Supplementary e-Table 1 Characteristics of 37 studies included for the review

Study	Country	Study design	Patients (n) (M/F)	Age (years)[a]	Smoking (n (%))	Follow-up lengths	Outcome	Number of deaths (%)[b]
Abe 2012 [35]	Japan	Retrospective cohort	73 (58/15)	67.5±8.2	Mean 937 (SD 658) (Smoking index)	-	All-cause mortality (3-month)	48 (65.8)
Akira 2008 [36]	Japan	Retrospective cohort	58 (44/14)	Median 66 (Range 45-82)	43 (74.1)	-	All-cause mortality (In-hospital)	25 (43.1)
Anzai 2013 [37]	Japan	Retrospective cohort	50 (41/9)	71.0±7.1[c]	(74.0)	-	All-cause mortality (Overall)	29 (58.0)
Atsumi 2018 [38]	Japan	Retrospective cohort	59 (49/10)	Median 74 (IQR 66-78)	Median 800 (IQR 500-1200) (Brinkman index)	-	All-cause mortality (60-day)	54 (91.5)
Cao 2016 [39]	China	Retrospective cohort	30 (23/7)	65.0±9.4	9 (30.0)	-	All-cause mortality (Overall)	26 (86.7)
Collard 2010 [40]	Korea	Retrospective cohort	47 (36/11)	66.0±8.0	40 (85.1)	-	All-cause mortality (Overall)	24 (51.1)
Enomoto 2015 [41]	Japan	Retrospective cohort	31 (28/3)	Median 69 (Range 50-84)	27 (87.1)	Median 53 months (Range 2-205)	All-cause mortality (3-month/12-month)	12 (38.7) (3 months) 23 (74.2) (12 months)
Enomoto 2018 [42]	Japan	Retrospective cohort	37	-	-	-	All-cause mortality (3-month)	10 (27.0)
Enomoto 2019 [43]	Japan	Retrospective cohort	37	-	-	-	All-cause mortality (3-month)	7 (18.9)
Fujimoto 2012 [44]	Japan	Retrospective cohort	60 (49/11)	Median 71 (IQR 63-75)	48 (80.0)	Median 370 days (Range 39-1230)	Disease-related mortality (Overall)	48 (80.0)

Furuya 2017 [45]	Japan	Retrospective cohort	47 (42/5)	Range 64-84	-	Median 173 days (Range 4-1137)	All-cause mortality (Overall)	27 (57.4)
Isshiki 2015 [46]	Japan	Retrospective cohort	41 (36/5)	72.6±6.4	36 (87.8)	Median 12 months (Range 1-143)	All-cause mortality (Overall)	29 (70.7)
Kang 2018 [47]	Korea	Retrospective cohort	66 (36/30)	70.8±9.0[c]	30 (45.5)	-	All-cause mortality (In-hospital)	29 (43.9)
Kataoka 2015 [48]	Japan	Retrospective cohort	40 (36/4)	Mean 72 (IQR 66-78)	-	-	All-cause mortality (3-month)	19 (47.5)
Kawamura 2017 [49]	Japan	Retrospective cohort	85 (66/19)	Median 76 (IQR 70-80)	-	-	All-cause mortality (60-day)	43 (50.6)
Kim 2006 [50]	Korea	Retrospective cohort	11	63.4±6.3 (n=8)	6 (75.0) (n=8)	-	All-cause mortality (In-hospital)	7 (63.6)
Kishaba 2018 [51]	Japan	Retrospective cohort	65 (40/25)	74.7±11.3	37 (56.9)	-	All-cause mortality (3-month)	-
Kishaba 2014 [52]	Japan	Retrospective cohort	58 (38/20)	75.0±9.6	58 (100.0)	Median 10.2 months (Range 0.1-112)	All-cause mortality (3-month)	- (70.7)
Koyama 2017 [53]	Japan	Retrospective cohort	47 (42/5)	Median 74 (Range 58-86)	42 (89.4)	-	All-cause mortality (3-month) Quality of life	19 (40.4)
Lee 2012 [54]	Korea	Retrospective cohort	24 (19/5)	64.3±9.4[c]	19 (79.2)	Median 74 days (IQR15-492)	All-cause mortality (Overall)	20 (83.3)
Nikaido 2018 [55]	Japan	Retrospective cohort	21 (21/0)	69.7±6.7[c]	-	-	All-cause mortality (60-day)	7 (33.3)

Novelli 2016 [56]	Italy	Retrospective cohort	11 (7/4)	Median 65 (IQR 55-75)	8 (72.7)	Median 18 months	All-cause mortality (3-month)	- (27.0)
Oishi 2016 [57]	Japan	Retrospective cohort	50 (46/4)	71.7±6.1	42 (84.0)	Median 42 days (Range 1-1656)	Disease-related mortality (Overall)	38 (76.0)
Papiris 2015 [58]	Greece	Retrospective cohort	17	-	-	-	All-cause mortality (Overall)	11 (39.3)
Sakamoto 2018 [59]	Japan	Retrospective cohort	80 (68/12)	72.9±6.3	67 (83.8)	Median 13 months (Range 1-137)	All-cause mortality (3-month)	- (46.3)
Sand 2018 [60]	Japan	Retrospective cohort	28 (28/0)	71.0±7.0	23 (82.1)	-	All-cause mortality (Overall)	13 (46.4) (at 100 days)
Saraya 2018 [61]	Japan	Retrospective cohort	27 (18/9)	Median 74 (IQR 70-84)	16 (66.7) (n=24)	-	All-cause mortality (60-day)	8 (29.6)
Sokai 2017 [62]	Japan	Retrospective cohort	59 (54/5)	71.7±8.2	49 (83.1)	-	All-cause mortality (180-day)	- (59.2)
Song 2011 [63]	Korea	Retrospective cohort	90 (69/21)	65.3±7.9	59 (65.6)	-	All-cause mortality (In-hospital)	45 (50.0)
Suzuki 2018 [64]	Japan	Retrospective cohort	62 (56/6)	Median 71 (IQR 64.8-76)	50 (80.6)	-	All-cause mortality (90-day)	32 (51.6)
Takei 2017 [65]	Japan	Retrospective cohort	18	-	-	-	All-cause mortality (90-day/Overall)	-
Tomioka 2007 [66]	Japan	Retrospective cohort	27 (18/9)	Mean 71 (Range 60-85)	20 (74.1)	-	All-cause mortality (In-hospital)	15 (55.6)
Tsushima 2014	Japan	Retrospective	20 (14/6)	76.8±1.9[c]	-	-	All-cause mortality	7 (35.0)

[67]		cohort					(28-day)	
Vianello 2019	Italy	Retrospective	20 (15/5)	67.0±10.4[c]	9 (45.0)	Maximum 370 days	All-cause mortality	10 (50.0)
[68]		cohort					(In-ICU /Overall)	(In-ICU)
Woottoon 2011	Korea	Prospective	43 (88%/12%)	Mean 65	(84.0)	-	All-cause mortality	- (51.2)
[69]		cohort					(60-day/Overall)	(60 days)
Yamazoe 2018	Japan	Retrospective	57		-	-	All-cause mortality	35 (61.4)
[70]		cohort					(In-hospital/Overall)	(In-hospital)
Yokoyama 2010	Japan	Retrospective	11 (7/4)	72.3±7.7	8 (72.7)	-	All-cause mortality	6 (54.5)
[71]		cohort					(3-month)	

a, indicates mean±standard deviation unless otherwise specified; b, indicates the number of deaths at each point in time unless otherwise specified; c, calculated using the sample size and median, range or interquartile range in two comparative groups;

IQR, interquartile range;

Supplementary e-Table 2 31 potential prognostic factors for all-cause mortality

Demographic characteristics
age, sex, smoking history, BMI, disease duration
Disease severity (staging) of underling IPF or acute phase
GAP system, JRS classification, APACHE II score
Symptoms (at onset)
Duration of dyspnoea, fever
Pulmonary function tests (at baseline)
FVC, DLCO, FEV1
Radiological features (at onset)
Pattern of distribution, GGO, reticular opacity, extent of GGO and consolidation, extent of abnormality
Laboratory findings (at onset)
PaO2/FiO2 ratio, CRP, LDH, KL-6, SP-D, WBC, D-dimer, FDP, BAL lymphocyte, BAL neutrophil
Treatment before acute exacerbation
Pirfenidone, corticosteroid, oxygen therapy

APACHE, acute physiology and chronic health evaluation; BAL, bronchoalveolar lavage; BMI, body mass index; CRP, C-reactive protein; DLCO, diffusion capacity of the lung for carbon monoxide; FDP, fibrin degradation product; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; GAP, gender, age and physiology; GGO, ground glass opacity; HR, hazard ratio; HRCT, high resolution computed tomography; IPF, idiopathic pulmonary fibrosis; JRS, Japanese Respiratory Society; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; PaO2/FiO2, partial pressure of arterial oxygen/fraction of inspired oxygen; SP-D, surfactant protein-D; WBC, white blood cell;

