Supplemental Table 1: Predictors of mortality in patients with tuberculosis admitted to the intensive care unit

PREDICTORS	Remarks (references)
Demographic parameters and risk factors	
Age	Advanced age predicted mortality in tuberculous pneumonia (OR 1.052, 95% CI, 1.010-1.095)[1]
Gender	Male gender (OR 2.16, 95% CI, 1.02-4.61)[2] Female (OR 21.42, 95% CI, 1.70-270.59)[3]
Smoking	Smoking (OR 4.54, 95% CI, 1.008-20.507)[4]
Chronic pancreatitis	Chronic pancreatitis (prevalence among non-survivors vs. survivors, 33.3% vs. 4.7%, p 0.001)[5]
HIV	(a) Recent diagnosis of HIV (adjusted HR, 0.27, 95% CI, 0.10-0.72, p 0.009)[6] (b) Nadir CD4 counts less than 50 cells/cu.mm (Adjusted HR 4.58, 95% CI, 1.64-12.74, p 0.004)[6] (c) CD4 count < 200 per cu.mm[7]
Laboratory parameters	
Serum albumin	(a) Serum albumin < 2 g/dL (OR 3.73, 95% CI, 1.09-15.31)[8] (b) Low serum albumin[2,9,10] (three studies, of which OR provided in two of them [OR 0.39, 95% CI, 0.21-0.71 and 0.073, 95% CI, 0.016-0.335 respectively][2,9] It was also able to predict the patients requiring MV (OR 0.39, 95% CI, 0.26-0.59)[2]
Hyponatremia	(a) Serum sodium mean (SD) value of 104.4(60) in non survivors vs. 135.1(4.5) in survivors, p < 0.05[11] (b) Nine subjects (32%) had hyponatremia of which eight died*[12]
C-reactive protein	Elevated CRP (OR 0.324, 95% CI, 0.146-0.716, p 0.005)[9]
Factors related to tuberculosis	
Diagnosis	(a) Longer time to diagnosis [11.8 (4.1) vs. 3.2 (2.7) days] more common in non-survivors[13]* (b) presence of smear positive for AFB (OR 5.667, 95% CI, 1.178-27.254) and positive PCR for M tuberculosis (OR 8.4, 95% CI, 1.6-44.104)[4]
Type of tuberculosis	(a) Miliary tuberculosis (OR 9.04, 95% CI, 1.25-65.3)[14] (b) Isolated pulmonary tuberculosis (OR 5.667, 95% CI, 1.034-22.293, p 0.037)[4] (c) Presence of ARDS (non-survivors vs. survivors, 33.3% vs. 4.7%, p 0.008)[5]
Radiology	(a) Consolidation on chest radiograph [7] (HR 7.731, 95% CI, 1.036-57.680[15], OR 33.26, 95% CI, 2.88-386.39[3] and OR 2.41, 95% CI, 1.17-4.98[2]) (b) Sequel of previous pulmonary tuberculosis (HR 6.61, 95% CI, 1.21-36.04, p 0.029)[16] (c) Wider extent of lesions (OR 1.307, 95% CI, 1.042-1.641, p 0.021)[9]and (OR 7.93, 95% CI, 2.44-25.77)[3] (d) Number of lobes involved (OR 1.83 per lobe, 95% CI, 1.12-2.98)[8]
Treatment-related	(a) Treatment delay > 30 d (OR 3.73, 95% CI, 1.06-13.00)[8] (b) Not receiving treatment with ATT (adjusted HR 3.59, 95% CI, 1.00-12.88)[17]
Use of corticosteroids	Lower risk of death in patients with tuberculous pneumonia (OR 0.544, 95% CI, 0.417-0.671)[1]
ICU parameters	
Severity scores	APACHE II: (a) A higher baseline APACHE II scores (OR 1.08, 95% CI, 1.04-1.13, p 0.002)[18] and a higher score in non-survivors vs. survivors [21 (4.9) vs. 15.9 (5.3) p < 0.05)[11]] (b) APACHE II score > 20 (HR 4.90, 95% CI, 1.43-16.80 p 0.012)[16] SOFA: (a)SOFA score on the day of diagnosis of ARDS (OR 0.809, 95% CI, 0.691-0.946, p 0.008)[19] (b) increase in SOFA score, (OR 1.375 per unit rise in SOFA, 95% CI, 1.179-1.605)[20] SAPS II: Higher score was independent predictor of mortlaity[21] CURB: Lower scores had lesser risk of death (OR 0.916, 95% CI, 0.844-0.995, p 0.037)[9]

