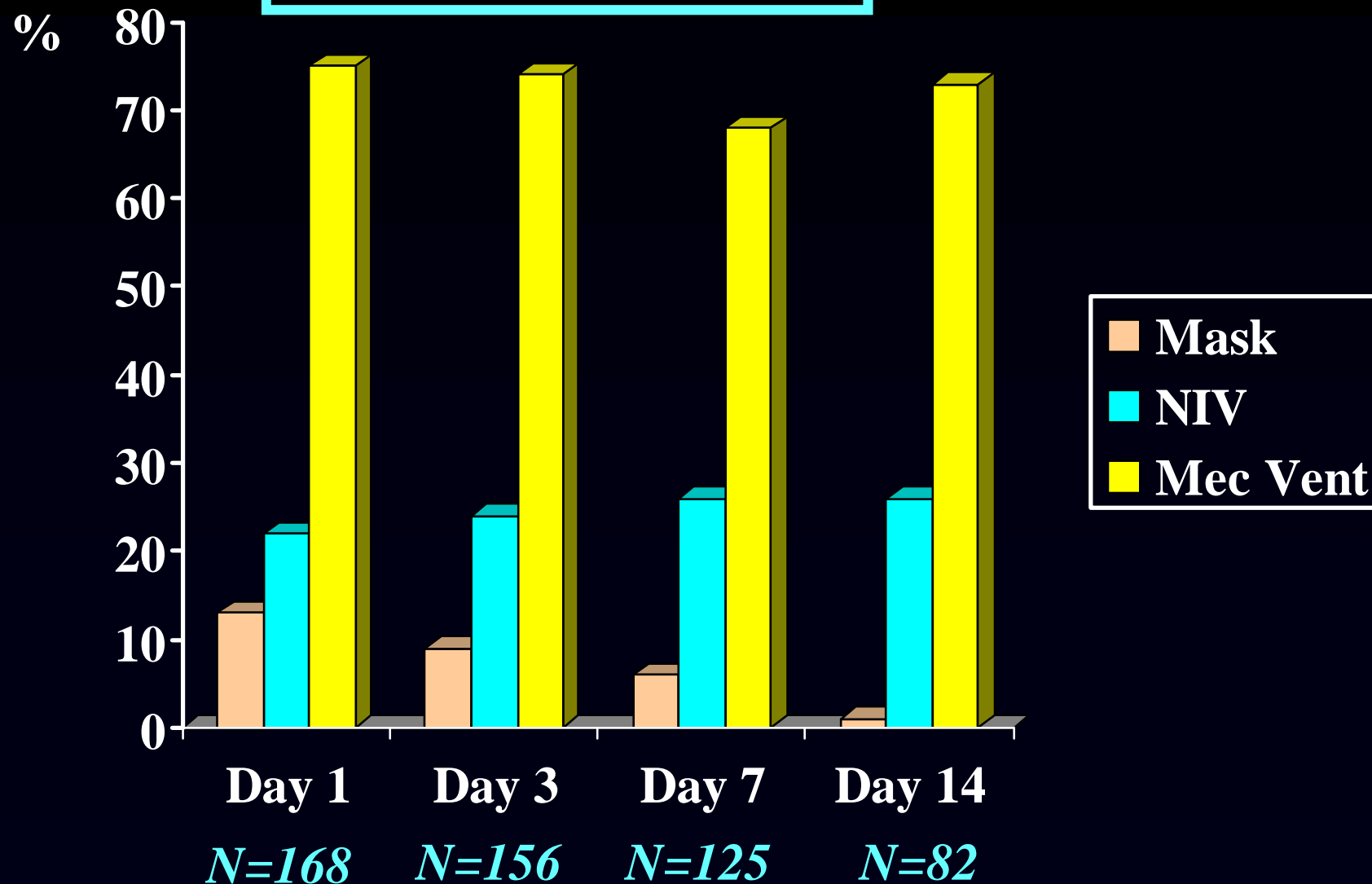
Variable	Non-Ventilated (n=8)	Non-Invasive ventilation		Initially Intubated n= 16
		Successful (n=2)	Failure (n=6)	
APACHE II Score				
Mean (SD)	9.5 (4.9)	9.5 (0.7)	15.3 (5.6)	15.2 (7.6)
IQR 25-75	4 – 16	9 -10	10 – 24	8 -38
SOFA score				
Mean (SD)	4.7 (1.7)	2.5 (0.7)*	8.1 (2.3)**	7.8 (3.5)
IQR 25 – 75	3 – 7	2 – 3	5 – 11	4 – 16
Age , yr				
Mean (SD)	39.2 (14.7)	42.5 (13.4)	44.0 (15.1)	38.7 (14.0)
IQR 25 – 75	17 – 58	33 - 52	10 – 57	16 – 70
Opacity lung quadrants				
Mean (SD)	2.9 (1.2)	2.5 (2.1)	2.8 (0.9)	3.3 (1.1)
LDH , U/L				
Mean (SD)	751 (361)	1140 (374)	918 (408)	2170 (3400)
IQR 25 – 75	195 – 1166	880 – 1400	354 – 1450	440 – 12200
CK, U/L				
Mean (SD)	2480 (4500)	2800 (3200)	4850 (4200)	2300 (3800)
IQR 25 – 75	66 – 9300	500 – 5100	122 - 9400	207 – 10800
28-day Mortality,n(%)***	0	0	2 (33)	4 (25)

