SOCIETAT CATALANA
DE MEDICINA INTENSIVA I CRÍTICA

ARDS:

Epidemiology and Prognostic Factors

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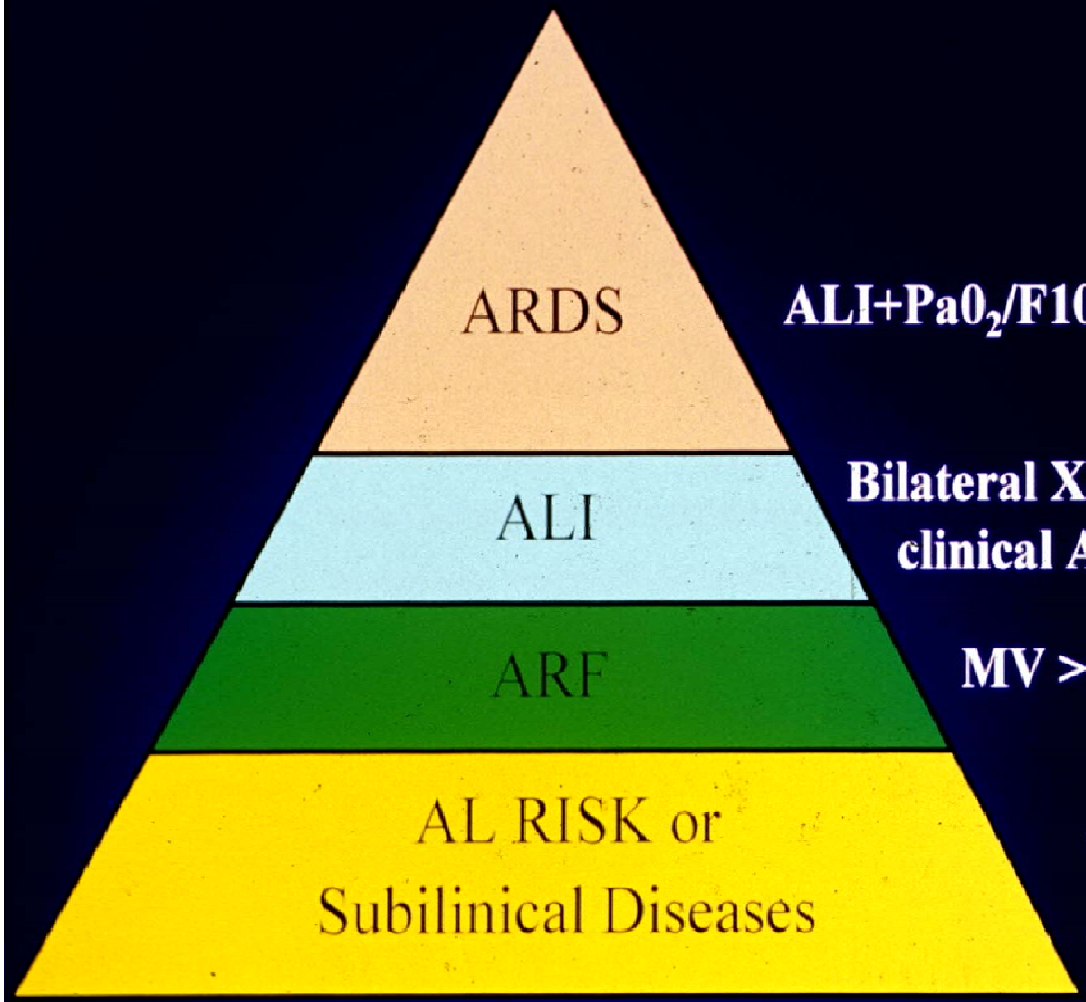
OUTLINE

- Diagnosis and Definition
- Incidence
- Outcome
- Prognostic Factors
- Early Detection
- Future Directions

WHY IS THE DEFINITION AND STRATIFICATION OF ARDS IMPORTANT?

- **Importance for Researchers:**
  - ✓ Clinical trial design, Epidemiological studies, linking basic and clinical research.
- **Importance to Clinicians:**
  - ✓ Apply research findings for therapeutics, and prognosis
- **Importance to Administrators:**
  - ✓ Resource Allocation

AECC ARDS DEFINITION



ALI+$Pa0_2/F10_2$< 200mmHg

Bilateral X-Ray Infiltrates, PWP < 18mmHg or clinical Absence LVF, $Pa0_2/F10_2$ < 300mmHg

MV > 24h, Acute Onset

Trauma, Sepsis, Pneumonia, Aspiration.

Am J Respir Crit Care Med 1994;149:818

AECC Definition and Autopsy

Patients	Clinical Criteria for ARDS		No Clinical Criteria for ARDS		Sensitivity (95% CI), %†	Specificity (95% CI), %‡	Positive Likelihood Ratio (95% CI)§	Negative Likelihood Ratio (95% CI)‖
	Diffuse Alveolar Damage, *n*	No Diffuse Alveolar Damage, *n*	Diffuse Alveolar Damage, *n*	No Diffuse Alveolar Damage, *n*				
All patients (*n* = 382)	84	43	28	227	75 (66–82)	84 (79–88)	4.7 (3.5–6.3)	0.3 (0.2–0.4)
Patients with risk factors for ARDS (*n* = 284)	84	43	27	130	76 (67–83)	75 (68–81)	3.0 (2.3–4.0)	0.3 (0.2–0.5)
Patients with pulmonary risk factors (*n* = 106)	27	19	17	43	61 (47–74)	69 (57–79)	2.0 (1.3–3.1)	0.6 (0.4–0.8)
Patients with extrapulmonary risk factors (*n* = 178)	57	24	10	87	85 (75–92)	78 (70–85)	3.9 (2.7–5.7)	0.2 (0.1–0.3)

* ARDS = acute respiratory distress syndrome.
† Sensitivity = True positives/(true positives + false negatives). True positives were patients with clinical criteria for ARDS and with diffuse alveolar damage in autopsy. False negatives were patients without clinical criteria for ARDS and with diffuse alveolar damage at autopsy.
‡ Specificity = True negatives/(true negatives + false positives). True negatives were patients without clinical criteria for ARDS and without diffuse alveolar damage at autopsy. False positives were patients with clinical criteria for ARDS and without diffuse alveolar damage at autopsy.
§ Positive likelihood ratio = sensitivity/(1 − specificity).
‖ Negative likelihood ratio = (1 − sensitivity)/specificity.