Supplementary e-Table 3 Risk of bias in 37 studies included for the review, assessed by the Quality in Prognostic Studies tool[a]

Study	study participation	study attrition	prognostic factor measurement	outcome measurement	study confounding	statistical analysis and reporting
Abe 2012 [35]	**high risk**	**high risk**	**high risk**	low risk	**high risk**	**high risk**
Akira 2008 [36]	medium risk	low risk	low risk	low risk	medium risk	**high risk**
Anzai 2013 [37]	low risk	low risk	medium risk	low risk	medium risk	**high risk**
Atsumi 2018 [38]	low risk	low risk	low risk	low risk	medium risk	**high risk**
Cao 2016 [39]	medium risk	low risk	low risk	low risk	**high risk**	**high risk**
Collard 2010 [40]	medium risk	**high risk**	medium risk	low risk	**high risk**	**high risk**
Enomoto 2015 [41]	medium risk	**high risk**	medium risk	low risk	medium risk	**high risk**
Enomoto 2018 [42]	medium risk	**high risk**	low risk	low risk	medium risk	**high risk**
Enomoto 2019 [43]	medium risk	**high risk**	medium risk	low risk	medium risk	**high risk**
Fujimoto 2012 [44]	low risk	**high risk**	low risk	low risk	**high risk**	medium risk
Furuya 2017 [45]	low risk	**high risk**	low risk	low risk	**high risk**	**high risk**
Isshiki 2015 [46]	low risk	**high risk**	low risk	low risk	medium risk	**high risk**
Kang 2018 [47]	low risk	low risk	low risk	low risk	**high risk**	**high risk**
Kataoka 2015 [48]	low risk	**high risk**	medium risk	low risk	**high risk**	medium risk
Kawamura 2017 [49]	low risk	low risk	low risk	low risk	**high risk**	**high risk**
Kim 2006 [50]	medium risk	**high risk**	**high risk**	low risk	medium risk	**high risk**
Kishaba 2018 [51]	low risk	**high risk**	medium risk	low risk	**high risk**	**high risk**
Kishaba 2014 [52]	medium risk	**high risk**	medium risk	low risk	medium risk	**high risk**
Koyama 2017 [53]	low risk	low risk	medium risk	low risk	**high risk**	**high risk**

Lee 2012 [54]	low risk	**high risk**	low risk	low risk	**high risk**	**high risk**
Nikaido 2018 [55]	low risk	low risk	low risk	low risk	**high risk**	**high risk**
Novelli 2016 [56]	medium risk	**high risk**	low risk	low risk	**high risk**	**high risk**
Oishi 2016 [57]	medium risk	**high risk**	medium risk	low risk	**high risk**	**high risk**
Papiris 2015 [58]	low risk	**high risk**	low risk	low risk	medium risk	**high risk**
Sakamoto 2018 [59]	low risk	**high risk**	low risk	low risk	medium risk	**high risk**
Sand 2018 [60]	medium risk	**high risk**	low risk	low risk	**high risk**	**high risk**
Saraya 2018 [61]	medium risk	**high risk**	low risk	low risk	**high risk**	**high risk**
Sokai 2017 [62]	low risk	**high risk**	low risk	low risk	medium risk	medium risk
Song 2011 [63]	medium risk	low risk	medium risk	low risk	**high risk**	**high risk**
Suzuki 2018 [64]	low risk	**high risk**	low risk	low risk	**high risk**	medium risk
Takei 2017 [65]	medium risk	**high risk**	low risk	low risk	**high risk**	**high risk**
Tomioka 2007 [66]	low risk	low risk	low risk	low risk	**high risk**	**high risk**
Tsushima 2014 [67]	medium risk	low risk	low risk	low risk	**high risk**	**high risk**
Vianello 2019 [68]	**high risk**	**high risk**	low risk	low risk	**high risk**	**high risk**
Woottoon 2011 [69]	medium risk	**high risk**	medium risk	low risk	**high risk**	**high risk**
Yamazoe 2018 [70]	low risk	**high risk**	low risk	low risk	**high risk**	medium risk
Yokoyama 2010 [71]	medium risk	low risk	**high risk**	low risk	**high risk**	**high risk**

a, Text in bold refers to high risk of bias.

Supplementary e-Table 4 The result of univariate analysis of potential prognostic factors for all-cause mortality

Potential prognostic factors[a]	Analysis	Studies (n)[b]	Subjects (n)	Point estimate (+/-)[c]	Result of meta-analysis and non-pooled studies (95% CI)[d]
Demographic features					
Age	Meta	8	405	4/2	HR 1.00 (0.98-1.02) (/1 year)
		3	236	3/0	OR 1.02 (0.98-1.05) (/1 year)
	Not pooled	Kishaba 2014 [52]	58	-/-	HR 1.00 (p=0.83) (year)
		Anzai 2013 [37]	50	1/0	MD 3.50 (-0.48-7.48) (year) (non-survivor vs. survivor)
		Tsushima 2014 [67]	20	0/1	***MD -4.30 (-6.04--2.56) (yaer) (non-survivor vs. survivor)***
Sex	Meta	7	377	3/4	HR 0.93 (0.65-1.34) (vs. female)
		5	306	3/2	OR 1.28 (0.74-2.21) (vs. female)
	Not pooled	Kishaba 2014 [52]	58	0/1	HR 0.90 (p=0.76)
Smoking history	Meta	3	145	2/1	HR 0.98 (0.35-2.75) (vs. never-smoker)
		4	243	3/1	OR 0.99 (0.59-1.67) (vs. never-smoker)
		3	116	1/1	HR 1.00 (0.89-1.11) (/10 pack-year)
	Not pooled	Atsumi 2018 [38]	59	0/1	HR 0.95 (0.88-1.02) (/200 Brinkman index)
		Kishaba 2014 [52]	58	1/0	***HR 1.01 (p=0.03) (pack-year)***
BMI	Not pooled	Kang 2018 [47]	66	0/1	MD -0.13 (-2.12-1.86) (non-survivor vs. survivor)
		Suzuki 2018 [64]	62	1/0	HR 1.04 (0.94-1.15) (/1 kg/m^2)
		Lee 2012 [54]	24	0/1	HR 0.93 (0.82-1.05)
Disease duration before AE	Not pooled	Papiris 2015 [58]	17	1/0	HR 1.01 (1.00-1.03)
		Enomoto 2019 [43]	37	-/-	HR 1.00 (p=0.82) (/1 month)
		Song 2011 [63]	90	0/1	OR 0.99 (0.98-1.01) (months)

		Akira 2008 [36]	58	1/0	MD 2.00 (-11.6-15.6) (months) (non-survivor vs. survivor)
		Novelli 2016 [56]	11	0/1	8 vs. 20 (months) (non-survivor vs. survivor)
Disease severity (staging) of underling IPF or acute phase					
GAP system[e]	Not pooled	Atsumi 2018 [38]	59	1/0	***HR 1.45 (1.10-1.93) (/1 point)***
		Enomoto 2018 [42]	37	1/0	HR 1.08 (0.48-2.44) (/1 stage)
		Sakamoto 2018 [59]	80	1/0	OR 1.64 (0.98-2.70) (/1)
JRS classification[f]	Not pooled	Atsumi 2018 [38]	59	1/0	***HR 1.50 (1.17-1.94) (/1 stage)***
		Enomoto 2018 [42]	37	1/0	HR 2.12 (0.86-5.23)
		Sakamoto 2018 [59]	80	1/0	OR 1.28 (0.53-3.13) (advanced (III, IV))
APACHE II score	Meta	3	194	3/0	***HR 1.09 (1.04-1.15)(/1 point)***
	Not pooled	Nikaido 2018 [55]	21	1/0	MD 2.80 (-1.19-6.79) (non-survivor vs. survivor)
Symptoms					
Duration of dyspnoea	Not pooled	Song 2011 [63]	90	0/1	***OR 0.94 (0.90-0.98) (days)***
		Kishaba 2014 [52]	58	1/0	HR 1.01 (p=0.65) (days)
		Kang 2018 [47]	66	0/1	MD -6.43 (-15.9-3.04) (days) (non-survivor vs. survivor)
Fever	Meta	3	206	2/1	OR 1.66 (0.74-3.70)
	Not pooled	Enomoto 2019 [43]	37	0/1	HR 0.51 (p=0.39)
Pulmonary function					
FVC	Meta	5	199	1/3	HR 0.99 (0.98-1.01) (/1% predicted value)
		3	193	1/0	OR 1.01 (0.99-1.02) (/1% predicted value)
DLCO	Meta	4	171	1/2	HR 0.99 (0.98-1.01) (/1% predicted value)
	Not pooled	Kang 2018 [47]	66	0/1	MD -6.38 (-15.8-3.04) (% predicted value) (non-survivor vs. survivor)