MV	(a) Diagnostic accuracy to predict mortality was highest for the need for MV (85%), it had a sensitivity, specificity, positive and negative predictive values 83.8%, 88.5%, 95.4% and 65.7% respectively.[3] (b) Invasive MV was independent predictor of death in the following studies: Valade et al (OR 11.36, 95% CI, 1.55-83.48)[14] Filiz et al (OR 7.58, 95% CI, 6.873-8.167)[20] Duro et al (OR 4.25, 95% CI, 1.019-17.729)[4] Erbes et al (MV in non-survivors vs. survivors, 73.3% vs. 25.6% p 0.002)[5] (c) Development of requirement for MV during ICU stay (OR 20, 95% CI, 5.261-171.062)[4]
Physiological	(a) PaO_2/FiO_2 ratio < 108.5 [11] (b) Baseline driving pressure (OR 1.1, 95% CI, 1.03-1.17, p 0.003)[18]
Complications in ICU	
Organ failures	(a) Number of organ failures (OR 3.11 per failing organ, 95% CI, 1.45-6.65)[8] (b) MOF (HR 2.651, 95% CI, 1.163-6.040) [15] (c) MODS (OR 8.59, 95% CI, 1.85-101.27) [22] and (OR 6.0, 95% CI, 1.090-33.016)[4]
Sepsis and shock	(a) Sepsis: Erbes et al (Sepsis in non-survivors vs. survivors, 60% vs. 18.6%, p 0.001)[5] Ryu et al (HR 5.84, 95% 1.63-20.95, p 0.007)[16] (b) Shock: Shock unrelated to sepsis (OR 3.446, 95% CI, 1.286-15.102)[1] (c) Vasopressor requirement in ICU: Independent predictor of mortality in the following studies Valade et al (OR 8.45, 95% CI, 1.29-55.18)[14] Calligaro et al (adjusted HR 4.33, 95% CI, 1.49-12.60)[17] Duro et al (OR 30, 95% CI, 5.261-171.062)[4]
Acute renal failure	ARF was independent predictor of mortality[5] (non-survivors vs. survivors, 46.7% vs. 0%, p 0.001)
Nosocomial infections	Nosocomial pneumonia: Erbes et al (Nosocomial pneumonia in non-survivors vs. survivors, 86.7% vs. 48.8%, p 0.014)[5] Presence of nosocomial pneumonia (OR 5.77, 95% CI, 1.33-44.36) and delay in its treatment > 24 hours*[22] Development of hospital acquired infection (OR 6.0, 95% CI, 1.090-33.016)[4]

APACHE – acute physiology and chronic health evaluation; AFB – acid fast bacilli; ARDS – acute respiratory distress syndrome; ARF – acute renal failure; ATT – antitubercular therapy; CI – confidence interval; CRP – C-reactive protein; CURB – confusion, urea, respiratory rate, blood pressure; DM – diabetes mellitus; GI – gastrointestinal; HIV – human immunodeficiency virus; HR – hazards ratio; ICU – intensive care unit; MODS – multiorgan dysfunction syndrome; MOF – multiorgan failure; MV – mechanical ventilation; OR – odds ratio; PCR – polymerase chain reaction; SAPS - Simplified Acute Physiology Score; SOFA – sequential organ failure assessment; SD – standard deviation

*Multivariate analysis not available

Supplemental table 2: Studies describing the role of glucocorticoids in critically ill tuberculosis subjects admitted to intensive care unit