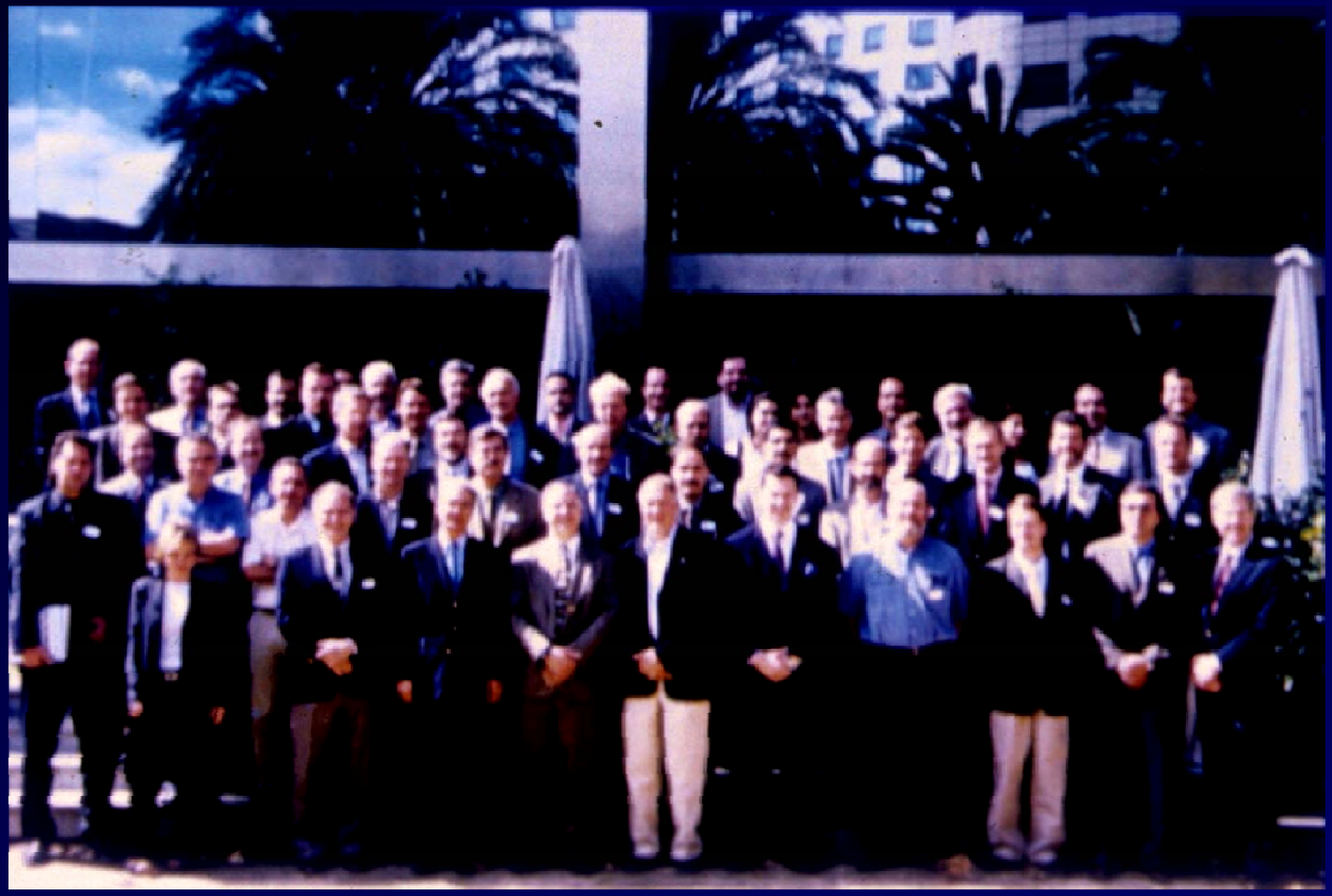
Ann Intern Med 2004;141:440-45

AMERICAN-EUROPEAN CONSENSUS CONFERENCE (AECC) DEFINITION

	AECC Definition	Limitations
Timing	Acute onset	No definition of acute
ALI category	All patients with PaO_2/FiO_2 <300	Misinterpreted as 200< PaO_2/FiO_2 <300 leading to confusing ALI/ARDS term
Oxygenation	PaO_2/FiO_2 ≤ 300 mmHg (regardless of PEEP)	Inconsistency of PaO_2/FiO_2 ratio due to the effect of PEEP and/or FiO_2
Chest Radiograph	Bilateral infiltrates seen on frontal chest radiograph	Poor interobserver reliability of chest radiograph interpretation
PAWP	PAWP ≤ 18 mmHg when measured or no clinical evidence of left atrial hypertension	Increased PAWP and ARDS may coexist
Risk Factor	None	Not formally included in definition

THIRD EUROPEAN-AMERICAN CONSENSUS CONFERENCE ON ARDS

(Barcelona, September 2000)



DIAGNOSTIC CRITERIA FOR VARIOUS FORMS OF ACUTE PULMONARY DYSFUNCTION

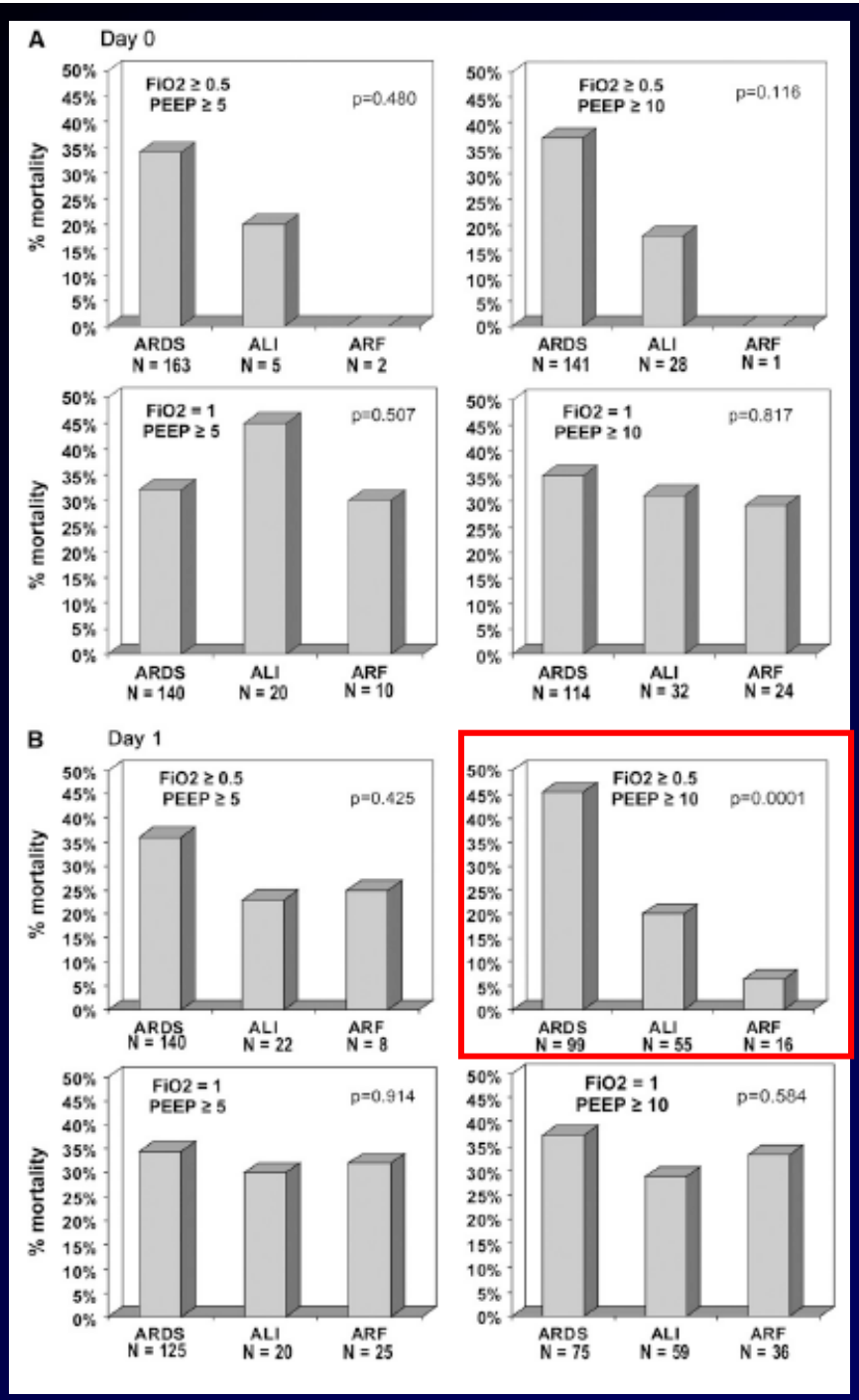
ACUTE PULMONARY DYSFUNCTION	PaO2 / FIO2	Chest Radiograph
ACUTE LUNG INJURY	0 - 300 mmHg	Bilateral infiltrates
ARDS	0 - 200 mmHg	Bilateral infiltrates
ACUTE LUNG FAILURE	0 - 300 mmHg	Any infiltrate

ACUTE < 7 days

PaO2 / FIO2=sustained hypoxemia + PEEP $\geq$5 cmH2O

CXR= bilateral opacities (patchy or asymetrical) consistent with pulmonary edema

Clinical or echocardiography absence LVF



PEEP/FIO_2 TRIAL AND SEVERITY OF ARDS

Am J Respir Crit Care Med 2007;176:795-804

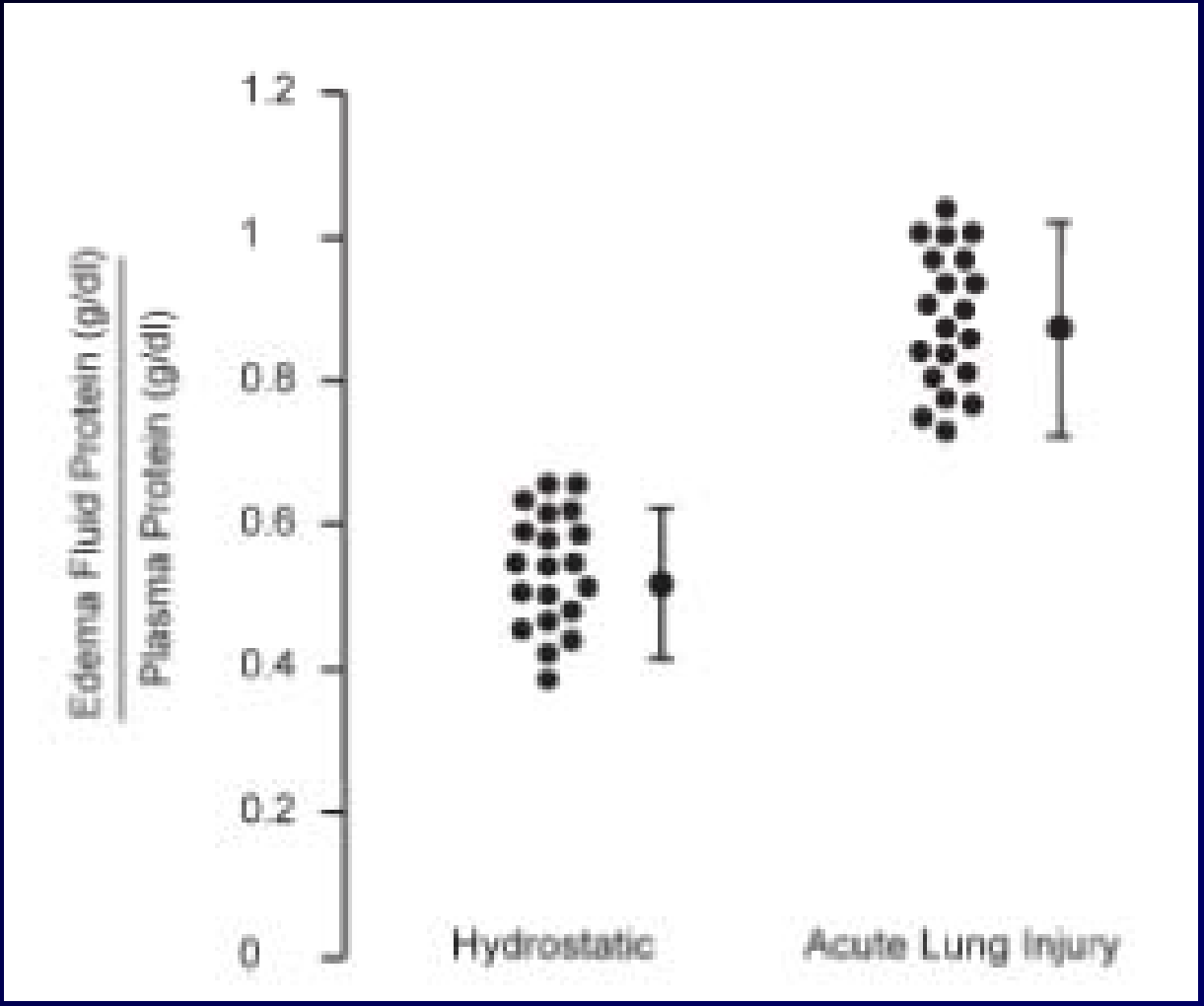
BERLIN DIAGNOSTIC: CRITERIA FOR ARDS (2011)