MANAGEMENT

H1N1 in Canadian ICUs

Kumar et al
CCCTG
JAMA 302:1496;2009

Ventilation requirements



H1N1 in Canadian ICUs

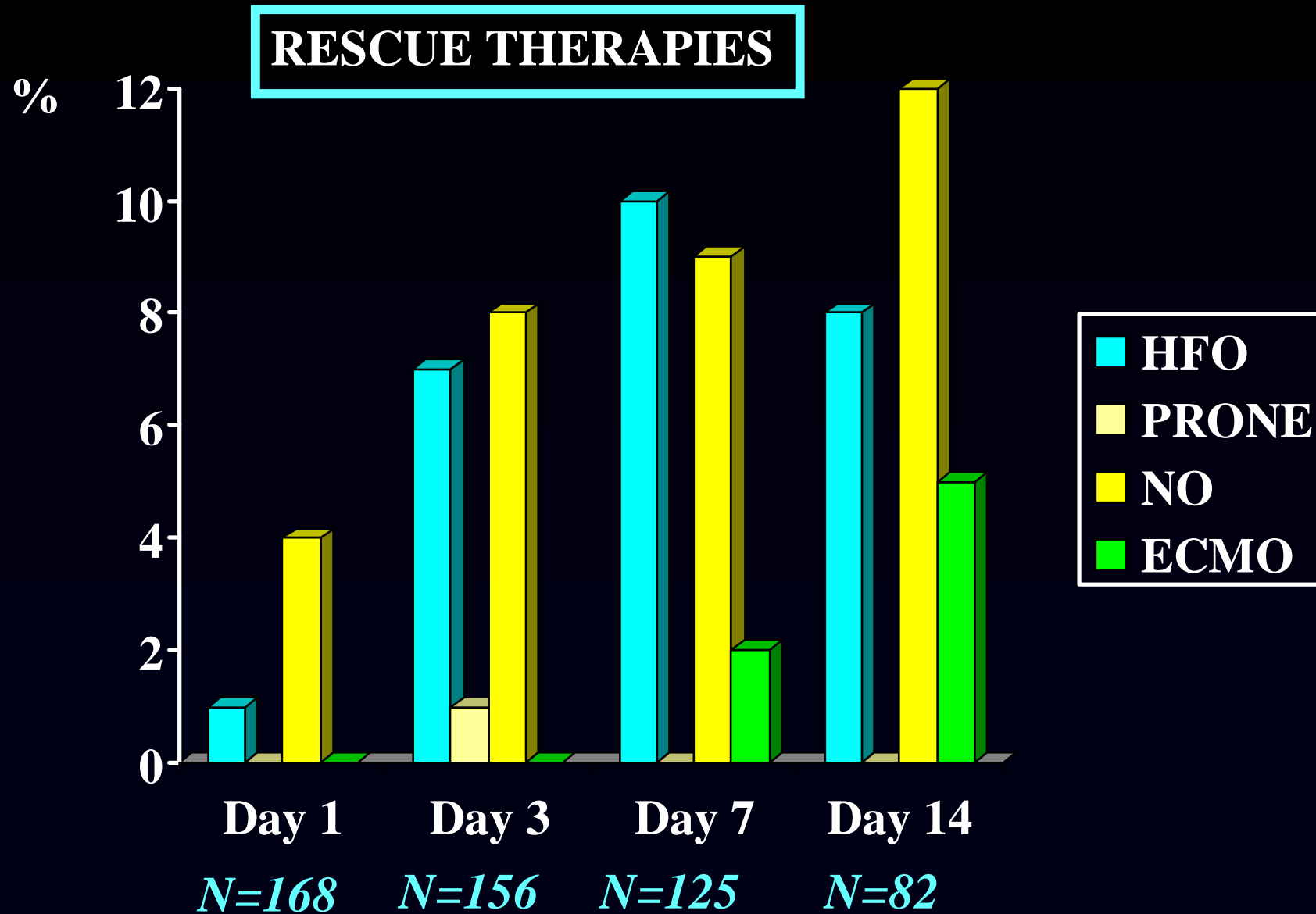
Kumar et al
CCCTG
JAMA 302:1496;2009

In addition, approximately **one-third** of patients in our cohort required advanced ventilatory support and rescue therapies for profound hypoxemic respiratory failure, including high levels of inspired oxygen and PEEP, pressure control, and airway pressure release ventilation, high-frequency oscillatory ventilation, prone positioning ventilation, neuromuscular blockade, inhaled nitric oxide, and extracorporeal membrane oxygenation. The fact that severe

