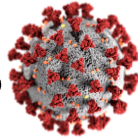


EVENT DEFINITION FORM

Event: Acute respiratory distress syndrome
Outcome/covariate: outcome
Version: 1.0
Status: final

Contributing authors

authors	Role	
Marta Rojo Villaescusa	Drafting v0.1	June 24 2020
Miriam Sturkenboom	Review epi/codes	June 28, 2020
Marta Rojo Villaescusa	Codemapper/ BGR	
Miriam Sturkenboom	Review codes	August 14-2020
Leila Belbachir	Medical review	23-08-2020
Leila & Miriam	Update after discussion	25-08-2020
Caitlin Dodd	Algorithm proposal	03-09-2020
Carlos Durán	Rev. narrow/possible assignment	28-03-2020
Miriam Sturkenboom	Inclusion of codes for final ACCESS report	23-08-2021



1. Event definition Search existing definitions, learned societies, Brighton Collaboration

The acute respiratory distress syndrome (ARDS) was defined in 2011 by a panel of experts comprised of the European Society of Intensive Care endorsed by the American Thoracic Society and the society of Critical Care Medicine, known as the Berlin definition.^[1]

The Berlin definition of ARDS is shown in table 1.

Table 1. The Berlin Definition of Acute Respiratory Distress Syndrome.^[1]

Acute Respiratory Distress Syndrome	
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging^a	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation^b	
• Mild	200 mm Hg < PaO ₂ /FIO ₂ ≤ 300 mm Hg with PEEP or CPAP ≥5 cm H ₂ O ^c
• Moderate	100 mm Hg < PaO ₂ /FIO ₂ ≤ 200 mm Hg with PEEP ≥5 cm H ₂ O
• Severe	PaO ₂ /FIO ₂ ≤ 100 mm Hg with PEEP ≥5 cm H ₂ O

Abbreviations: CPAP, continuous positive airway pressure; FIO₂, fraction of inspired oxygen; PaO₂, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.

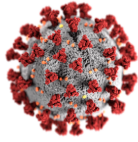
^a Chest radiograph or computed tomography scan.

^b If altitude is higher than 1000 m, the correction factor should be calculated as follows: [PaO₂/FIO₂_(barometric pressure/760)].

^c This may be delivered noninvasively in the mild acute respiratory distress syndrome group.

2. Synonyms / lay terms for the event

- acute lung injury
- adult respiratory distress syndrome
- ARDS
- noncardiogenic pulmonary edema
- increased-permeability pulmonary edema



3. Laboratory tests that are specific for event

Regularly obtaining complete blood count with differential, comprehensive metabolic panel, serum magnesium, serum ionized calcium, phosphorus levels, blood lactate level, coagulation panel, troponin, cardiac enzymes, and Creatine Kinase Myocardial Band (CK-MB) are recommended if clinically indicated.^[2]

4. Diagnostic tests that are specific for event

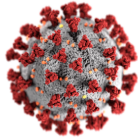
- **Chest radiography** to check acute onset, bilateral lung infiltrates of a non-cardiac origin.^[2]
- Partial pressure of arterial oxygen PaO₂/ (fraction of inspired oxygen) FiO₂ ratio of less than 300 mmHg.
- **CT scan** of the chest may be required in cases of pneumothorax, pleural effusions, mediastinal lymphadenopathy, or barotrauma to properly identify infiltrates as pulmonary in location.^[2]
- **Pulmonary artery catheter measurements.** Invasive method to assess left ventricular function in order to differentiate from or quantify the contribution of congestive heart failure to the overall clinical picture.^[2]
- **Echocardiography or thoracic bioimpedance or pulse contour analysis.** Non-invasive method for the assessment of left ventricular function to differentiate from or quantify the contribution of congestive heart failure to the overall clinical picture.^[2]
- **Bronchoscopy** to assess pulmonary infections and obtain material for culture.^[2]

5. Drugs that are used to treat event

The main treatment strategy is supportive care and focuses on 1) reducing shunt fraction, 2) increasing oxygen delivery, 3) decreasing oxygen consumption, and 4) avoiding further injury.^[2]