	Mild ARDS	Moderate ARDS	Severe ARDS
Timing	Within 1 week of a known clinical insult or new/worsening respiratory symptoms		
Oxygenation[a]	PaO_2/FiO_2 201-300 with PEEP/CPAP ≥ 5 cmH_2O	PaO_2/FiO_2 ≤ 200 with PEEP ≥ 5 cmH_2O	PaO_2/FiO_2 ≤ 100 with PEEP ≥ 10 cmH_2O
Imaging (chest x-ray or CT scan)[b]	Bilateral opacities	Bilateral opacities	Opacities involving at least 3 quadrants
Origin of Edema	Respiratory failure not fully explained by cardiac failure or fluid overload; need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present		
Additional Physiological Derangements	Not required	Not required	$V_{E(corr)}$ ≥ 10 L/min[c] or C_{rs} < 40 mL/cmH_2O[d]

BERLIN DIAGNOSTIC CRITERIA FOR ARDS: Problems

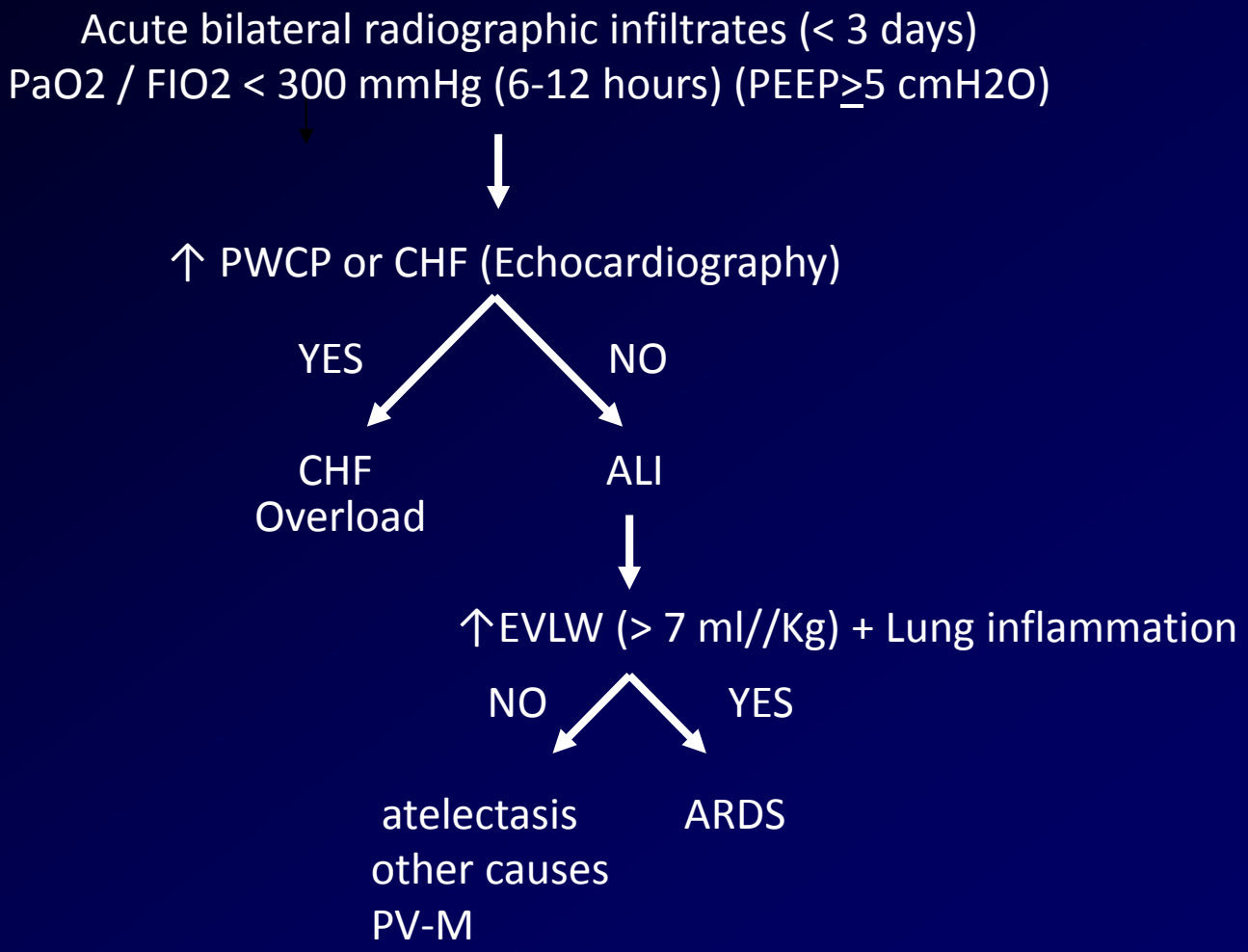
- Not validated
- Create confusion
- Permeability?
- Lung edema?
- Pulmonary inflamation?
- Severe ARDS: Crs