		Sakamoto 2018 [59]	80	1/0	OR 1.01 (0.98-1.03)
FEV1	Not pooled	Kang 2018 [47]	66	0/1	MD -4.36 (-14.1-5.37) (% predicted value) (non-survivor vs. survivor)
		Koyama 2017 [53]	47	0/1	MD -11.0 (-23.8-1.82) (% predicted value) (non-survivor vs. survivor)
		Papiris 2015 [58]	17	-/-	HR 1.00 (0.94-1.06) (% predicted value)
Features on HRCT					
Pattern	Not pooled	Kim 2006 [50]	11	1/0	OR 30.3 (0.96-959.6) (multifocal vs. peripheral)
		Anzai 2013 [37]	50	1/0	OR 8.00 (0.82-78.0) (diffuse+multifocal vs. peripheral)
		Sakamoto 2018 [59]	80	1/0	OR 1.39 (0.55-3.45) (diffuse)
		Akira 2008 [36]	58	1/0	***HR 5.39 (2.60-11.2) (diffuse+multifocal vs. peripheral)***
		Kawamura 2017 [49]	85	0/1	HR 0.41 (0.10-1.71) (multifocal)
GGO	Not pooled	Sokai 2017 [62]	59	1/0	HR 1.01 (0.99-1.03)
		Papiris 2015 [58]	17	1/0	HR 1.65 (0.74-3.70)
		Lee 2012 [54]	24	1/0	HR 1.03 (1.00-1.06) (GGO score)
Reticular opacity	Not pooled	Akira 2008 [36]	58	1/0	HR 1.03 (1.00-1.06) (reticulation and honeycombing (%))
		Lee 2012 [54]	24	0/1	HR 0.96 (0.91-1.01) (reticulation score)
		Kishaba 2014 [52]	58	1/0	HR 1.32 (p=0.06) (traction bronchiectasis and honeycombing score)
		Sokai 2017 [62]	59	0/1	HR 0.98 (0.95-1.02) (reticulation and honeycombing (%))
Extent of GGO and	Not pooled	Kishaba 2014 [52]	58	1/0	***HR 1.85 (p=0.03) (score)***
consolidation		Akira 2008 [36]	58	1/0	***HR 1.05 (1.02-1.07) (%)***
		Sokai 2017 [62]	59	1/0	HR 1.02 (1.00-1.04) (%)
Extent of abnormality	Meta	3	120	3/0	HR 1.02 (1.00-1.05) (/1 score)
		Akira 2008 [36]	58	1/0	***HR 1.07 (1.04-1.10) (%)***

Laboratory findings					
PaO2/FiO2 ratio	Meta	6	325	0/5	***HR 0.95 (0.92-0.97) (/10 mmHg)***
		3	236	0/3	***OR 0.92 (0.89-0.95) (/10 mmHg)***
		4	118	0/4	MD -76.3 (-153.9-1.28) (non-survivor vs. survivor)
	Not pooled	Novelli 2016 [56]	11	0/1	195 vs. 240 (non-survivor vs. survivor)
		Sokai 2017 [62]	59	1/0	HR 1.45 (0.71-3.03) (≥200)
CRP	Meta	4	243	3/0	***HR 1.05 (1.02-1.08) (/1mg/dl)***
		6	242	7/0	***SMD 0.69 (0.19-1.18) (non-survivor vs. survivor)***
	Not pooled	Kishaba 2014 [52]	58	0/1	HR 0.98 (p=0.47) (mg/dl)
		Song 2011 [63]	90	1/0	***OR 1.09 (1.01-1.17) (mg/dl)***
		Sakamoto 2018 [59]	80	1/0	OR 1.05 (0.97-1.14) (mg/dl)
LDH	Meta	7	425	6/0	***HR 1.02 (1.01-1.02) (/10 IU/L)***
		4	118	4/0	***SMD 0.48 (0.11-0.84) (non-survivor vs. survivor)***
	Not pooled	Kang 2018 [47]	66	1/0	OR 1.02 (1.00-1.04)
		Sakamoto 2018 [59]	80	1/0	OR 1.01 (1.00-1.01) (IU/L)
KL-6	Meta	4	265	3/0	***HR 1.02 (1.01-1.04) (/100 U/mL)***
		4	118	2/2	MD -23.6 (-119.7-72.5) (×10 U/mL) (non-survivor vs. survivor)
	Not pooled	Kishaba 2014 [52]	58	1/0	***HR 2.01 (p=0.001) (IU/L)***
		Enomoto 2018 [42]	37	-/-	HR 1.00 (1.00-1.00) (U/mL)
		Collard 2010 [40]	47	0/1	OR 0.41 (0.06-2.93) (log unit)
		Sakamoto 2018 [59]	80	-/-	OR 1.00 (1.00-1.00) (U/mL)
SP-D	Meta	4	243	0/2	HR 0.99 (0.99-1.00) (/10 ng/ml)
	Not pooled	Anzai 2013 [37]	50	1/0	MD 25.0 (-155.6-205.6) (non-survivor vs. survivor) (ng/ml)

		Nikaido 2018 [55]	21	1/0	MD 172.2 (-76.3-420.7) (non-survivor vs. survivor) (ng/ml)
		Collard 2010 [40]	47	1/0	OR 1.23 (0.36-4.21) (log ng/ml)
		Sakamoto 2018 [59]	80	1/0	OR 1.01 (1.00-1.01) (ng/ml)
WBC	Meta	6	242	5/1	***MD 1.35 (0.19-2.51) (×10^6/mm^3) (non-survivor vs. survivor)***
	Not pooled	Kataoka 2015 [48]	40	-/-	OR 1.00 (1.00-1.00) (/mm^3)
		Sakamoto 2018 [59]	80	-/-	OR 1.00 (1.00-1.00) (/mm^3)
		Kishaba 2014 [52]	58	-/-	HR 1.00 (p=0.47) (/mm^3)
		Enomoto 2019 [43]	37	-/-	***HR 1.00 (p=0.03) (/ul)***
D-dimer	Not pooled	Suzuki 2018 [64]	62	1/0	***HR 1.03 (1.01-1.05) (/1 μg/ml)***
		Sakamoto 2018 [59]	80	0/1	OR 0.99 (0.94-1.04) (mg/ml)
		Nikaido 2018 [55]	21	1/0	MD 3.10 (-7.48-13.7) (μg/ml) (non-survivor vs. survivor)
FDP	Not pooled	Nikaido 2018 [55]	21	1/0	MD 3.0 (-21.6-27.6) (μg/ml) (non-survivor vs. survivor)
		Tsushima 2014 [67]	20	1/0	***MD 115.6 (73.5-157.7) (μg/ml) (non-survivor vs. survivor)***
		Sakamoto 2018 [59]	80	-/-	OR 1.00 (0.98-1.02) (μg/ml)
BAL lymphocyte	Not pooled	Song 2011 [63]	90	0/1	***OR 0.91 (0.83-0.99) (%)***
		Suzuki 2018 [64]	62	0/1	HR 0.97 (0.92-1.01) (/1%)
		Kishaba 2014 [52]	58	-/-	HR 1.00 (p=0.97)
BAL neutrophil	Not pooled	Song 2011 [63]	90	1/0	OR 1.06 (1.00-1.12) (%)
		Suzuki 2018 [64]	62	1/0	***HR 1.01 (1.00-1.03) (/1%)***
		Kishaba 2014 [52]	58	0/1	HR 0.94 (p=0.33)
Treatment before AE					
Pirfenidone	Meta	3	164	3/0	HR 1.34 (0.81-2.24)

		Sakamoto 2018 [59]	80	0/1	OR 0.85 (0.28-2.56)
Corticosteroid	Meta	3	161	2/1	HR 0.96 (0.61-1.52)
		Song 2011 [63]	90	0/1	OR 0.83 (0.35-1.94) (corticosteroid with or without cytotoxic agent)
		Sakamoto [59]	80	1/0	OR 1.75 (0.64-4.76)
Oxygen therapy	Meta	4	160	4/0	***HR 1.88 (1.15-3.09)***

a, Text in italic bold refers to potential prognostic factors, which demonstrated consistent and statistically significant results in the majority of studies. If the result of meta-analysis was significant, all studies included for the analysis were assumed to be significant to determine whether the majority of studies demonstrated significant results.

b, The number of included studies was described for meta-analysis while an individual study was specified for non-pooled studies.

c, Plus (+) indicates a positive association between mortality and potential prognostic factors based on point estimates while minus (-) indicates the negative association. Studies with null effects such as zero by MDs and one by HRs were not counted in this column. The direction of point estimates of all pooled and non-pooled studies were considered.

d, Parenthesis indicates 95% confidence interval unless otherwise specified. Text in bold refers to statistically significant results. Per unit for relative values such as ORs and HRs was described only if data was available and otherwise only unit was described.

e, The system considers gender, age and two lung physiology variables, i.e., FVC and DLCO. Points are assigned to each component of the system and there are three stages depending on the total points with a higher value indicating severer disease.

f, The classification consists of PaO_2 at rest and minimum SpO_2 during the six-minute walking test. There are four stages based on a combination of the value of both PaO2 and SpO2 with a higher stage indicating severer disease.