The following medications are used for management of acute respiratory distress syndrome:^[3]

Management of hypoxaemia	
Supplemental oxygen	Intubation/mechanical ventilation (most patients) Non-invasive ventilation for mild ARDS or to decrease intubation rates
Inflammation management (corticosteroids)	Prolonged low doses (1 mg·kg ⁻¹ ·day ⁻¹) methylprednisolone treatment accelerates ARDS resolution and improves several clinical outcomes
Fluid management	Aim for central venous pressure <4 mmHg or PAOP <8 mmHg to decrease pulmonary oedema
Decrease oxygen consumption	Antipyretics, sedatives, analgesics, and paralysis agents
Increase oxygen delivery	Inotropics to increase filling pressure (if no pulmonary oedema) Inhaled vasodilators (nitric oxide, prostacyclin and prostaglandin)
Supportive care	Sedation and analgesia



Neuromuscular blockade if severe ARDS

Nutritional support (enteral)

6. Procedures used specific for event treatment

Management of hypoxemia

- Prone positioning.
- Restrict transfusions to maintain haemoglobin to 7–9 g·dL⁻¹.^[3]

Supportive care

- Haemodynamic monitoring/management via central venous catheter.^[3]
- Glucose control.^[3]
- Tracheostomy. It facilitates weaning from the ventilator, making it easy to clear the secretions and is more comfortable for the patient. The tracheostomy is usually done at 2 to 3 weeks.^[2]
- Percutaneous Endoscopic Gastrostomy (PEG).

7. Setting (outpatient specialist, in-hospital, GP, emergency room) where condition will be most frequently /reliably diagnosed

Emergency room and in-hospital setting.

8. Diagnosis codes or algorithms used in different papers to extract the events in Europe/USA: seek literature for papers that have studied this event, and see how they extracted/measured the event.

- **Veeravagu et al.**^[4]

ICD-9-CM codes 518.5 and 518.82

- **Reynolds et al.**^[5]

Respiratory disease codes from the International Classification of Diseases, 9th revision (ICD-9)

518.5 Pulmonary insufficiency following trauma and surgery

518.82 Other pulmonary insufficiency, not elsewhere classified

96.70 Continuous mechanical ventilation of unspecified duration

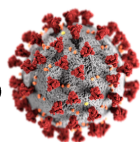
96.71 Continuous mechanical ventilation for < 96 h consecutively

96.72 Continuous mechanical ventilation for ≥96 h consecutively

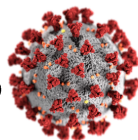
- **Chen et al.**^[6]