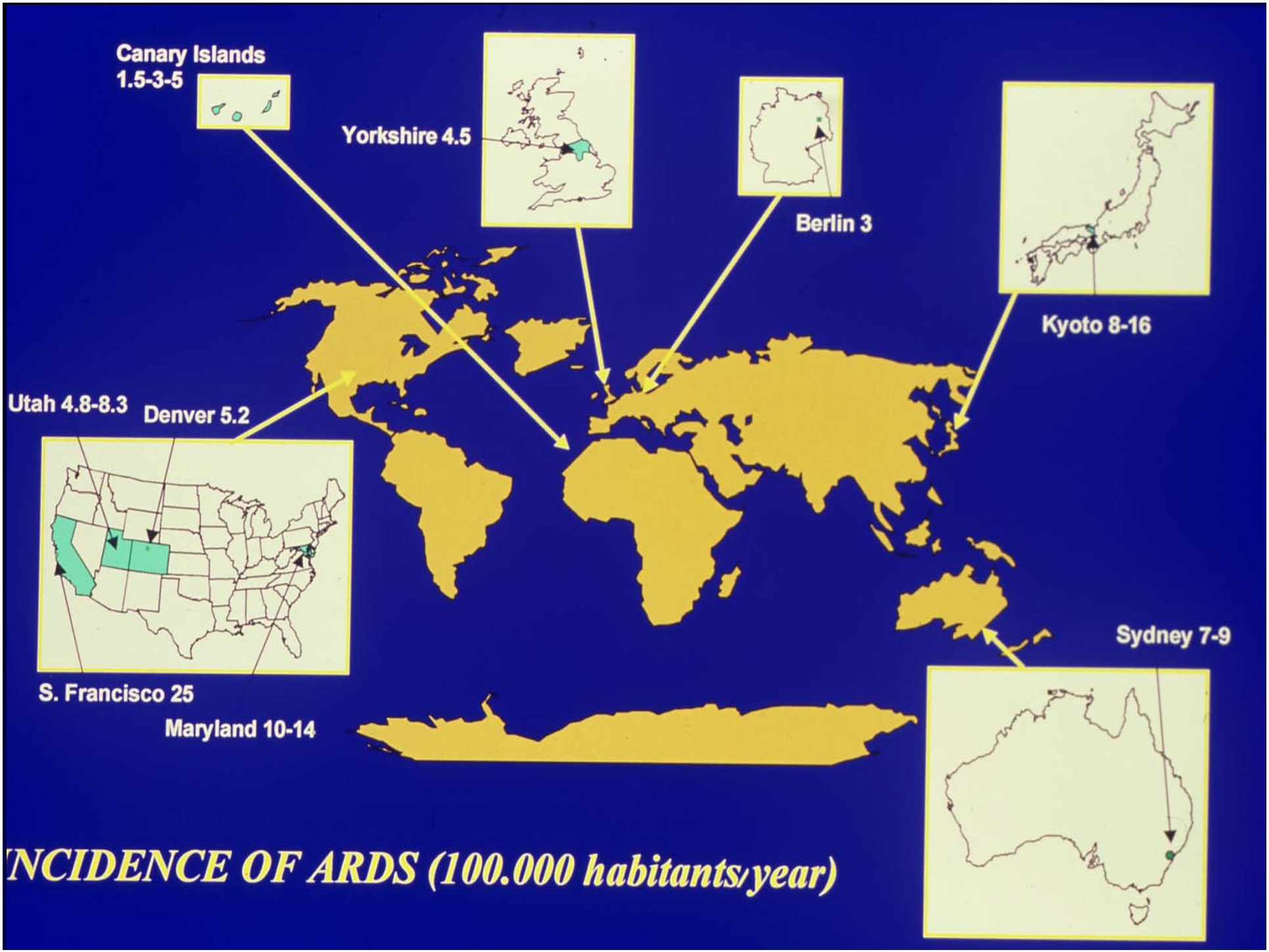
INCREASED LUNG PERMEABILITY IN ALI/ARDS



Am J Respir Cell Mol Biol 2005;33:319-327

ARDS DIAGNOSIS ALGORITHM




Canary Islands
1.5-3-5
Yorkshire 4.5
Berlin 3
Kyoto 8-16
Utah 4.8-8.3
Denver 5.2
S. Francisco 25
Maryland 10-14
Sydney 7-9
NCIDENCE OF ARDS (100.000 habitants/year)

INCIDENCE OF ALI/ARDS IN ARDS AND OUTCOME (1996-1999)

Study	Incidence	Mortality
ARDS NET (1996-1999)	64/10^5 /yr 2.2/ICU bed/yr	40%
ALIVE (1999)	12.7%/ICU adms.	42-58.8%
AUSTRALIA (1999)	22-34/10^5 /yr	32-38%
KING COUNTRY (1999)	70/10^5 /yr	30%
BRITISH COLUMBIA (1997)	8.4/10^5 /yr	37.5%
A. ESTEBAN (1998)	4.5% ARF	52%

INCIDENCE OF ACUTE LUNG INJURY AND ARDS AND MORTALITY FROM THESE CONDITIONS*

Variable	Acute Lung Injury	ARDS
Cases — no.	1,113	828
Crude incidence — no. per 100,000 person-yr	78.9	58.7
Age-adjusted incidence — no. per 100,000 person-yr†	86.2	64.0
Mortality (95% CI) — %	38.5 (34.9–42.2)	41.1 (36.7–45.4)
Estimated annual cases — no.†	190,600	141,500
Estimated annual deaths — no.†	74,500	59,000
Estimated annual hospital days — no.†	3,622,000	2,746,000
Estimated annual days in ICU — no.†	2,154,000	1,642,000

* ARDS denotes acute respiratory distress syndrome, and CI confidence interval.
† U.S. estimates, age-adjusted to the 2000 Census, are shown.

G.Rubenfeld N Engl Med 2005;353:1685-93

ALIEN Study: Lung Protective MV

(Nov 2008-Oct 2009)

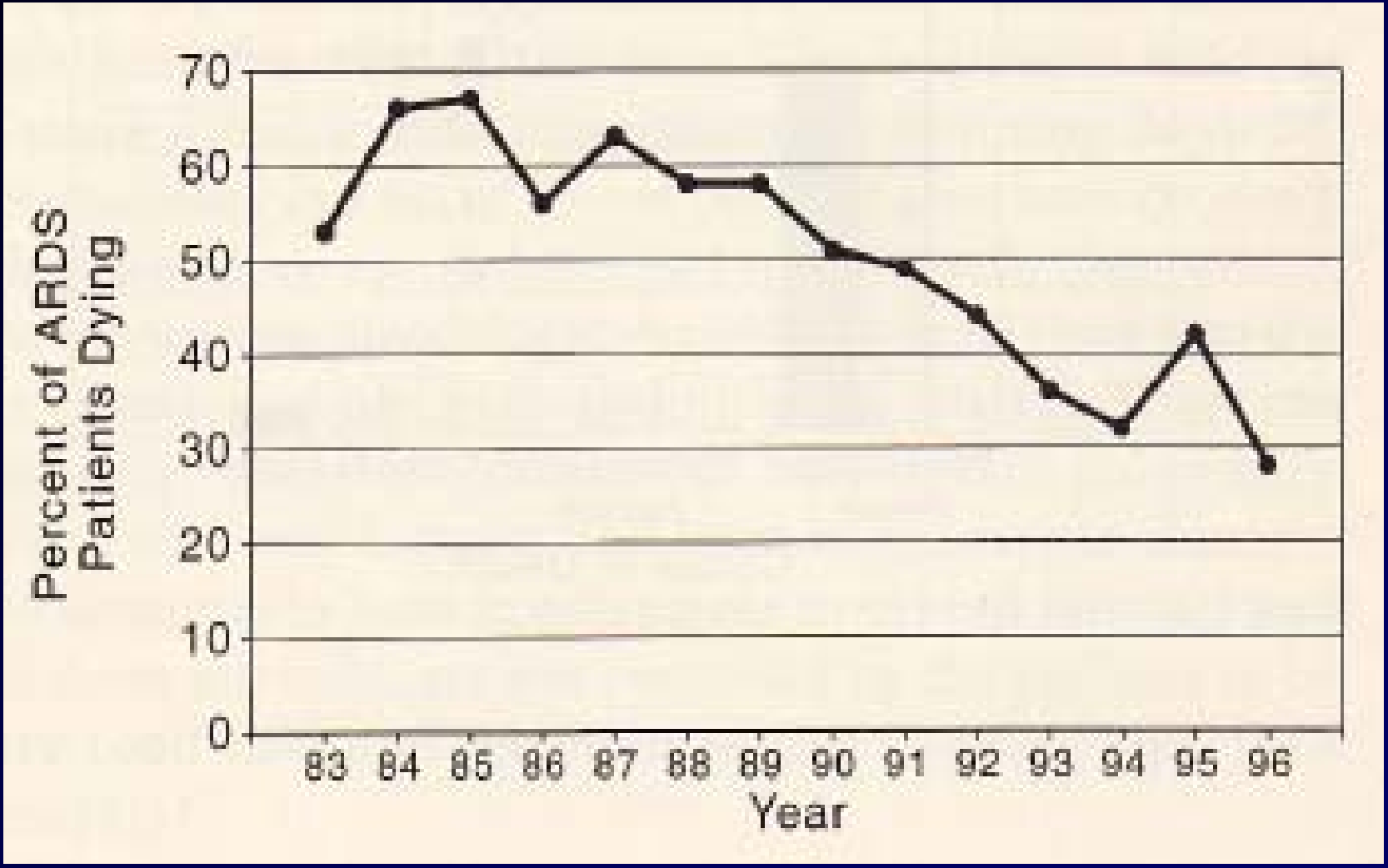
- MV pts 3,462/11,363 ICU admissions
- ARDS 255: 2.2% of ICU admissions

