

Online Data Supplement

eTable 1: Criteria for defining at-risk status* (Only one criterion had to be present to be defined as at-risk)

Risk factor	Definition
Trauma	Multiple fractures (fracture of two long bones, an unstable pelvic fracture, or one long bone and a pelvic fracture) and/or pulmonary contusions (infiltrates on chest radiographs within 8 hours of admission to the emergency room and evidence of blunt trauma to the chest such as fractured ribs or ecchymosis overlying the infiltrate).
Sepsis	Consensus criteria(1): a known or suspected source of systemic infection and at least two of the following: a) temperature >38°C or <36°C; b) heart rate >90 beats/min; c) respiratory rate >20 breaths/min or PaCO ₂ <32 mm Hg; d) WBC count >12,000/mm ³ , <4000/mm ³ , or >10% bands.
Transfusion	8 or more units of blood product transfused within 24 hours.
Aspiration	Witnessed or documented aspiration of gastric contents into the trachea or documented retrieval of gastric contents from the oropharynx, endotracheal tube, or tracheobronchial tree.
Pneumonia	Two or more of the following: a) new infiltrate on chest radiograph; b) temperature >38.3°C or <36.0°C or WBC >12,000 or <4,000 or >10% bandemia; c) positive microbiological culture from the lower respiratory tract or blood with an appropriate organism

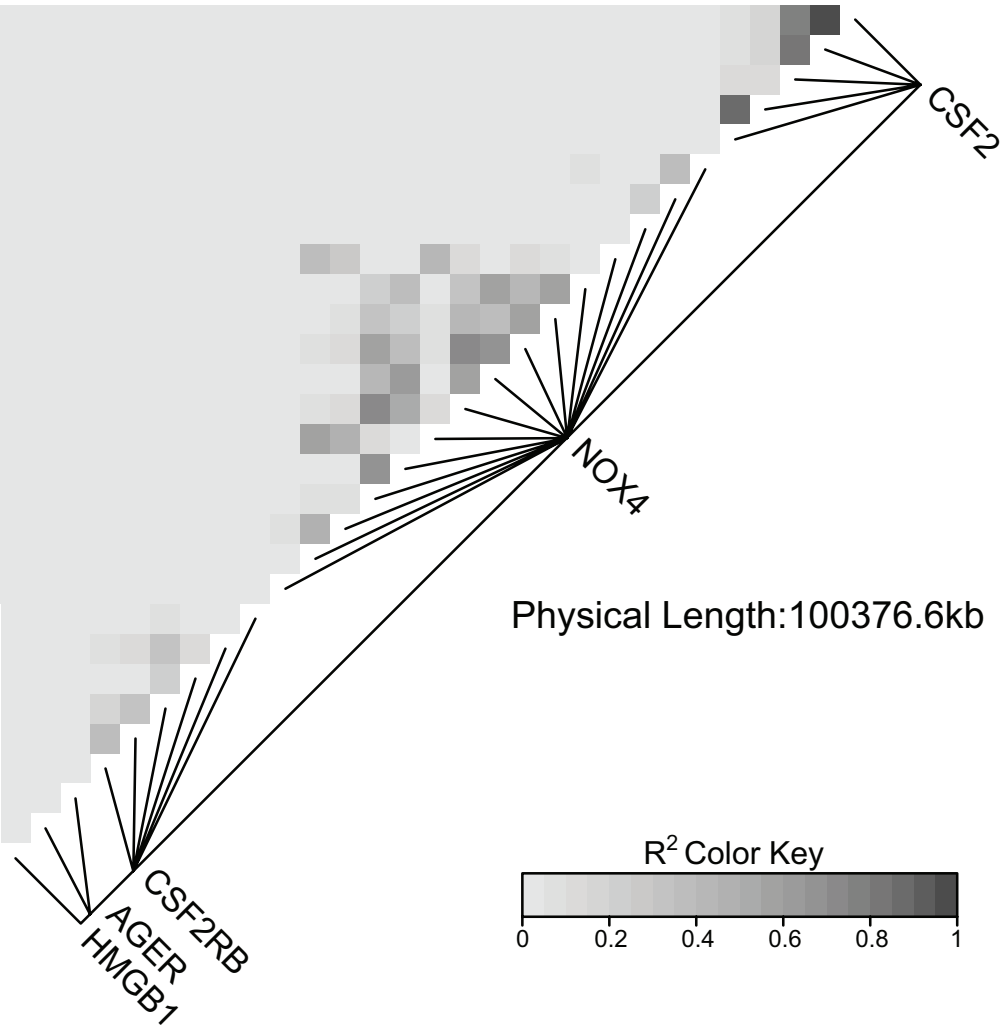
*Slightly modified from Gong et al.(2) to match definitions used by the NHLBI ARDS Network.

eTable 2: Inclusion and exclusion criteria	
Inclusion criteria	
Onset within 24h of	
	Requirement for positive pressure ventilation through an endotracheal tube
	PaO ₂ /FIO ₂ ≤ 300*
	Bilateral infiltrates consistent with pulmonary edema on frontal chest radiograph
	No clinical evidence of left-sided heart failure to account for bilateral pulmonary infiltrates
Exclusion criteria	
	Age younger than 13 years
	Neuromuscular disease that impairs ability to ventilate without assistance
	Pregnancy
	Chronic hypercapnia (PaCO ₂ >45 mmHg) or hypoxemia (PaO ₂ <55 mmHg)
	Severe pulmonary hypertension (mPAP>40mmHg)

	Chronic ventilator dependency
	Morbid obesity (greater than 1 kg weight / cm height)
	Severe burns (>40% body surface area)
	Terminal disease, including cancer
	End-stage liver disease
	Diffuse alveolar hemorrhage or bone marrow transplant
	Recent (≤ 30 d) coronary syndrome
	Lack of commitment to full life support
	Moribund patient
*Cutoff was adjusted for ambient barometric pressure for patients in Utah and Colorado. Adjusted PaO ₂ /FIO ₂ threshold was calculated by dividing local barometric pressure by 760 and then multiplying by 300.	

eFigure 1

Heatmap: Pairwise LD in R² of tested SNPs



References

1. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest*. 1992;101(6):1644-55.
2. Gong MN, Zhou W, Williams PL, Thompson BT, Pothier L, Christiani DC. Polymorphisms in the mannose binding lectin-2 gene and acute respiratory distress syndrome. *Crit Care Med*. 2007;35(1):48-56.