N = 168

H1N1 in Canadian ICUs

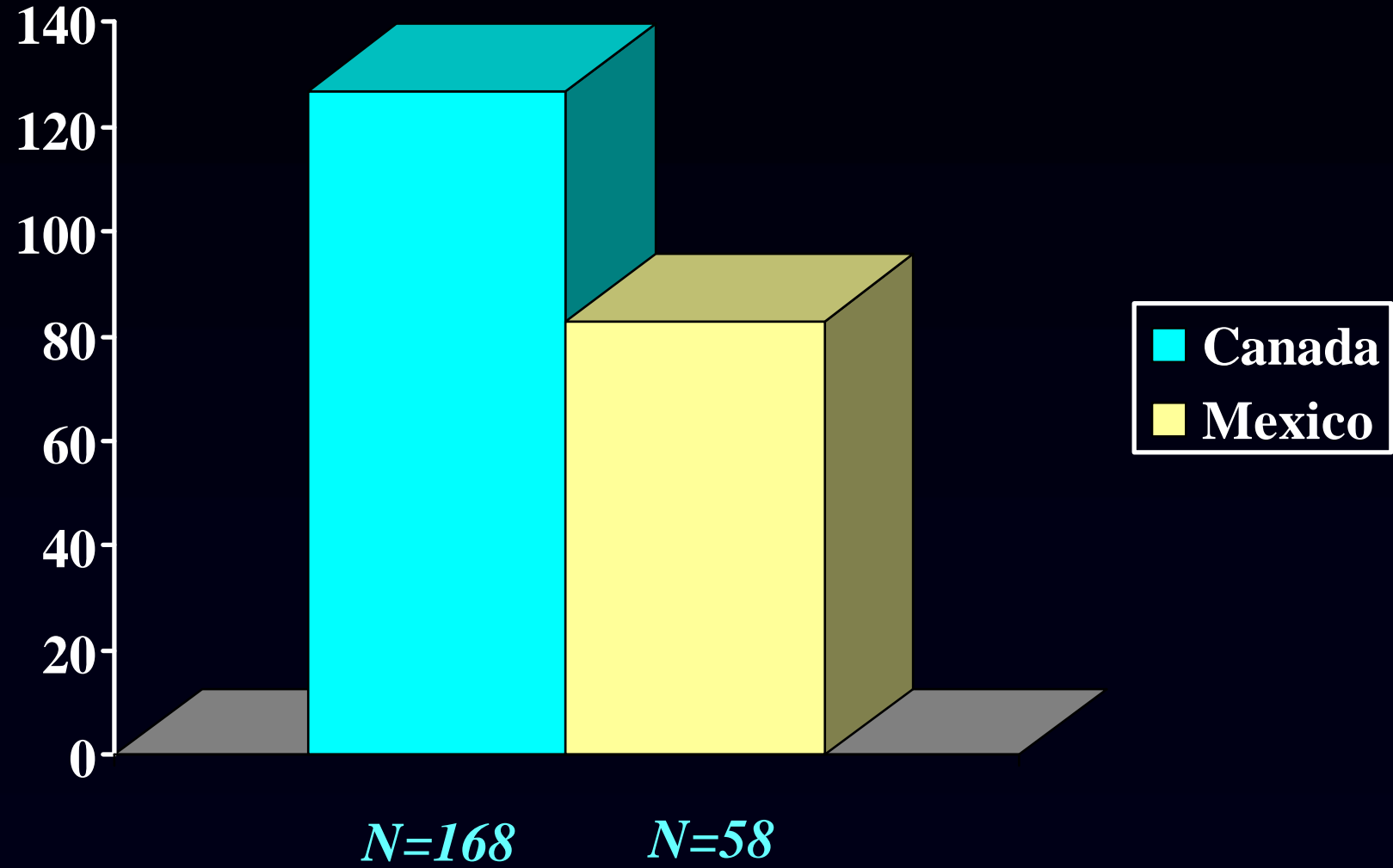
Kumar et al
CCCTG
JAMA 302:1496;2009



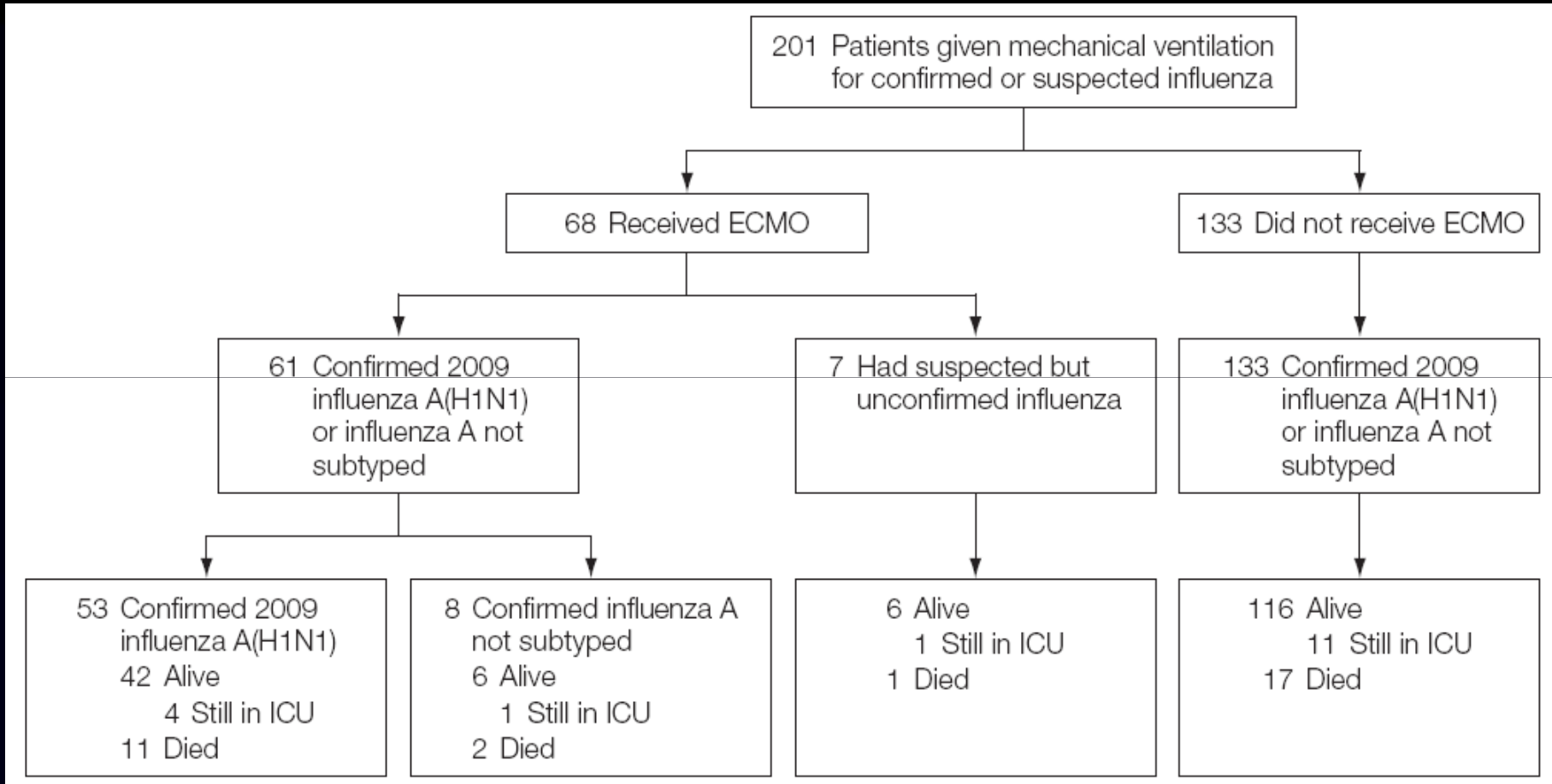
PF ratio on admission

**Dominguez-Cherit et al
JAMA 302:1536;2009**

**Kumar et al (CCCTG)
JAMA 302:1496;2009**



**ANZ ECMO
JAMA 302:1535;2009**



June 01 – AUG 31; 2009
15 units

Parameter	ECMO (n = 61)	Mechanical Ventilation But Without ECMO (n = 133)	P Value
Age, median (IQR), y	36 (27-45)	44 (31-54)	.02
Male sex	29 (48)	63 (47)	.54
BMI, median (IQR)	29 (23-36)	29 (24-37)	.92
Chronic lung disease	18 (30)	35 (26)	.64
APACHE III comorbidity ^b	5 (8)	30 (23)	.02