  7.4% of MV>24 hr
- Incidence: 7.2/100,000/year
- Hospital mortality: 47.8%

Intensive Care Med 2011;37:1932-41

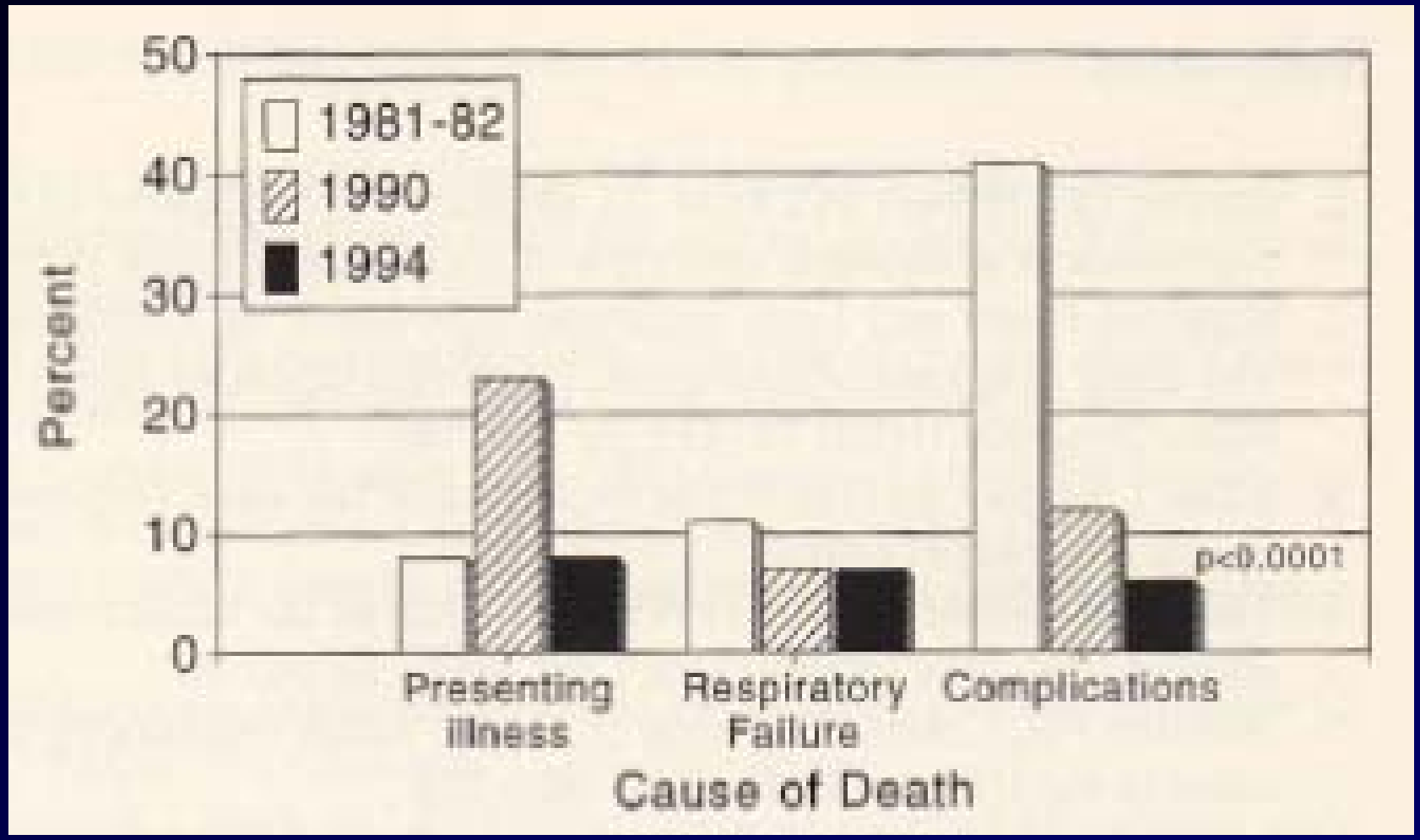
IMPROVED SURVIVAL OF ARDS

(1983-1993)



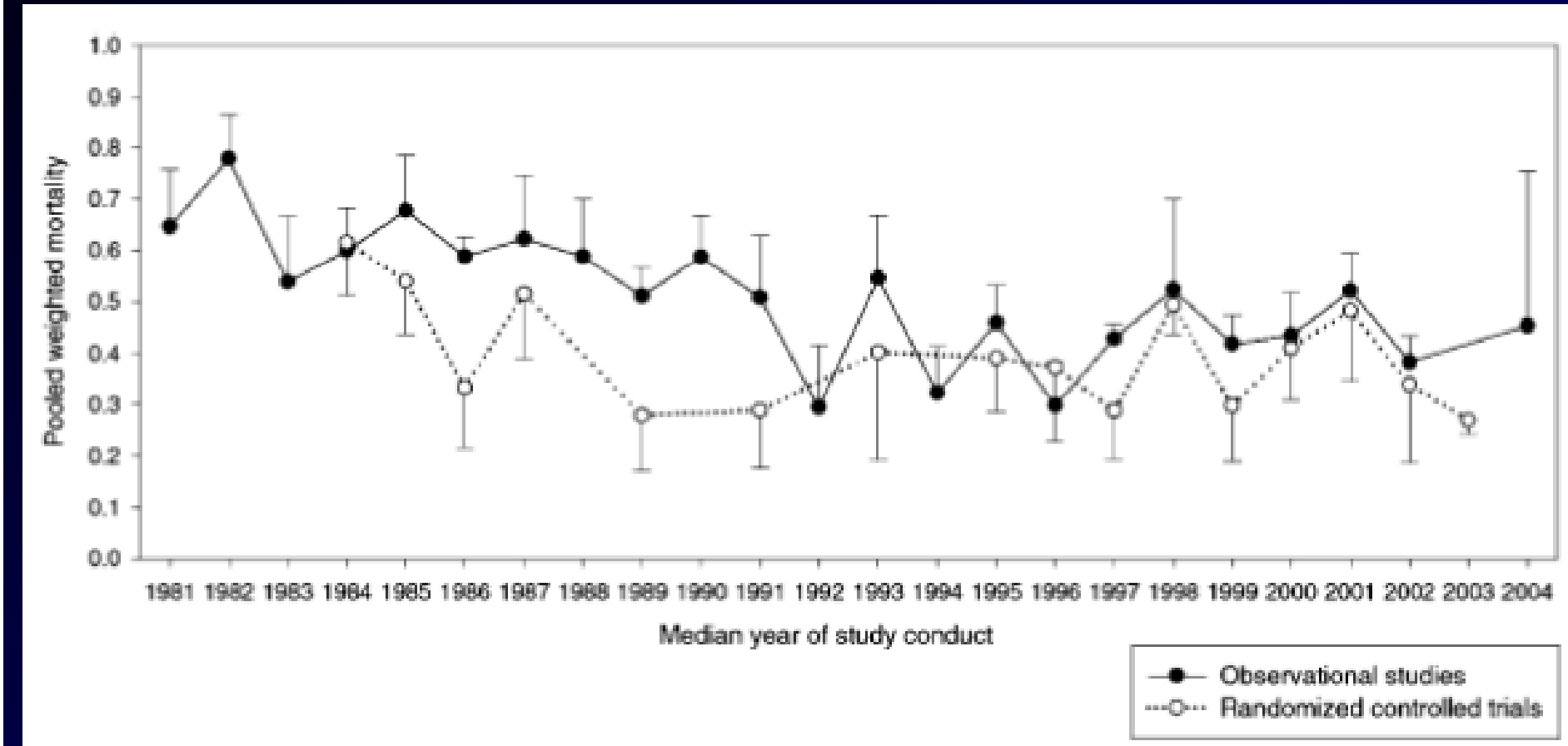
JAMA 1995;273:301-309

IMPROVED SURVIVAL OF ARDS:
Complications Decrease



JAMA 1995;273:301-309

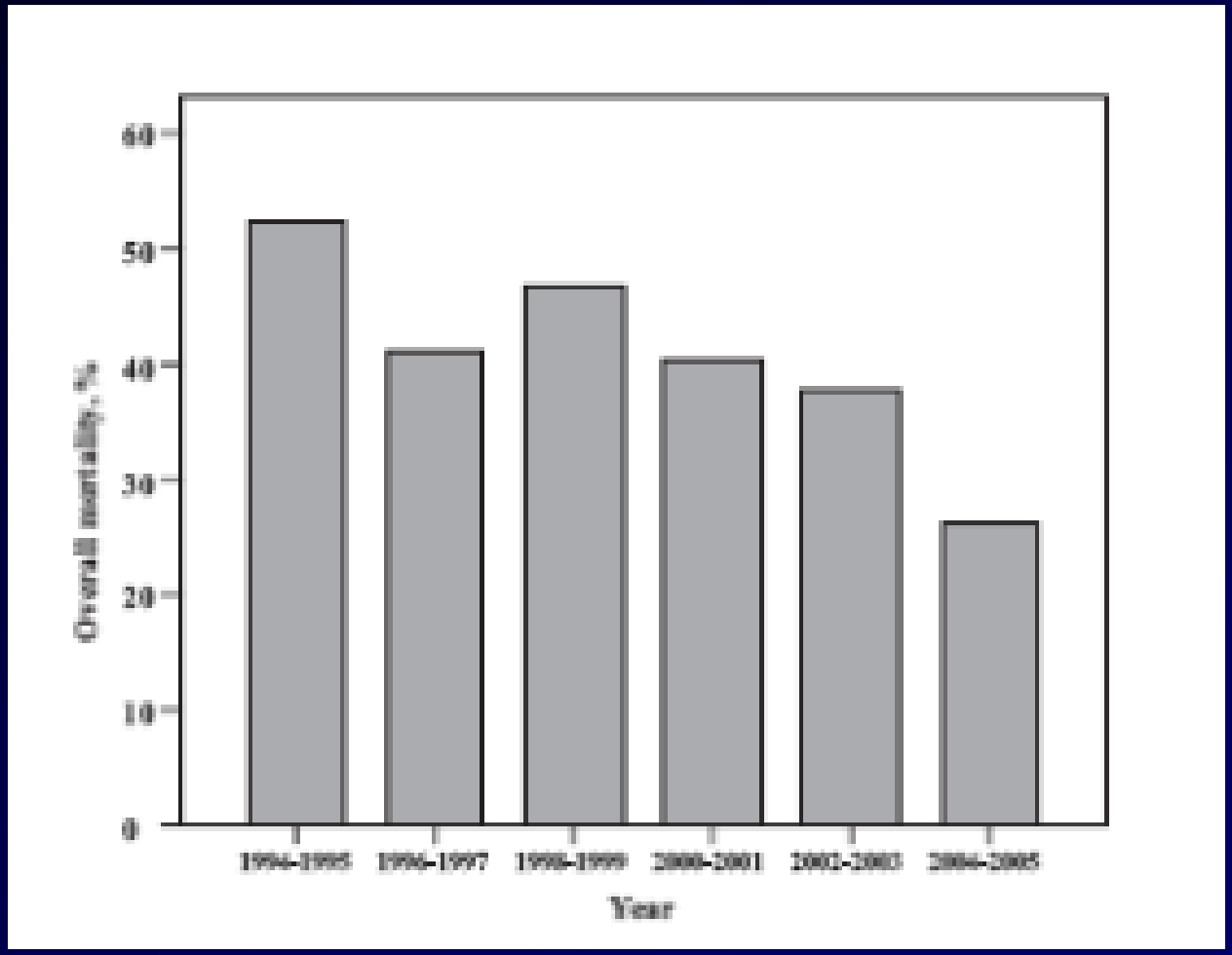
HAS MORTALITY FROM ARDS DECREASE OVER TIME?