AE, acute exacerbation; APACHE, acute physiology and chronic health evaluation; BAL, bronchoalveolar lavage; BMI, body mass index; CRP, C-reactive protein; CI, confidence interval; DLCO, diffusion capacity of the lung for carbon monoxide; FDP, fibrin

degradation product; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; GAP, gender, age and physiology; GGO, ground glass opacity; HR, hazard ratio; HRCT, high resolution computed tomography; IPF, idiopathic pulmonary fibrosis; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; MD, mean difference; Meta, meta-analysis; OR, odds ratio; PaO_2, partial pressure of arterial oxygen; PaO2/FiO2 ratio, partial pressure of arterial oxygen/fraction of inspired oxygen ratio, SMD, standardized mean difference; SP-D, SpO2, saturation of percutaneous oxygen; surfactant protein-D; WBC, white blood cell;

Supplementary e-Table 5 The result of multivariate analysis of potential prognostic factors for all-cause mortality

Potential prognostic factors[a]	Studies (n)	Subjects (n)	Effect estimates (95% CI)[b]	Adjusted factors
Demographic features				
Age	Akira 2008 [36]	58	HR 1.00 (0.96-1.04) (year)	sex, smoking history, FVC, DLCO, pattern and extent of abnormality on HRCT, LDH
	Kang 2008 [47]	66	OR 0.97 (0.91-1.04) (year)	Unclear
	Yamazoe 2018 [70]	57	OR 0.96 (0.87-1.07) (year)	PaO2/FiO2 ratio, CRP, WBC, Hb, antibiotic therapy
Sex	Akira 2008 [36]	58	HR 0.91 (0.34-2.43) (vs. female)	age, smoking history, FVC, DLCO, pattern and extent of abnormality on HRCT, LDH
Smoking history	Akira 2008 [36]	58	HR 2.47 (0.91-6.70) (vs. never-smoker)	age, sex, FVC, DLCO, pattern and extent of abnormality on HRCT, LDH
	Sokai 2017 [62]	59	HR 0.51 (0.23-1.31)	GGO and consolidation, LDH, KL-6, oxygen therapy, asymmetrical exacerbation
Disease severity (staging) of underling IPF or acute phase				
GAP system[c]	Atsumi 2018 [38]	59	HR 0.98 (0.62-1.51) (/1 point)	Unclear
APACHE II score	Kawamura 2017 [49]	85	***HR 1.10 (1.01-1.19)***	Unclear
Symptoms				
Fever	Kang 2018 [47]	66	OR 1.35 (0.41-4.50)	Unclear
Pulmonary function				
FVC	Akira 2008 [36]	58	HR 0.98 (0.96-1.01) (% predicted value)	age, sex, smoking history, DLCO, pattern and extent of abnormality on HRCT, LDH
	Kang 2018 [47]	66	OR 1.00 (0.96-1.04) (% predicted value)	Unclear

DLCO	Akira 2008 [36]	58	HR 1.02 (1.00-1.04) (% predicted value)	age, sex, smoking history, FVC, pattern and extent of abnormality on HRCT, LDH
Features on HRCT				
Pattern	Akira 2008 [36]	58	***HR 4.63 (1.90-11.3)*** (diffuse+multifocal vs. peripheral)	age, sex, smoking history, FVC, DLCO, extent of abnormality on HRCT, LDH
Extent of GGO and consolidation	Kishaba 2014 [52]	58	***HR 2.29 (p=0.03)***	Unclear
	Akira 2008 [36]	58	HR 0.98 (0.95-1.02) (%)	Unclear
	Sokai 2017 [62]	59	HR 0.99 (0.96-1.02) (%)	smoking history, LDH, KL-6, oxygen therapy, asymmetrical exacerbation
Extent of abnormality	Akira 2008 [36]	58	***HR 1.07 (1.02-1.12) (%)***	age, sex, smoking history, FVC, DLCO, pattern of abnormality on HRCT, LDH
	Atsumi 2018 [38]	59	HR 1.18 (0.99-1.39) (/10 score)	Unclear
	Enomoto 2018 [42]	37	***HR 1.22 (1.01-1.48) (score)***	age
Laboratory findings				
PaO2/FiO2 ratio	Kang 2018 [47]	66	***OR 0.99 (0.98-1.00)***	Unclear
	Yamazoe 2018 [70]	57	OR 1.00 (0.99-1.01)	age, CRP, WBC, Hb, antibiotic therapy
	Kishaba 2018 [51]	65	***HR 0.99 (0.99-1.00)***	LDH, delta LDH, delta KL-6, criteria of AE
	Suzuki 2018 [64]	62	***HR 0.31 (0.14-0.67) (>300 vs. ≤300)***	Unclear
	Sakamoto 2018 [59]	80	***OR 0.99 (0.99-1.00)***	Unclear
CRP	Song 2011 [63]	90	***OR 2.47 (1.03-5.91) (mg/dl)***	Unclear
	Yamazoe 2018 [70]	57	OR 1.00 (0.90-1.13) (mg/dl)	age, PaO2/FiO2 ratio, WBC, Hb, antibiotic therapy

	Kataoka 2015 [48]	40	OR 1.18 (1.00-1.39) (mg/dl)	respiratory rate
LDH	Kang 2018 [47]	66	OR 1.00 (1.00-1.00)	Unclear
	Akira 2008 [36]	58	***HR 1.002 (1.000-1.004)***	age, sex, smoking history, FVC, DLCO, pattern and extent of abnormality on HRCT
	Kishaba 2018 [51]	65	***HR 1.003 (1.001-1.005) (IU/L)***	PaO2/FiO2 ratio, delta LDH, delta KL-6, criteria of AE
	Enomoto 2018 [42]	37	***HR 1.01 (1.00-1.01) (IU/L)***	age
	Sokai 2017 [62]	59	***HR 1.02 (1.00-1.05) (/10IU/L)***	smoking history, GGO and consolidation, KL-6, oxygen therapy, asymmetrical exacerbation
KL-6	Suzuki 2018 [64]	62	***HR 1.24 (1.05-1.46) (/500U/mL)***	Unclear
	Sokai 2017 [62]	59	HR 0.99 (0.96-1.02) (/100U/mL)	smoking history, GGO and consolidation, LDH, oxygen therapy, asymmetrical exacerbation
WBC	Yamazoe 2018 [70]	57	***OR 1.38 (1.04-1.83) (/μl)***	age, PaO2/FiO2 ratio, CRP, Hb, antibiotic therapy
D-dimer	Suzuki 2018 [64]	62	***HR 1.04 (1.02-1.06) (/1/μg/mL)***	Unclear
BAL lymphocyte	Song 2011 [63]	90	OR 0.87 (0.74-1.02) (%)	Unclear
BAL neutrophil	Suzuki 2018 [64]	62	***HR 1.02 (1.00-1.03) (%)***	Unclear
Treatment before AE				
Oxygen therapy	Enomoto 2018 [42]	37	***HR 3.68 (1.05-12.9)***	age
	Sokai 2017 [62]	59	***HR 2.34 (1.04-5.28)***	smoking history, GGO and consolidation, LDH, asymmetrical exacerbation

a, Text in italic bold refers to potential prognostic factors, which demonstrated consistent and statistically significant results in the majority of studies.

b, Parenthesis indicates 95% confidence interval unless otherwise specified. Text in bold refers to statistically significant results. Per unit for relative values such as ORs and HRs was described only if data was available and otherwise only unit was described.

c, The system considers gender, age and two lung physiology variables, i.e., FVC and DLCO. Points are assigned to each component of the system and there are three stages depending on the total points with a higher value indicating severer disease.