Pregnancy or postpartum	10 (16)	12 (9)	.21
Diabetes mellitus	9 (15)	23 (17)	.64
H1N1 positive	56 (92)	107 (80)	.05
At ICU admission			
Mechanical ventilation	53 (87)	117 (88)	.80
Vasopressor	35 (57)	46 (34)	.02
Renal replacement therapy	5 (8)	9 (7)	.95

June 01 – AUG 31; 2009 15 ECMO units

**ANZ ECMO
JAMA 302:1535;2009**

Characteristics	All Infections (N = 68)
Ventilation parameters, median (IQR)	
Lowest PaO ₂ /FIO ₂ ratio	56 (48-63)
Highest FIO ₂	1.0 (1.0-1.0)
Highest PEEP, cm H ₂ O	18 (15-20)
Highest peak airway pressure, cm H ₂ O	36 (33-38)
Lowest pH	7.2 (7.1-7.3)
Highest PaCO ₂ , mm Hg	69 (54-83)
Highest tidal volume, mL/kg	5.6 (4.6-6.7)
Quadrants of radiograph infiltrate, No.	4 (4-4)
Acute lung injury score ^a	3.8 (3.5-4.0)
Pneumothorax pre-ECMO, No. (%)	10 (15)
Rescue ARDS therapies used, No. (%)	
Recruitment maneuver	38 (67)
Prone positioning	12 (20)
High-frequency oscillation	3 (5)
Nitric oxide	20 (32)
Prostacyclin	14 (22)

June 01 – AUG 31; 2009 15 ECMO units

Parameter	ECMO (n = 61)	Mechanical Ventilation But Without ECMO (n = 133)	<i>P</i> Value
Duration or length of stay, median (IQR), d			
Mechanical ventilation	18 (9-27)	8 (4-14)	.001
ICU	22 (13-32)	12 (7-18)	.001
Hospital	28 (15-43)	20 (13-31)	.07
Mortality			
in ICU	14 (23)	12 (9)	.01
in hospital	14 (23)	17 (13)	.06