Phua J. Am J Respir Crit Care Med 2009;179:220-227

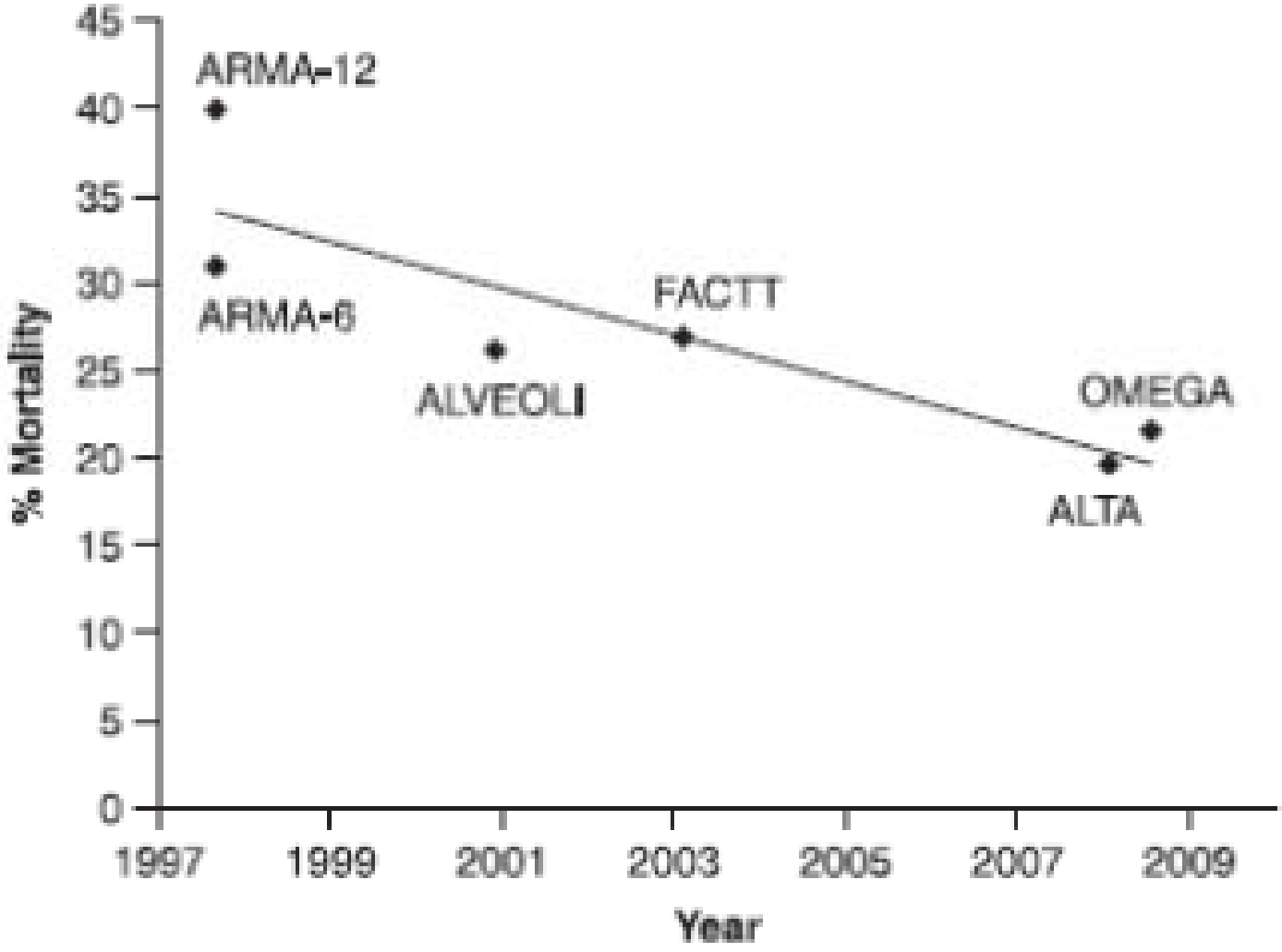
ALI/ARDS MORTALITY DECREASE OVER TIME

(72 Studies)



Zambon M. CHEST 2008;133:1120-27

ARDS-Net 60-day MORTALITY



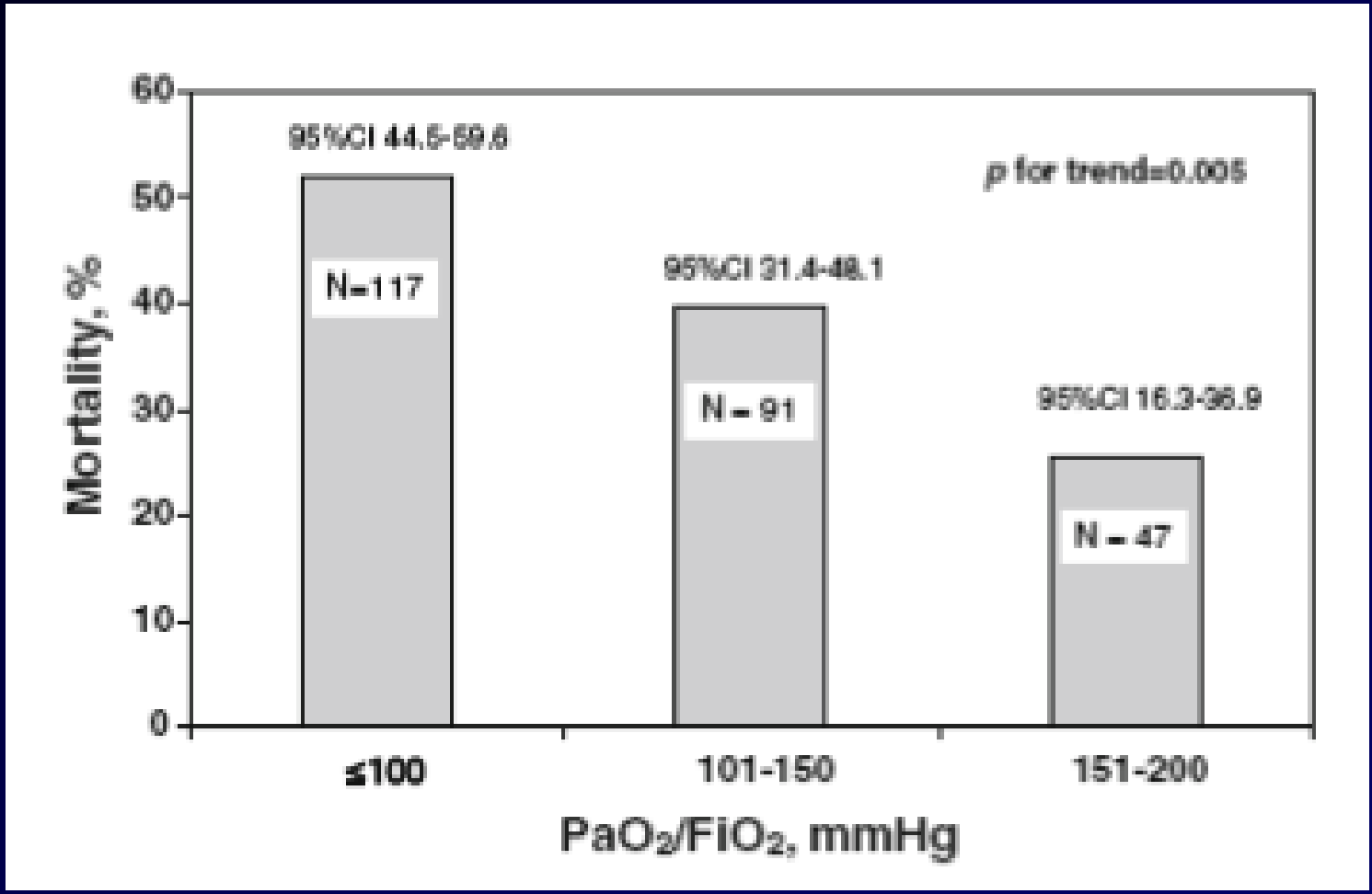
Spragg RG. Am J Respir Crit Care Med 2010;181:1121-1127