AE, acute exacerbation; APACHE, acute physiology and chronic health evaluation; BAL, bronchoalveolar lavage; CRP, C-reactive protein; CI, confidence interval; DLCO, diffusion capacity of the lung for carbon monoxide; FVC, forced vital capacity; GAP, gender, age and physiology; GGO, ground glass opacity; Hb, haemoglobin; HR, hazard ratio; HRCT, high resolution computed tomography; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; OR, odds ratio; PaO2/FiO2 ratio, partial pressure of arterial oxygen/fraction of inspired oxygen, WBC, white blood cell

Supplementary e-Table 6 Assessment of quality of evidence of prognostic factors by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system

Outcome: all-cause mortality										
			GRADE factors							
Prognostic factors[a]	Analysis[b]	Phase	Study limitations	Inconsistency[c]	Indirectness	Publication bias	Imprecision	Moderate/large effect size	Dose response gradient	Overall quality
APACHE II score	Uni	1	+	-	-	+	-	-	-	Very Low
	Multi	1	+	N/A	-	+	-	-	-	Very low
PaO2/FiO2 ratio	Uni	1	+	-	-	+	-	+	-	Low
	Multi	1	+	-	-	+	-	-	-	Very low
LDH	Uni	1	+	-	-	+	-	-	-	Very low
	Multi	1	+	-	-	+	-	-	-	Very low
WBC	Uni	1	+	-	-	+	-	-	-	Very low
	Multi	1	+	N/A	-	+	-	-	-	Very low
Oxygen therapy	Uni	1	+	-	-	+	-	-	-	Very low
(before AE)	Multi	1	+	-	-	+	+	+	-	Very low

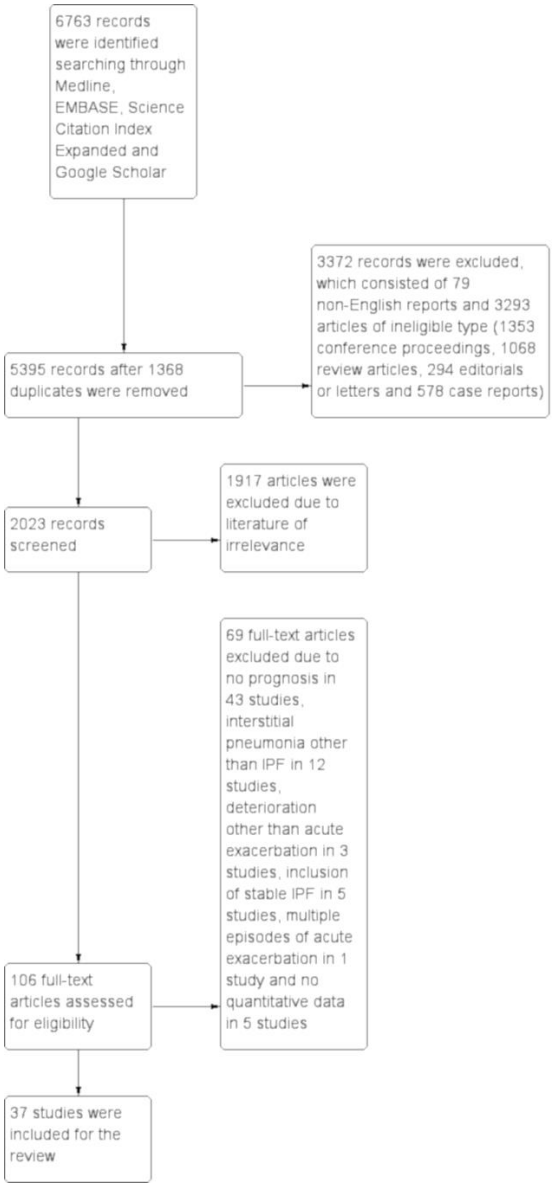
a, A total of 5 clinical information was determined as prognostic factors from 30 potential prognostic factors based on the consistent and significant result on both univariate and multivariate analyses.

b, ‘uni’ indicating univariate analysis while ‘multi’ indicating multivariate analysis.

c, N/A indicating not applicable due to only one study available.

AE, acute exacerbation; APACHE, acute physiology and chronic health evaluation; BAL, bronchoalveolar lavage; HRCT, high resolution computed tomography; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; PaO2/FiO2 ratio, partial pressure of arterial oxygen/fraction of inspired oxygen ratio, WBC, white blood cell;

Supplementary e-Figure

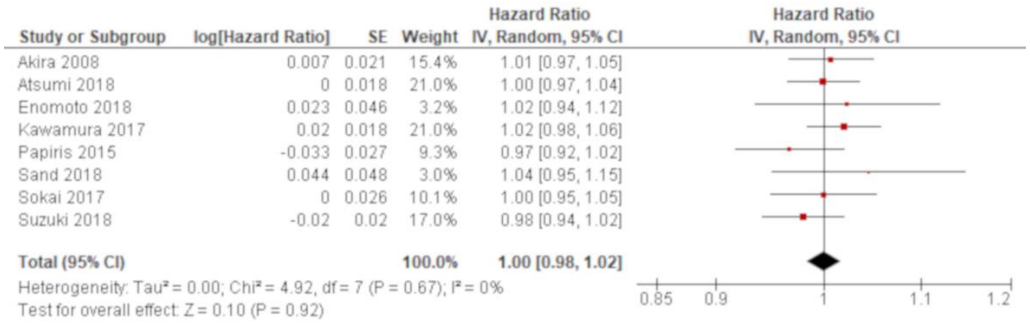


Supplementary e-Figure 1. Study flow diagram

A total of 6763 reports were identified through Medline, EMBASE, Science Citation Index Expanded and Google Scholar. After excluding 1368 duplicates, 79 non-English records, 3293 reports of ineligible types (consisting of 1353 conference proceedings,

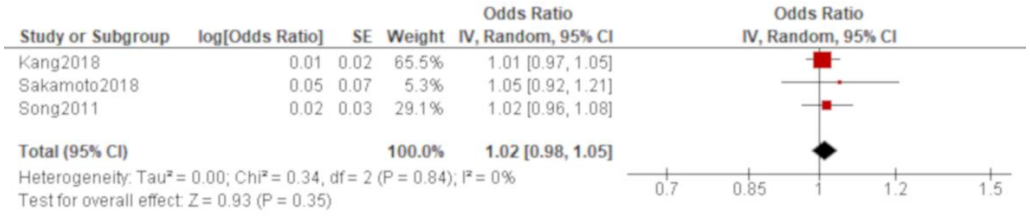
1068 review articles, 294 editorials or letters and 578 case reports) and 1917 irrelevant articles, the remaining 106 reports were obtained as full-texts. Out of these, 69 reports were excluded due to no prognosis in 43 studies, interstitial pneumonia other than idiopathic pulmonary fibrosis (IPF) in 12 studies, deterioration other than acute exacerbation in 3 studies, inclusion of stable IPF in 5 studies, multiple episodes of acute exacerbation in 1 study and no quantitative data in 5 studies. Finally, 37 articles/studies were eligible for this review.

Kamiya H, Panlaqui OM. *BMJ Open* 2020; 10:e035420. doi: 10.1136/bmjopen-2019-035420



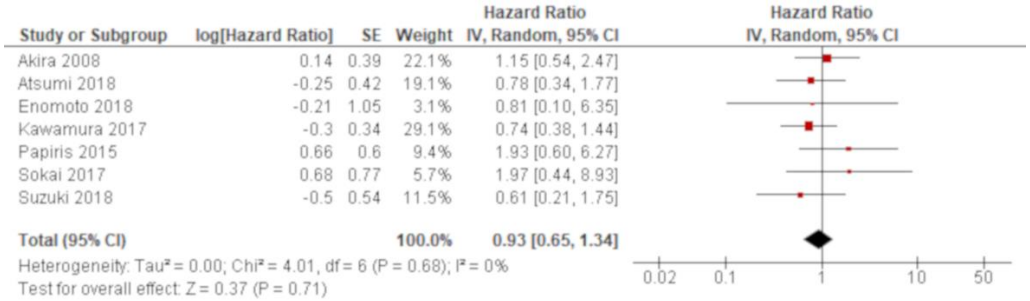
Supplementary e-Figure 2. Forrest plot of the result of univariate analysis for age (combined by hazard ratio)

The result of univariate analysis in 8 studies was pooled for meta-analysis and a total of 405 patients were included. Age was not significantly associated with all-cause mortality with a hazard ratio (HR) of 1.00 (95% confidence interval: 0.98 to 1.02, p=0.92). There was no heterogeneity (chi^2=4.92, p=0.67, I^2=0%).



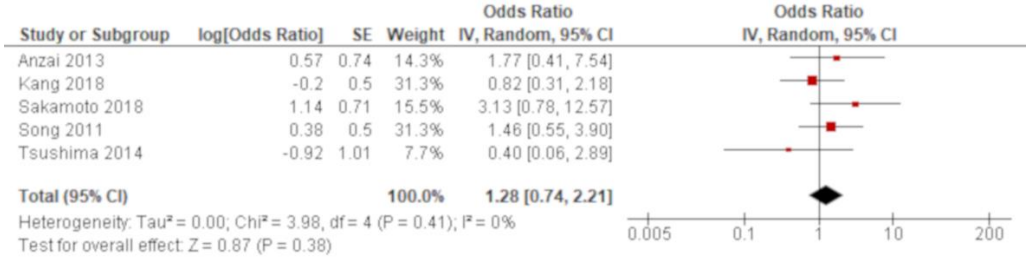
Supplementary e-Figure 3. Forrest plot of the result of univariate analysis for age (combined by odds ratio)

The result of univariate analysis in 3 studies was pooled for meta-analysis and a total of 236 patients were included. Age was not significantly associated with all-cause mortality with an odds ratio (OR) of 1.02 (95% confidence interval: 0.98 to 1.05, p=0.35). There was no heterogeneity (chi^2=0.34, p=0.84, I^2=0%).