June 01 – AUG 31; 2009 15 ECMO units

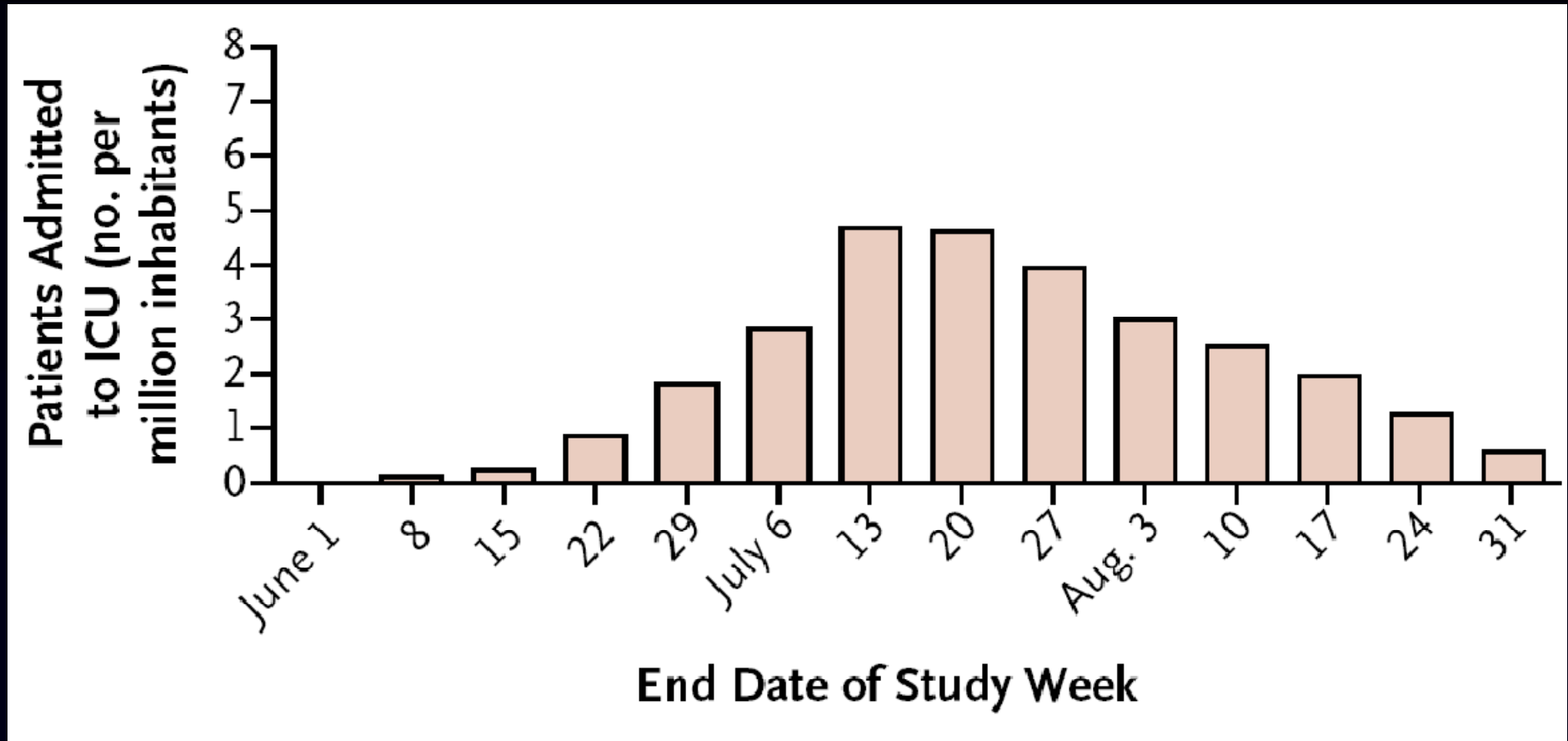
Outcome Measure	All Infections (N = 68)
Length of stay, median (IQR), d	
ICU	27 (16-37)
Hospital	39 (23-47)
Duration, median (IQR), d	
Mechanical ventilation	25 (13-34)
ECMO support	10 (7-15)
Survival at ICU discharge	48 (71)
Still in ICU	6 (9)
Survival at hospital discharge	32 (47)
Still in hospital ^b	16 (24)
Ambulant at hospital discharge ^c	31 (97)
SaO ₂ on room air at hospital discharge, median (IQR), % ^c	97 (95-98)
Discharge destination	
Died	14 (21)
Home	22 (32)
Other hospital	1 (1)
Rehabilitation facility	9 (13)
Cause of death ^d	
Hemorrhage	4 (29)
Intracranial hemorrhage	6 (43)
Infection	1 (7)
Intractable respiratory failure	4 (29)