ATTRIBUTABLE MORTALITY

Disease	Attributable mortality
ALI[a]	17,000–43,000
Acute respiratory failure[b]	60,000–120,000
Acute myocardial infarction[c]	199,454
Breast cancer[c]	41,528
HIV disease[c]	14,802
Asthma[c]	4,657

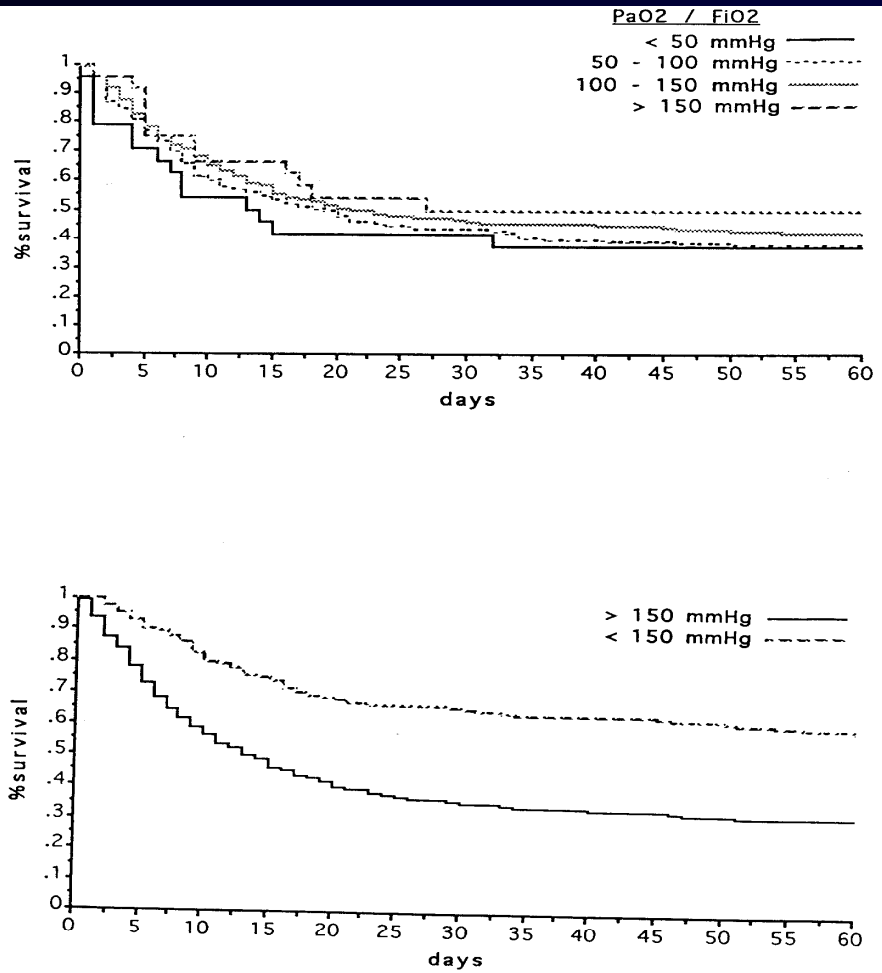
[a]Assumes incidence range 20–50 per 10^5 person-years, mortality of 40%, and U.S. 2000 census population of 215 million > age 15.
[b]Assumes incidence range 70–140 per 10^5 person-years and mortality of 40%, and U.S. 2000 census population of 215 million > age 15.
[c]Based on U.S. 1999 death certificate data (56).

ARDS HYPOXEMIA DEGREE and MORTALITY: ALIEN Study



Villar J. Intensive Care Med 2011;37:1932:1941

GAS EXCHANGE AND SURVIVAL IN 583 ARDS OF EUROPEAN COLLABORATIVE ARDS STUDY



Survival at 60 days in 583 ARDS according to gas exchange (PaO_2/FIO_2) at ICU admission (Fig A) and after 24 hours of treatment (Fig B, $p<0{,}0001$).

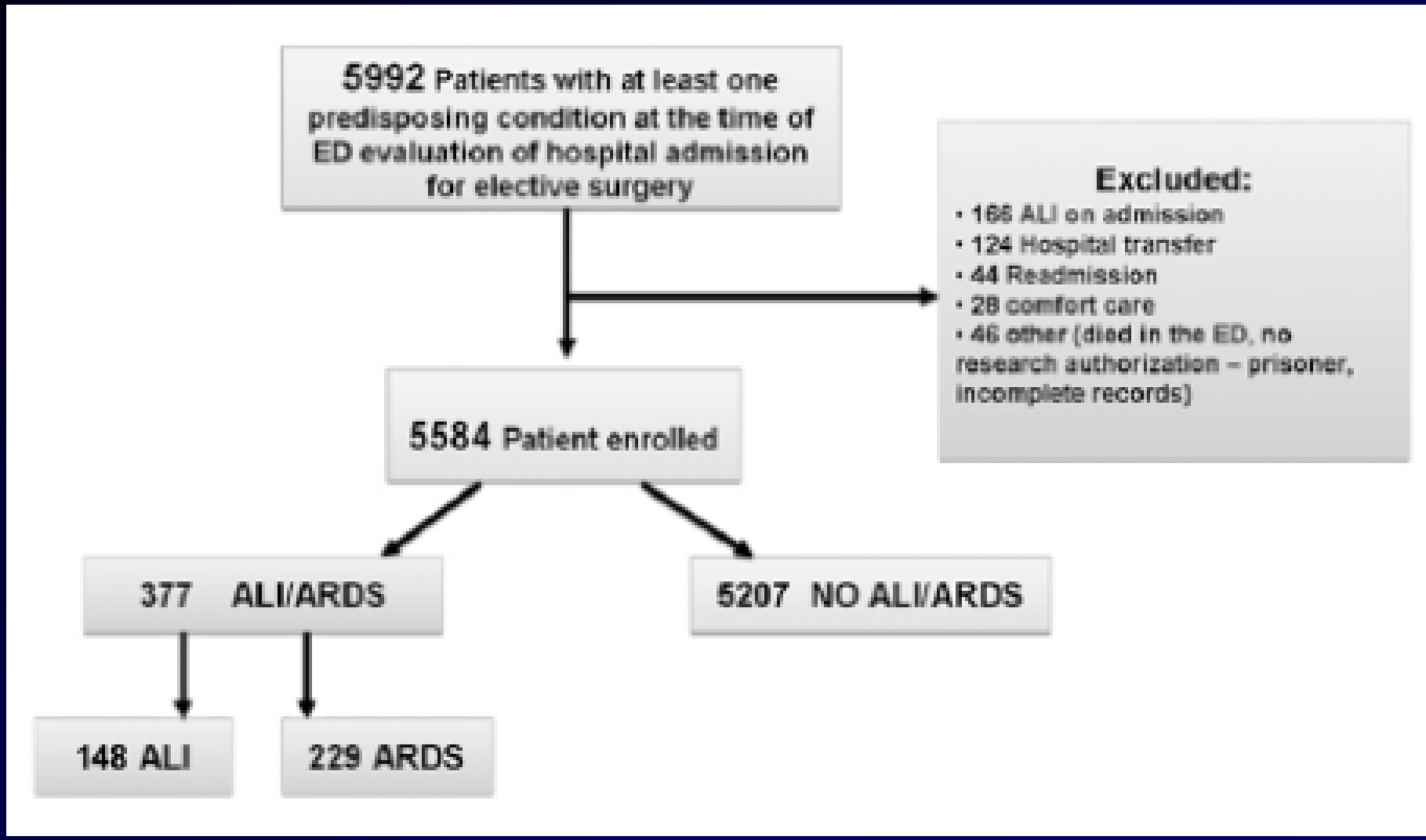
Intensive Care Med 1998;24:1018-10289

MORTALITY RATE WITH AND WITHOUT ARDS BY CLINICAL CONDITION, ADJUSTED FOR AGE, ISS, AND APACHE II SCORE

Condition	Mortality Rate no.with ARDS/ no.at risk (%) ARDS	No ARDS	No ARDS, Adjusted Mortality Rate (%)	Crude Mortality Ratio*	95% CI†
All clinical risks	111/179 (62.0)	98/516 (19.0)	26.6‡	3.3	2.6-4.0
Multiple transfusions	32/46 (69.6)	24/69 (34.8)		2.0	1.4-2.9
Sepsis syndrome	51/74 (68.9)	50/101 (49.5)	55.2§	1.4	1.1-1.8
Any trauma	40/69 (58.0)	26/202 (12.9)	24.0¶	4.3	2.9-6.5
Pulmonary contusions	16/33 (48.5)	9/78 (11.5)		4.2	2.1-8.5
Multiple fractures	15/31 (48.4)	9/104 (8.6)		5.6	2.7-11.6
Aspiration	12/25 (48.0)	15/70 (21.4)		2.2	1.2-4.1
Drug overdose	9/26 (34.6)	7/174 (4.)		8.6	3.5-21.4
Near-drowning	1/3 (33.3)	2/5 (40.0)			