ICD-9-CM codes 518.82, 518.5

9. Codes used in ACCESS by



Coding system	Code	Code name	Concept	Concept name	Algorithm
ICD10/CM	J80	Adult respiratory distress syndrome	C0035222	Respiratory Distress Syndrome, Adult	Narrow
ICD10/CM	J81	Pulmonary oedema	C0034063	Pulmonary Edema	Possible
ICD10/CM	J81.1	Pulmonary edema NOS	C0034063	Pulmonary Edema	Possible
ICD10/CM	J96.9	Respiratory failure, unspecified	C1145670	Respiratory Failure	Narrow
ICD10/CM	R06.03	Acute respiratory distress	C0748355	Acute respiratory distress	Narrow
ICD10/CM	R09.2	Respiratory arrest			Narrow
ICD9CM	518.4	Acute pulmonary edema			Possible
ICD9CM	518.5	Pulmonary insufficiency following trauma and surgery	C0034076	Pulmonary insufficiency following trauma and surgery	Possible
ICD9CM	518.82	Other pulmonary insufficiency, not elsewhere classified	C0302379	Other pulmonary insufficiency, NEC in ICD9CM	Narrow
ICD9CM	96.71	Continuous invasive mechanical ventilation for less than 96 consecutive hours	C2349744	Continuous invasive mechanical ventilation for less than 96 consecutive hours	Narrow
ICD9CM	96.72	Continuous invasive mechanical ventilation for 96 consecutive hours or more	C2349745	Continuous invasive mechanical ventilation for 96 consecutive hours or more	Narrow
ICD9CM	799.1	Respiratory arrest			Narrow
ICPC2P	K77013	Oedema;pulmonary	C0034063	Pulmonary Edema	Possible
ICPC2P	R99004	Failure;respiratory	C1145670	Respiratory Failure	Narrow
RCD2	H541z	Pulmonary oedema NOS	C0034063	Pulmonary Edema	Possible
RCD2	H5853	Adult respiratory distress syn	C0035222	Respiratory Distress Syndrome, Adult	Narrow
RCD2	H59..	Respiratory failure	C1145670	Respiratory Failure	Narrow
RCD2	R2y1.	[D]Respiratory failure	C1145670	Respiratory Failure	Narrow
RCD2	R2y1z	[D]Respiratory failure NOS	C1145670	Respiratory Failure	Narrow
RCD2	H585.	Acquired respiratory distress syndrome			Narrow
RCD2	R0606	Respiratory distress			narrow
SCTSPA	19242006	edema pulmonar	C0034063	Pulmonary Edema	Possible
SNOMEDCT_US	19242006	Pulmonary edema	C0034063	Pulmonary Edema	Possible
SNOMEDCT_US	19242006	Pulmonary oedema NOS			possible
SNOMEDCT_US	51395007	Respiratory failure	C1145670	Respiratory Failure	Narrow
SNOMEDCT_US	65710008	Acute respiratory failure			narrow
SCTSPA	67782005	síndrome de distrés respiratorio agudo	C0035222	Respiratory Distress Syndrome, Adult	Narrow
SNOMEDCT_US	67782005	Acute respiratory distress syndrome	C0035222	Respiratory Distress Syndrome, Adult	Narrow
SNOMEDCT_US	67782005	Adult respiratory distress syndrome			narrow



10. Algorithm proposal

Broad Algorithm

- Concept sets (Pulmonary_edema, RDS, Respiratory_failure, Pulmonary_insufficiency, Mechanical_ventilation)
- Index date = first occurrence of a code in the concept sets (Pulmonary_edema, RDS, Respiratory_failure, Pulmonary_insufficiency, Mechanical_ventilation)

Narrow algorithm

- Concept sets (RDS, Respiratory_failure, Pulmonary_insufficiency)
- Index date = first occurrence of a code in the concept sets (RDS, Respiratory_failure, Pulmonary_insufficiency)

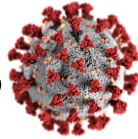
11. Background rates

The following search terms were used to extract background rates from the literature:
 ("acute respiratory distress syndrome"[Mesh]) AND ("incidence"[tw]) NOT (Comment[ptyp]
 OR Editorial[ptyp] OR News[ptyp] OR Newspaper Article[ptyp]) NOT ("animals"[Mesh]
 NOT "humans"[Mesh]) AND English[lang]
 Between 2010-2020

The background rates found by literature review can be found in the following publications

Table 2. References corresponding to the studies included in relation to the background rates

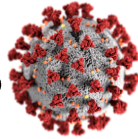
Number	Study reference
1 ^[7]	Sigurdsson MI, Sigvaldason K, Gunnarsson TS, Moller A, Sigurdsson GH. Acute respiratory distress syndrome: nationwide changes in incidence, treatment and mortality over 23 years. <i>Acta Anaesthesiologica Scandinavica</i> 2013;57(1):37–45.
2 ^[8]	Siddiqui S, Puthuchear Z, Phua J, Ho B, Tan J, Chuin S, et al. National survey of outcomes and practices in acute respiratory distress syndrome in Singapore. <i>PLoS ONE</i> 2017;12(6):e0179343.
3 ^[9]	López-Fernández Y, Azagra AM, de la Oliva P, Modesto V, Sánchez JI, Parrilla J, et al. Pediatric Acute Lung Injury Epidemiology and Natural History study: Incidence and outcome of the acute respiratory
4 ^[10]	Li G, Malinchoc M, Cartin-Ceba R, Venkata CV, Kor DJ, Peters SG, et al. Eight-year trend of acute respiratory distress syndrome: a population-based study in Olmsted County, Minnesota. <i>Am J Respir Crit Care Med</i> 2011;183(1):59–66.