June 01 – AUG 31; 2009
15 ECMO units

THE BURDEN

H1N1 in Australia and New Zealand

ANZIC
NEJM 361;2009

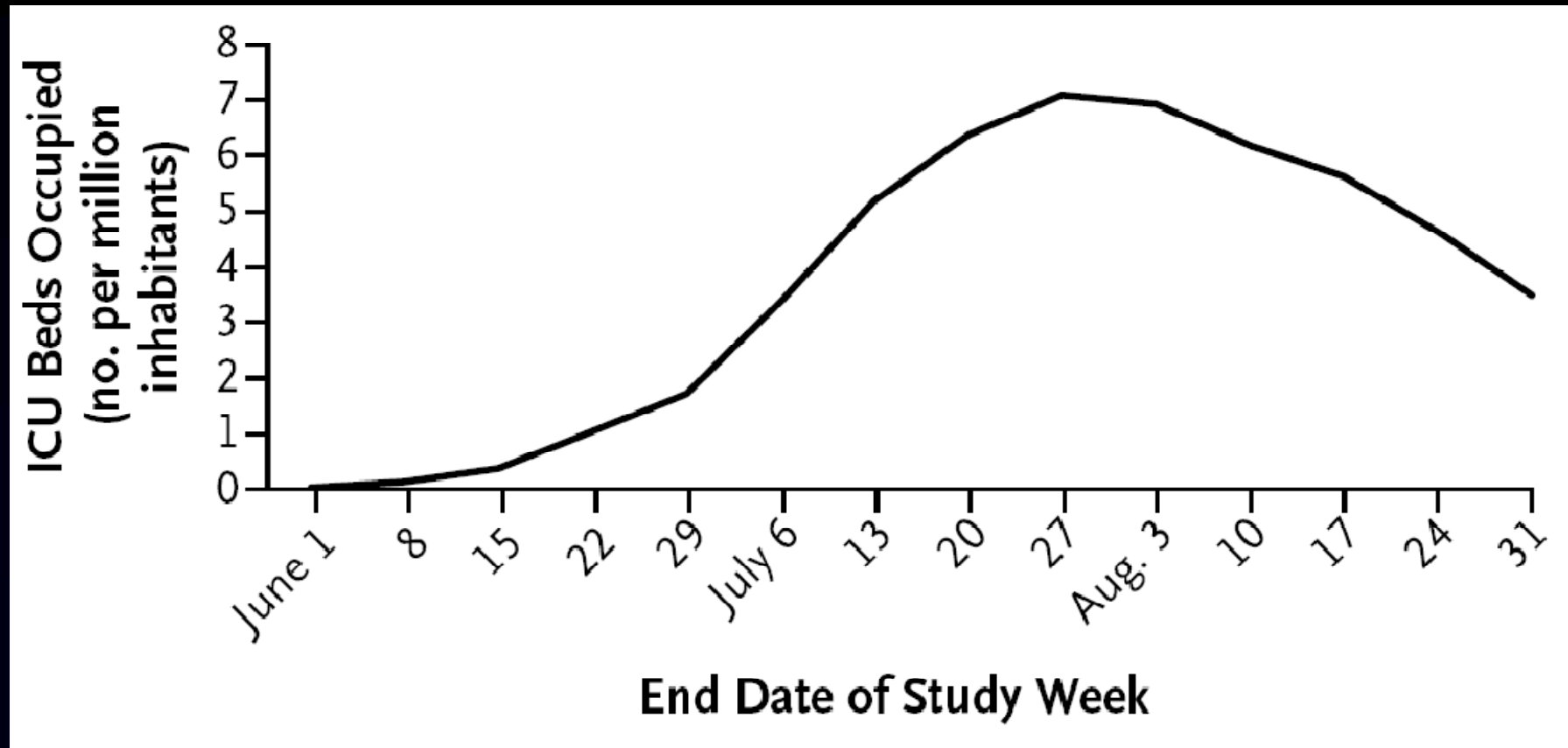


9 weeks

N=722

H1N1 in Australia and New Zealand