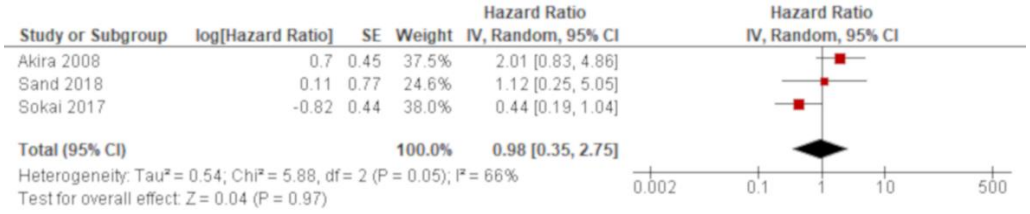
Supplementary e-Figure 4. Forrest plot of the result of univariate analysis for sex (male vs. female) (combined by hazard ratio)

The result of univariate analysis in 7 studies was pooled for meta-analysis and a total of 377 patients were included. Men were not significantly associated with all-cause mortality with a hazard ratio (HR) of 0.93 (95% confidence interval: 0.65 to 1.34, p=0.71). There was no heterogeneity (chi^2=4.01, p=0.68, I^2=0%).



Supplementary e-Figure 5. Forrest plot of the result of univariate analysis for sex (male vs. female) (combined by odds ratio)

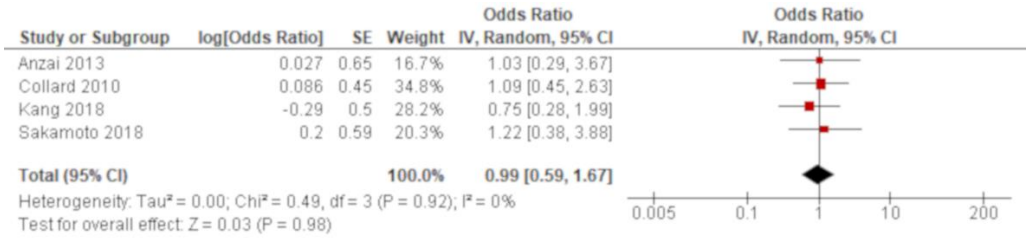
The result of univariate analysis in 5 studies was pooled for meta-analysis and a total of 306 patients were included. Men were not significantly associated with all-cause mortality with an odds ratio (OR) of 1.28 (95% confidence interval: 0.74 to 2.21, p=0.38). There was no heterogeneity (chi^2=3.98, p=0.41, I^2=0%).



Supplementary e-Figure 6. Forrest plot of the result of univariate analysis for smoking history (ever-smoker vs. never-smoker) (combined by hazard ratio)

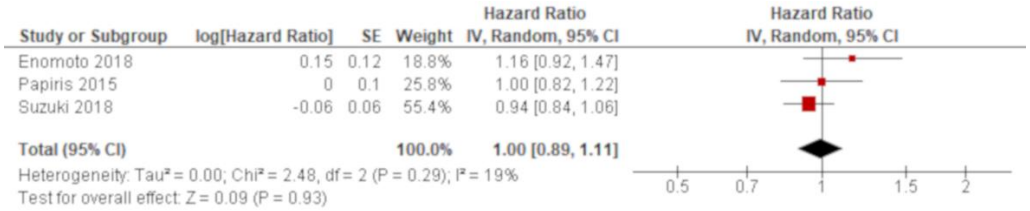
The result of univariate analysis in 3 studies was pooled for meta-analysis and a total of 145 patients were included. Smoking history was not significantly associated with all-cause mortality with a hazard ratio (HR) of 0.98 (95% confidence interval: 0.35 to 2.75, p=0.97). There was considerable heterogeneity with statistical significance (chi^2=5.88, p=0.05, I^2=66%). The 95% prediction interval ranged from 0.0000 to 95377. All studies were conducted in Japan and implemented nearly the same definition of AE of IPF. One study (Sokai 2017 [62]) demonstrated the effect estimate in the opposite direction from the other two studies. It included over 50 patients and analysed 180-day all-cause mortality whereas the other two studies included over 50 or fewer than 50 patients and analysed in-hospital or overall all-cause mortality.

Kamiya H, Panlaqui OM. *BMJ Open* 2020; 10:e035420. doi: 10.1136/bmjopen-2019-035420



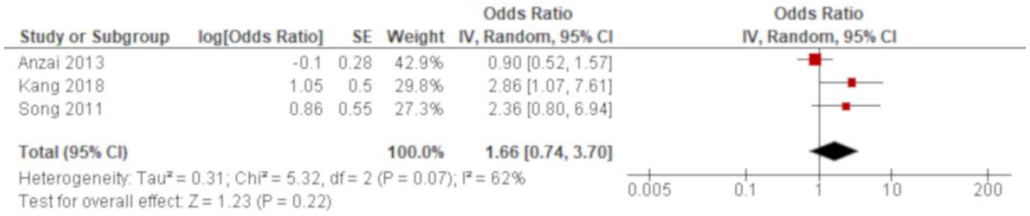
Supplementary e-Figure 7. Forrest plot of the result of univariate analysis for smoking history (ever-smoker vs. never-smoker) (combined by odds ratio)

The result of univariate analysis in 4 studies was pooled for meta-analysis and a total of 243 patients were included. Smoking history was not significantly associated with all-cause mortality with an odds ratio (OR) of 0.99 (95% confidence interval: 0.59 to 1.67, p=0.98). There was no heterogeneity (chi^2=0.49, p=0.92, I^2=0%).



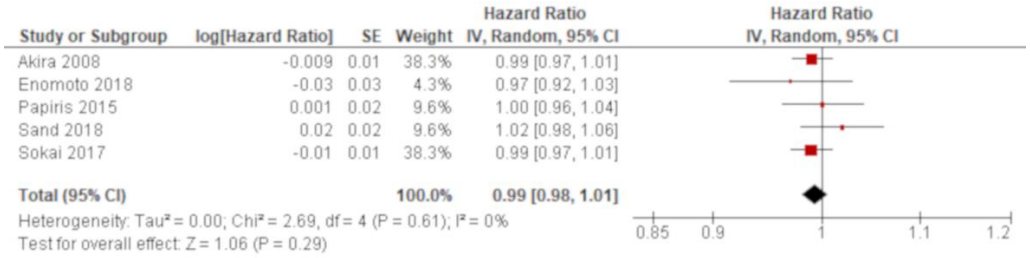
Supplementary e-Figure 8. Forrest plot of the result of univariate analysis for smoking history (pack-year)

The result of univariate analysis in 3 studies was pooled for meta-analysis and a total of 116 patients were included. Smoking history was not significantly associated with all-cause mortality with a hazard ratio (HR) of 1.00 (95% confidence interval: 0.89 to 1.11, p=0.93). There was mild heterogeneity with no statistical significance (chi^2=2.48, p=0.29, I^2=19%). The 95% prediction interval ranged from 0.51 to 1.97.



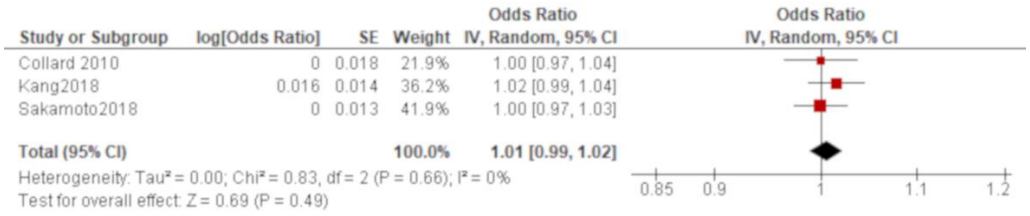
Supplementary e-Figure 9. Forrest plot of the result of univariate analysis for fever

The result of univariate analysis in 3 studies was pooled for meta-analysis and a total of 206 patients were included. Fever was not significantly associated with all-cause mortality with an odds ratio (OR) of 1.66 (95% confidence interval: 0.74 to 3.70, p=0.22). There was considerable heterogeneity with statistical significance (chi^2=5.32, p=0.07, I^2=62%). The 95% prediction interval ranged from 0.0003 to 10770. All studies implemented the same definition of AE of IPF. One study (Anzai 2013 [37]), which was conducted in Japan, demonstrated the effect estimate in the opposite direction from the other two studies. It included 50 patients and analysed overall all-cause mortality. The other two studies, which were conducted in Korea, included over 50 patients and analysed in-hospital all-cause mortality.



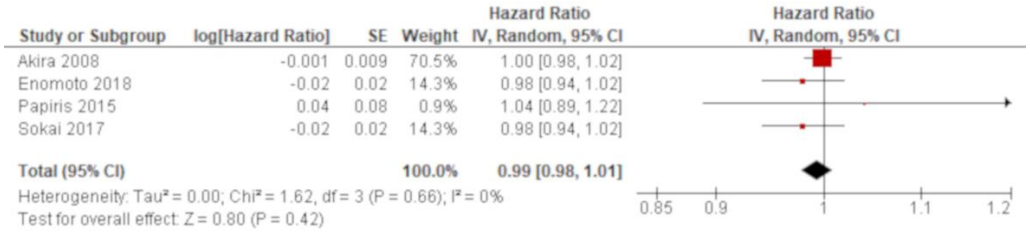
Supplementary e-Figure 10. Forrest plot of the result of univariate analysis for percentage of predicted value of forced vital capacity (%FVC) (combined by hazard ratio)

The result of univariate analysis in 5 studies was pooled for meta-analysis and a total of 199 patients were included. %FVC was not significantly associated with all-cause mortality with a hazard ratio (HR) of 0.99 (95% confidence interval: 0.98 to 1.01, p=0.29). There was no heterogeneity (chi^2=2.69, p=0.61, I^2=0%).