Author/year (number of patients)	Steroid used (n)		Steroid not used (n)		Indications	Remarks/conclusion
	Dead	Total	Dead	Total		
Levy et al. [23] 1987 (n=15)	-	6	-	9	-	No equivocal benefit or harm
Penner et al. [24] 1995 (n=13)	6	6	3	7	-	Of the 10 ARDS patients: 4/4 received steroid and all of them died vs. 3/6 in the no steroid group died
Zahar et al. [8] 2001 (n=99)	-	18	-	81	Miliary tuberculosis and respiratory failure (n=18)	-
Kim et al. [25] 2003 (n=34)	-	8	-	26	ARDS (n=6)	5 out of 6 ARDS died
Lee et al. [15] 2003 (n=41)	9	13	18	28	ARDS (n=13)	≥2mg/kg methylprednisolone after 7 d of ARDS
Erbes et al. [5] 2006 (n=58)	-	40	-	18	Severe inflammation related to tuberculosis (n=31) ARDS (n=7) COPD (n=2)	-
Sharma et al. [11] 2006 (n=29)	-	6	-	23	Severe hypoxemia ARDS while on ATT (n=4) Seven days after ARDS (n=2)	-
Kim et al. [1] 2008 (n=90)	24	44	35	46	ARDS (n=36) Other reasons (n=8) [they were started on glucocorticoids before diagnosing tuberculosis (6 as COPD, 2 as COP)]	Mean (SD) dose 59 (6.7) mg/d prednisolone equivalent Median (range) duration 20 (7-120) d Glucocorticoids use did not affect duration of MV or oxygenation ratio measured at day 7 Favourable outcome with corticosteroid use in tubercular pneumonia group (p 0.046)
Lin et al. [22] 2009 (n=59)	9	14	31	45	Administered for severe pulmonary lesions (details NA)	In patients with nosocomial pneumonia glucocorticoids use vs. no use was similar (6/29, 20.7% vs. 8/30, 26.7%, P = 0.761)
Lee et al. [19] 2011 (n=67)	-	27	-	40	ARDS (n=13)	≥ 1mg/kg methylprednisolone Mean (SD) duration 33.2 (45.1) days
Deng et al. [13] 2012 (n=85)	8	35	38	50	Miliary tuberculosis and ARDS (n=35)	Methylprednisolone 80 g/d iv for 5 days along with ATT may have mortality benefit
Mahmoud et al. [26] 2016 (n=11)	5	NA	2	NA	-	Seven patients died, of which five had received steroids
Yang et al. [27] 2016 (n=124)	34	70	27	54	ARDS (n=23) Shock (n=13) wheeze (n=9) Other reasons (n=25)	Median dose 50 mg/d (IQR 40-75 mg) prednisolone.
Loh et al.[10] 2016 (n=75)	21	29	26	46	-	-
Duro et al.[4] 2017 (n=39	0	5	21	34	Meningeal or pericardial disease only (n=5)	-

ARDS – acute respiratory distress syndrome; ATT – antitubercular therapy; COP – cryptogenic organizing pneumonia; COPD – chronic obstructive pulmonary disease; ICU – intensive care unit; IQR – interquartile range; IPTW – inverse probability of treatment weighted; LOS – length of stay; MV – mechanical ventilation; OR – odds ratio; SD – standard deviation

Supplemental table 3: Quality of the studies included in the review using QualSyst tool[28]