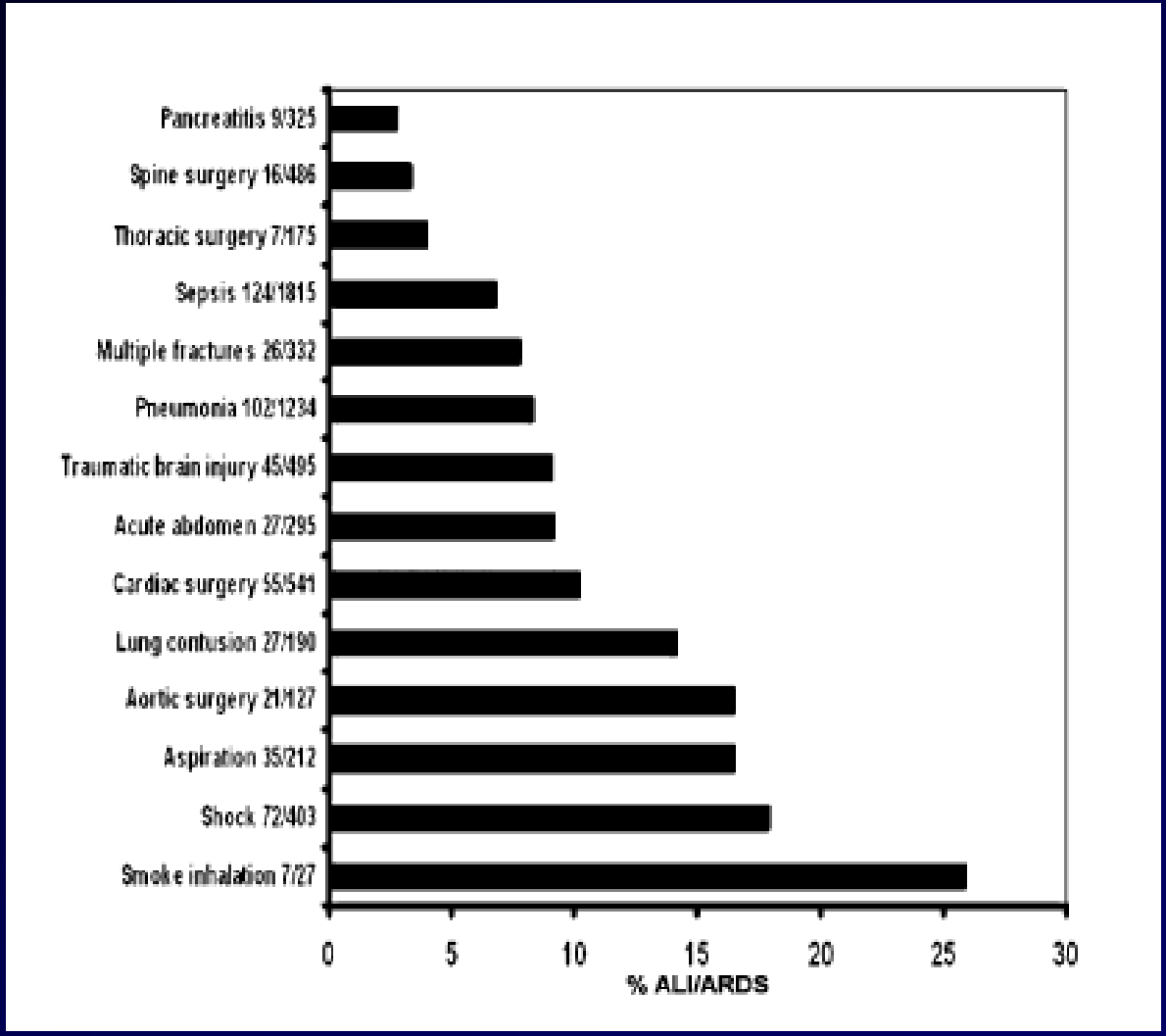
* Mortality
¶ Adjusted for age and ISS
† 95% CI
§ Adjusted for APACHE (first 24 h)
‡ Adjusted for age

Hudson L. Am J Respir Crit Care Med 1995;151:293-301



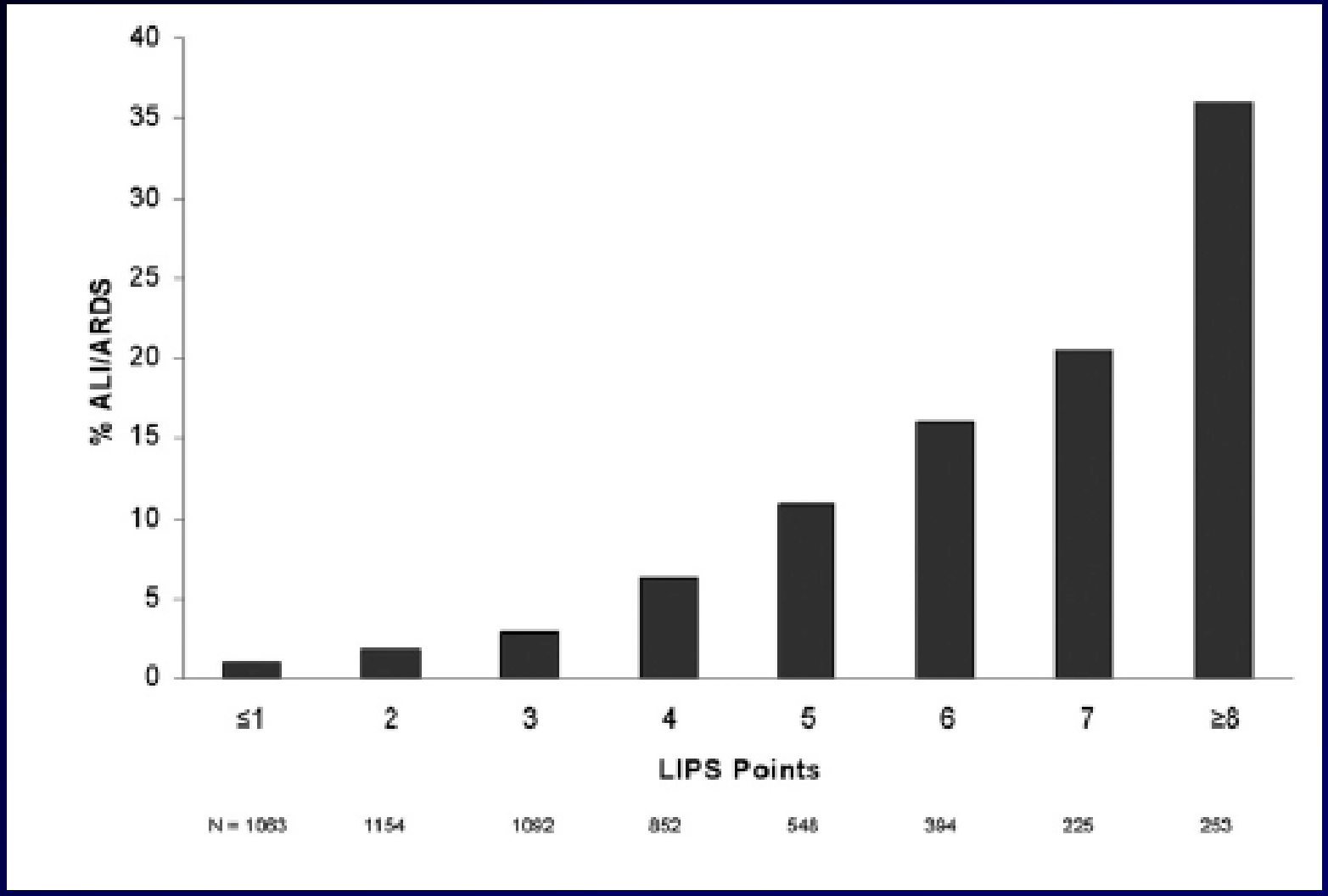
Gajic O. Am J Respir Crit Care Med 2011;183:462-470

ALI/ARDS FRECUENCY AND PREDISPOSING CONDITIONS



Gajic O. Am J Respir Crit Care Med 2011;183:462-470

ALI/ARDS RISK: LUNG INJURY PREDICTION SCORE (LIPS)



Gajic O. Am J Respir Crit Care Med 2011;183:462-470

FUTURE DIRECTIONS

- Prevention of ALI progress and Long-term sequelae
- Improve ARDS diagnosis by pulmonary biomarkers
- Composite outcome
- ARDS “TNM”: GOCA stratification
- Decrease mortality in RCT:
  - Increase number patients and centers
  - Increase generalizibility and inhomogeneity

Thank You!