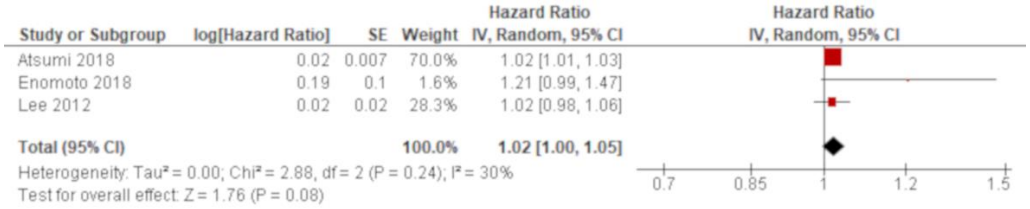
Supplementary e-Figure 11. Forrest plot of the result of univariate analysis for percentage of predicted value of forced vital capacity (%FVC) (combined by odds ratio)

The result of univariate analysis in 3 studies was pooled for meta-analysis and a total of 193 patients were included. %FVC was not significantly associated with all-cause mortality with an odds ratio (OR) of 1.01 (95% confidence interval: 0.99 to 1.02, p=0.49). There was no heterogeneity (chi^2=0.83, p=0.66, I^2=0%).



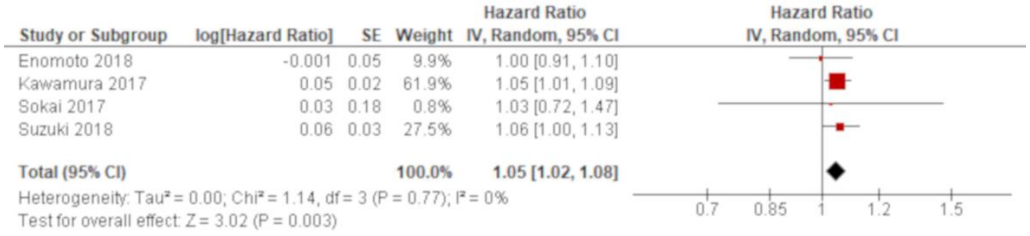
Supplementary e-Figure 12. Forrest plot of the result of univariate analysis for percentage of predictive value of diffusion capacity of the lung for carbon monoxide (%DLCO)

The result of univariate analysis in 4 studies was pooled for meta-analysis and a total of 171 patients were included. %DLCO was not significantly associated with all-cause mortality with a hazard ratio (HR) of 0.99 (95% confidence interval: 0.98 to 1.01, p=0.42). There was no heterogeneity (chi^2=1.62, p=0.66, I^2=0%).



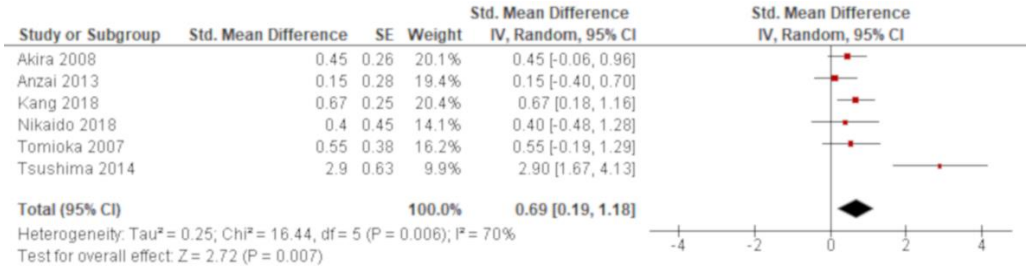
Supplementary e-Figure 13. Forrest plot of the result of univariate analysis for extent of abnormality on high resolution computed tomography (HRCT) scan

The result of univariate analysis in 3 studies was pooled for meta-analysis and a total of 120 patients were included. Extent of abnormality on HRCT scan was not significantly associated with all-cause mortality with a hazard ratio (HR) of 1.02 (95% confidence interval: 1.00 to 1.05, p=0.08). There was moderate heterogeneity with no statistical significance (chi^2=2.88, p=0.24, I^2=30%). The 95% prediction interval ranged from 0.85 to 1.23.



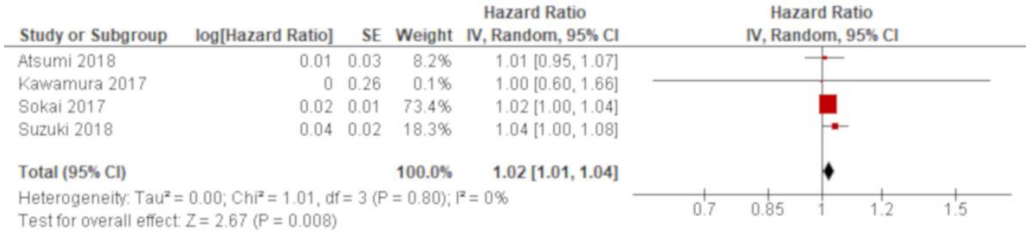
Supplementary e-Figure 14. Forrest plot of the result of univariate analysis for C-reactive protein (CRP) (combined by hazard ratio)

The result of univariate analysis in 4 studies was pooled for meta-analysis and a total of 243 patients were included. CRP was significantly associated with all-cause mortality with a hazard ratio (HR) of 1.05 (95% confidence interval: 1.02 to 1.08, p=0.003). There was no heterogeneity (chi^2=1.14, p=0.77, I^2=0%).



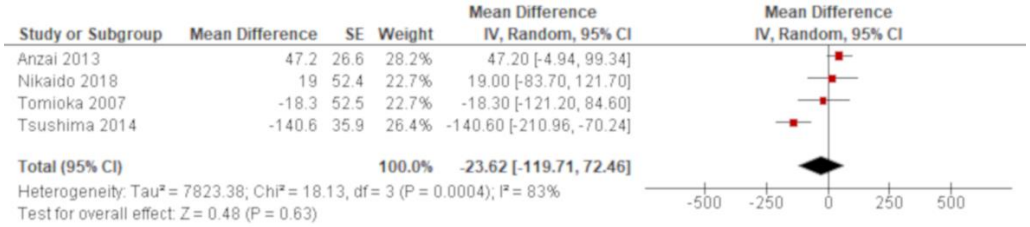
Supplementary e-Figure 15. Forrest plot of the result of univariate analysis for C-reactive protein (CRP) (combined by standardized mean difference)

The result of univariate analysis in 6 studies was pooled for meta-analysis and a total of 242 patients were included. CRP was significantly associated with all-cause mortality with a standardized mean difference (SMD) of 0.69 (95% confidence interval: 0.19 to 1.18, p=0.007). There was substantial heterogeneity (chi^2=16.44, p=0.006, I^2=70%). The 95% prediction interval ranged from -0.86 to 2.24. All studies except for one study (Kang 2018 [47]) were conducted in Japan and most of these studies included 50 or fewer patients. All studies implemented nearly the same definition of AE of IPF. The effect of one study (Tsushima 2014 [67]) was extremely different from that of the other five studies. It analysed 28-day all-cause mortality whereas the other five studies analysed either in-hospital, 60-day, 3-month or overall all-cause mortality. Meta-analysis excluding this study demonstrated a SMD of 0.45 (95%CI: 0.19 to 0.72) with no heterogeneity (chi^2=2.00, p=0.74, I^2=0%).



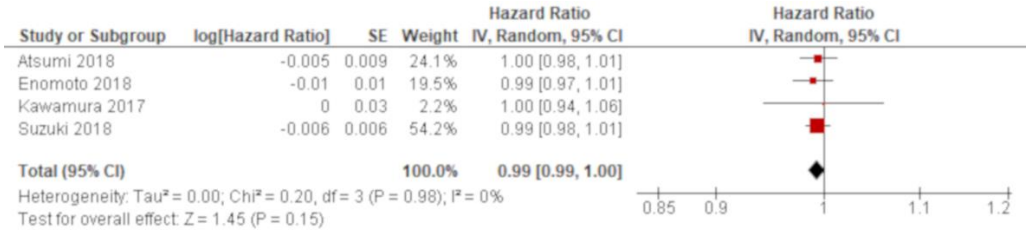
Supplementary e-Figure 16. Forrest plot of the result of univariate analysis for Krebs von den Lungen-6 (KL-6) (combined by hazard ratio)

The result of univariate analysis in 4 studies was pooled for meta-analysis and a total of 265 patients were included. KL-6 was significantly associated with all-cause mortality with a hazard ratio (HR) of 1.02 (95% confidence interval: 1.01 to 1.04, p=0.008). There was no heterogeneity (chi^2=1.01, p=0.80, I^2=0%).