	Criterion	Agarwal et al. (1977) [29]	Frame et al. (1987) [30]	Levy et al. (1987) [23]	Hayhurst et al. (1994) [12]	Penner et al. (1995) [24]	Vyskocil et al. (1995) [31]	Zahar et al. (2001) [8]	Hui et al. (2003) [32]	Kim et al. (2003) [25]	Lee et al. (2003) [15]	Erbes et al. (2006) [5]
1	Question / objective sufficiently described?	1	1	1	1	2	1	2	1	1	2	1
2	Study design evident and appropriate?	1	1	1	1	1	1	1	1	1	1	1
3	Context for the study clear?	1	1	1	1	2	1	1	1	1	1	1
4	Connection to a theoretical framework /wider body of knowledge?	1	1	1	1	2	1	1	1	1	1	1
5	Sampling strategy described, relevant and justified?	1	1	1	1	1	1	2	1	1	1	1
6	Data collection methods clearly described and systematic?	1	1	1	1	1	1	2	1	1	2	1
7	Data analysis clearly described and systematic?	1	1	1	0	1	1	2	2	1	2	1
8	Use of verification procedure(s) to establish credibility?	1	1	1	1	1	1	1	1	1	1	1
9	Conclusions supported by the results?	1	1	1	1	1	1	2	1	1	2	2
10	Reflexivity of the account?	1	1	1	1	1	1	1	1	1	1	1
	Total	10	10	10	9	15	10	15	11	10	14	11

	Criterion	Sharma et al. (2006) [11]	Ryu et al. (2007) [16]	Kim et al. (2008) [1]	Lin et al. (2009) [22]	Ulasli et al. (2009) [33]	Silva et al. (2010) [34]	Alshimemeri et al. (2011) [35]	Lee et al. (2011) [19]	Deng et al. (2012) [13]	Valade et al. (2012) [14]	Balkema et al. (2014) [7]	Lanoix et al. (2014) [21]
1	Question / objective sufficiently described?	2	2	2	1	1	1	1	1	2	1	2	1
2	Study design evident and appropriate?	1	1	1	1	1	1	1	1	1	1	2	1
3	Context for the study clear?	1	1	1	1	1	1	1	1	1	1	1	1
4	Connection to a theoretical framework /wider body of knowledge?	1	1	1	1	1	1	1	1	1	1	1	1
5	Sampling strategy described, relevant and justified?	1	1	1	1	1	2	1	1	1	1	2	1
6	Data collection methods clearly described and systematic?	2	1	1	1	1	2	0	1	2	1	2	1
7	Data analysis clearly described and systematic?	2	2	2	1	1	2	1	2	2	2	2	2
8	Use of verification procedure(s) to establish credibility?	1	1	1	1	1	1	1	1	1	1	1	1
9	Conclusions supported by the results?	1	1	1	2	1	2	1	2	1	1	2	2
10	Reflexivity of the account?	1	1	1	1	1	1	1	1	1	1	1	1
	Total	13	12	12	11	10	14	9	12	13	11	16	12

	Criterion	Mansour et al. (2014) [3]	Calligaro et al. (2015) [17]	Rollas et al. (2015) [36]	Bhurayanontachai et al. (2016) [2]	Filiz et al. (2016) [20]	Kim et al. (2016) [9]	Loh et al. (2016) [10]	Mahmoud et al. (2016) [26]	Pecego et al. (2016) [6]	Yang et al. (2016) [27]	Duro et al. (2017) [4]	Muthu et al. (2017) [18]
1	Question / objective sufficiently described?	1	2	1	1	1	1	1	1	1	2	1	2
2	Study design evident and appropriate?	2	2	1	1	1	1	1	1	1	1	1	1
3	Context for the study clear?	1	1	1	1	1	1	1	1	2	1	1	2
4	Connection to a theoretical framework /wider body of knowledge?	1	2	1	1	1	1	1	1	1	1	1	1
5	Sampling strategy described, relevant and justified?	2	2	1	2	1	1	1	1	1	1	1	1
6	Data collection methods clearly described and systematic?	1	2	1	2	1	1	1	1	1	2	2	1
7	Data analysis clearly described and systematic?	2	8	1	2	2	1	1	1	1	2	1	1
8	Use of verification procedure(s) to establish credibility?	1	1	1	1	1	1	1	1	1	1	1	1
9	Conclusions supported by the results?	2	2	1	1	2	1	1	1	1	1	1	1
10	Reflexivity of the account?	1	2	1	1	1	1	1	1	1	1	1	1
	Total	14	18	10	13	12	10	10	10	11	13	11	12