5 ^[6]	Chen W, Chen Y-Y, Tsai C-F, Chen SC-C, Lin M-S, Ware LB, et al. Incidence and Outcomes of Acute Respiratory Distress Syndrome: A Nationwide Registry-Based Study in Taiwan, 1997 to 2011. <i>Medicine (Baltimore)</i> 2015;94(43):e1849.
6 ^[11]	Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. <i>JAMA</i> 2016;315(8):788–800.
7 ^[12]	Villar J, Blanco J, Añón JM, Santos-Bouza A, Blanch L, Ambrós A, et al. The ALIEN study: incidence and outcome of acute respiratory distress syndrome in the era of lung protective ventilation. <i>Intensive Care Med</i> 2011;37(12):1932–41.
8 ^[13]	Hu X, Qian S, Xu F, Huang B, Zhou D, Wang Y, et al. Incidence, management and mortality of acute hypoxemic respiratory failure and acute respiratory distress syndrome from a prospective study of Chinese paediatric intensive care network. <i>Acta Paediatr</i> 2010;99(5):715–21.

12. References

1. Acute Respiratory Distress Syndrome: The Berlin Definition. *JAMA* 2012;307(23):2526–33.
2. Diamond M, Peniston Feliciano HL, Sanghavi D, Mahapatra S. Acute Respiratory Distress Syndrome (ARDS) [Internet]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020 [cited 2020 Jun 4]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK436002/>
3. Confalonieri M, Salton F, Fabiano F. Acute respiratory distress syndrome. *Eur Respir Rev* 2017;26(144):160116.
4. Veeravagu A, Jiang B, Rincon F, Maltenfort M, Jallo J, Ratliff JK. Acute respiratory distress syndrome and acute lung injury in patients with vertebral column fracture(s) and spinal cord injury: a nationwide inpatient sample study. *Spinal Cord* 2013;51(6):461–5.
5. Reynolds HN, McCunn M, Borg U, Habashi N, Cottingham C, Bar-Lavi Y. Acute respiratory distress syndrome: estimated incidence and mortality rate in a 5 million-person population base. 2(1):7.



6. Chen W, Chen Y-Y, Tsai C-F, Chen SC-C, Lin M-S, Ware LB, et al. Incidence and Outcomes of Acute Respiratory Distress Syndrome: A Nationwide Registry-Based Study in Taiwan, 1997 to 2011. *Medicine (Baltimore)* 2015;94(43):e1849.
7. Sigurdsson MI, Sigvaldason K, Gunnarsson TS, Moller A, Sigurdsson GH. Acute respiratory distress syndrome: nationwide changes in incidence, treatment and mortality over 23 years. *Acta Anaesthesiologica Scandinavica* 2013;57(1):37–45.
8. Siddiqui S, Puthuchery Z, Phua J, Ho B, Tan J, Chuin S, et al. National survey of outcomes and practices in acute respiratory distress syndrome in Singapore. *PLoS ONE* 2017;12(6):e0179343.
9. López-Fernández Y, Azagra AM, de la Oliva P, Modesto V, Sánchez JI, Parrilla J, et al. Pediatric Acute Lung Injury Epidemiology and Natural History study: Incidence and outcome of the acute respiratory distress syndrome in children. *Crit Care Med* 2012;40(12):3238–45.
10. Li G, Malinchoc M, Cartin-Ceba R, Venkata CV, Kor DJ, Peters SG, et al. Eight-year trend of acute respiratory distress syndrome: a population-based study in Olmsted County, Minnesota. *Am J Respir Crit Care Med* 2011;183(1):59–66.
11. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. *JAMA* 2016;315(8):788–800.
12. Villar J, Blanco J, Kacmarek RM. Current incidence and outcome of the acute respiratory distress syndrome: *Current Opinion in Critical Care* 2016;22(1):1–6.
13. Hu X, Qian S, Xu F, Huang B, Zhou D, Wang Y, et al. Incidence, management and mortality of acute hypoxemic respiratory failure and acute respiratory distress syndrome from a prospective study of Chinese paediatric intensive care network. *Acta Paediatr* 2010;99(5):715–21.