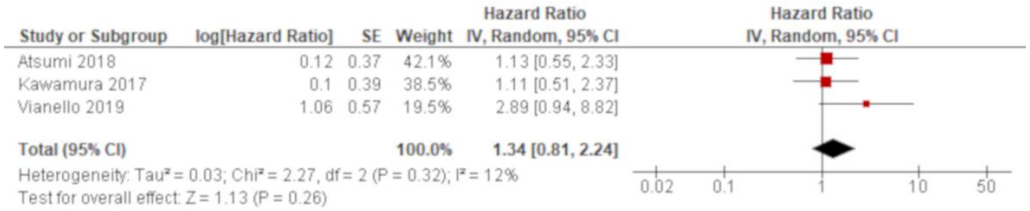
Supplementary e-Figure 17. Forrest plot of the result of univariate analysis for Krebs von den Lungen-6 (KL-6) (combined by mean difference)

The result of univariate analysis in 4 studies was pooled for meta-analysis and a total of 118 patients were included. KL-6 was not significantly associated with all-cause mortality with a mean difference (MD) of -23.6 (95% confidence interval: -119.7 to 72.5, p=0.63). There was substantial heterogeneity with statistical significance (chi^2=18.13, p=0.0004, I^2=83%). The 95% prediction interval ranged from -458.7 to 411.5. All studies were conducted in Japan and included 50 or fewer patients. All studies implemented nearly the same definition of AE of IPF. The effect of one study (Tsushima 2014 [67]) was extremely different from that of the other three studies. It analysed 28-day all-cause mortality whereas the other three studies analysed either in-hospital, 60-day or overall all-cause mortality. Meta-analysis excluding this study demonstrated an MD of 31.3 (95%CI: -11.1 to 73.7) with no heterogeneity (chi^2=1.30, p=0.52, I^2=0%).



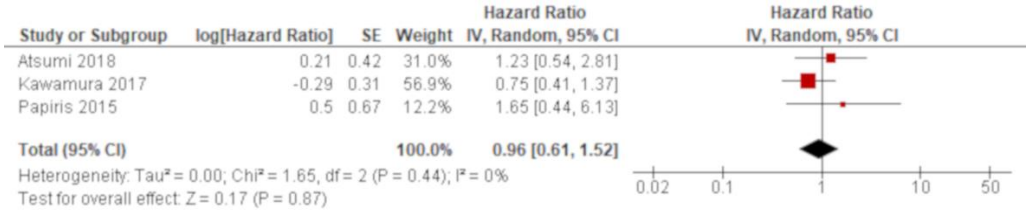
Supplementary e-Figure 18. Forrest plot of the result of univariate analysis for surfactant protein-D (SP-D)

The result of univariate analysis in 4 studies was pooled for meta-analysis and a total of 243 patients were included. SP-D was not significantly associated with all-cause mortality with a hazard ratio (HR) of 0.99 (95% confidence interval: 0.99 to 1.00, p=0.15). There was no heterogeneity (chi^2=0.20, p=0.98, I^2=0%).



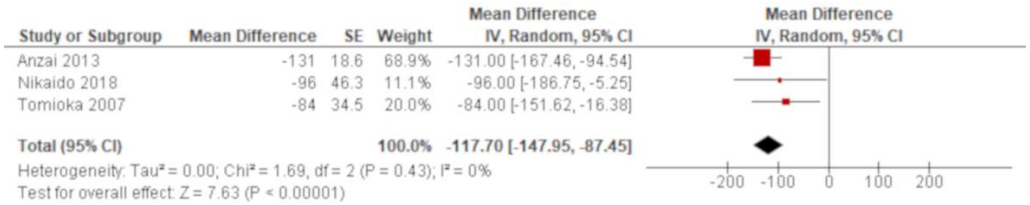
Supplementary e-Figure 19. Forrest plot of the result of univariate analysis for pirfenidone therapy before acute exacerbation

The result of univariate analysis in 3 studies was pooled for meta-analysis and a total of 164 patients were included. Pirfenidone therapy before acute exacerbation was not significantly associated with all-cause mortality with a hazard ratio (HR) of 1.34 (95% confidence interval: 0.81 to 2.24, p=0.26). There was mild heterogeneity with no statistical significance (chi^2=2.27, p=0.32, I^2=12%). The 95% prediction interval ranged from 0.02 to 75.6.



Supplementary e-Figure 20. Forrest plot of the result of univariate analysis for corticosteroid therapy before acute exacerbation

The result of univariate analysis in 3 studies was pooled for meta-analysis and a total of 161 patients were included. Corticosteroid therapy before acute exacerbation was not significantly associated with all-cause mortality with a hazard ratio (HR) of 0.96 (95% confidence interval: 0.61 to 1.52, p=0.87). There was no heterogeneity (chi^2=1.65, p=0.44, I^2=0%).



Supplementary e-Figure 21. Forrest plot of the result of univariate analysis for partial pressure of arterial oxygen to fraction of inspired oxygen (PaO2/FiO2) ratio (combined by mean difference)

As there was substantial heterogeneity in the result of meta-analysis using MD for PaO2/FiO2 ratio (Figure 4), meta-analysis was re-conducted after excluding one study (Tsushima 2014 [67]) that demonstrated an extremely different effect estimate from the other studies. The result was significant with an MD of -117.7 (95%CI: -148.0 to -87.5) and no heterogeneity was identified (chi^2=1.69, p=0.43, I^2=0%).

Supplementary e-Appendix: Search terms for each electronic database

Medline (Ovid)

1 exp Pulmonary Fibrosis/

2 exp Idiopathic Pulmonary Fibrosis/

3 exp Lung Diseases, Interstitial/

4 (pulmonary adj3 fibros$).mp.

5 (interstitial adj3 pneumoni$).mp.

6 exp Disease Progression /

7 (acute adj3 exacerbation?).mp.

8 (disease adj3 progression?).mp.

9 (disease adj3 exacerbation?).mp.

10 (deterioration?).mp.

11 incidence.sh.

12 exp Mortality/

13 follow-up studies.sh.

14 prognos$.tw.

15 predict$.tw.

16 course$.tw.

17 (1 or 2 or 3 or 4 or 5)

18 (6 or 7 or 8 or 9 or 10)

19 (11 or 12 or 13 or 14 or 15 or 16)

20 (17 and 18 and 19)

21limit 20 to yr="2002 -Current"

Kamiya H, Panlaqui OM. *BMJ Open* 2020; 10:e035420. doi: 10.1136/bmjopen-2019-035420

EMBASE (Ovid)

1 exp fibrosing alveolitis/

2 exp interstitial pneumonia/

3 exp lung fibrosis /

4 (pulmonary adj3 fibros$).mp.

5 (interstitial adj3 pneumoni$).mp.

6 exp disease exacerbation /

7 exp deterioration /

8 (acute adj3 exacerbation?).mp.

9 (disease adj3 progression?).mp.

10 (disease adj3 exacerbation?).mp.

11 risk$.mp.

12 diagnos$.mp.

13 follow-up.mp.

14 ep.fs.

15 outcome.tw.

16 exp disease course/

17 (1 or 2 or 3 or 4 or 5)

18 (6 or 7 or 8 or 9 or 10)

19 (11 or 12 or 13 or 14 or 15 or 16)

20 (17 and 18 and 19)

21 limit 20 to yr="2002 -Current"

Kamiya H, Panlaqui OM. *BMJ Open* 2020; 10:e035420. doi: 10.1136/bmjopen-2019-035420

Science Citation Index Expanded (Web of Science)

#1 TS=("interstitial NEAR/3 lung NEAR/3 disease$") OR TS=("interstitial NEAR/3 pneumonia$") OR TS=(alveolitis) OR TS=("pulmonary NEAR/3 fibros*")

#2 TS=(acute NEAR/3 exacerbation$) OR TS=(disease NEAR/3 progression$) OR TS=(disease NEAR/3 exacerbation$) OR TS=(deterioration$)

#3 TS=(prognos*) OR TS=(mortality) OR TS=(outcome) OR TS=(course$) OR TS=(follow-up) OR TS=(predict*) OR TS=(incidence) OR TS=(risk)

#4 #1 AND #2 AND #3

#5 #4 AND (2002-2019)

Kamiya H, Panlaqui OM. *BMJ Open* 2020; 10:e035420. doi: 10.1136/bmjopen-2019-035420

Google scholar

(“acute exacerbation” OR "disease progression" OR "disease exacerbation")
(“interstitial lung disease” OR “usual interstitial pneumonia” OR “idiopathic pulmonary fibrosis”) (prognosis OR mortality OR outcome)

Kamiya H, Panlaqui OM. *BMJ Open* 2020; 10:e035420. doi: 10.1136/bmjopen-2019-035420