ANZIC
NEJM 361:;2009

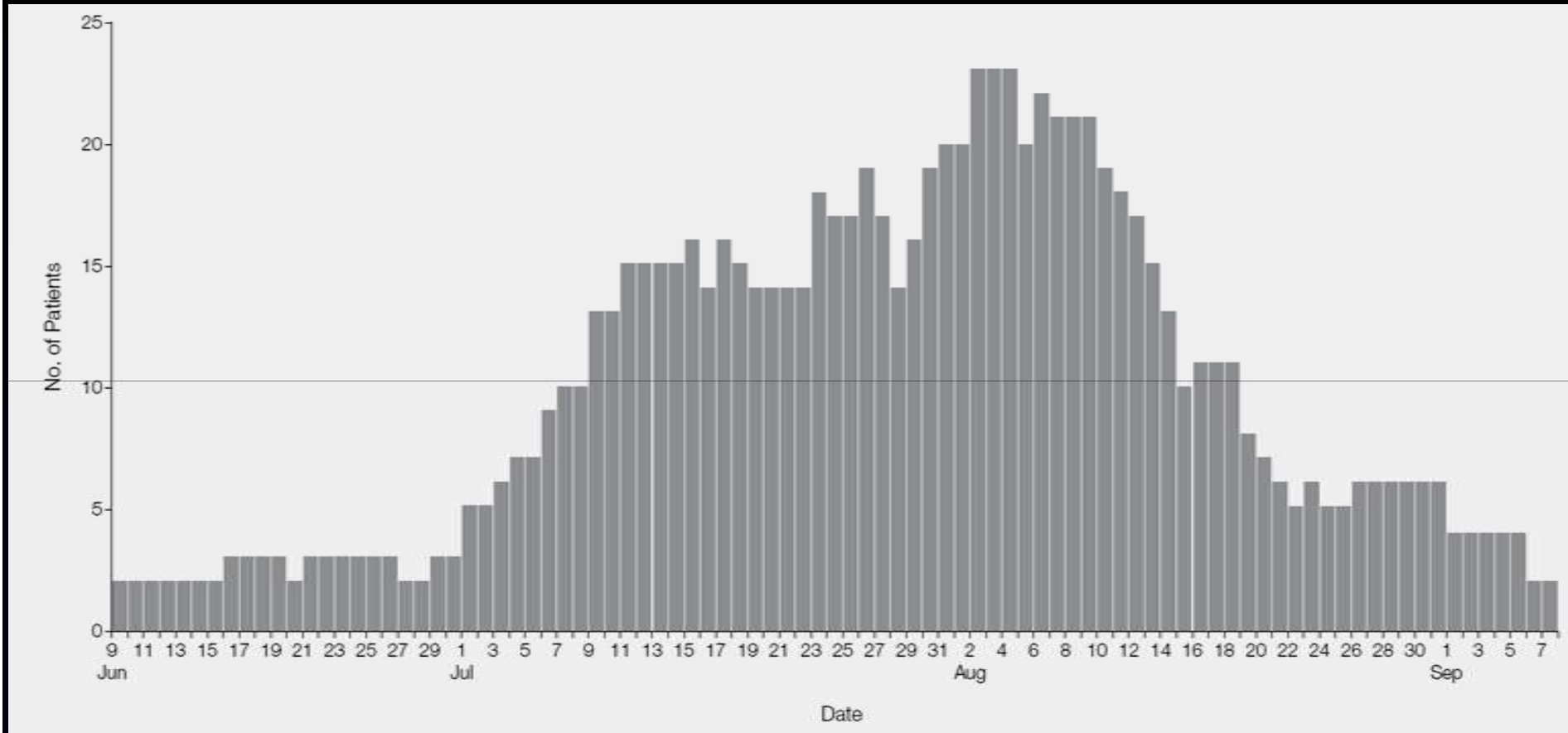


9 weeks

N=722

The burden on ECMO use

ANZ ECMO
JAMA 302:1535;2009



June 01 – AUG 31; 2009 15 ECMO units