Supplementary Material

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Supplementary Table 1: Search terms for frailty individual patient data meta-analysis.

	Concept 1	**Concept 2**	**Concept 3**
Key concepts	**COVID Patients**	**patients with frailty**	**Intervention**
Controlled vocabulary terms / Subject terms (MeSH terms, Entree terms)	"coronavirus"[MH] OR "coronavirus infections"[MH] OR "coronavirus"[TW] OR "corona virus"[TW] OR "HCoV"[TW] OR "nCov"[TW] OR "covid"[TW] OR "covid19"[TW] OR "Severe Acute Respiratory Syndrome Coronavirus 2"[TW] OR "SARS-CoV2"[TW] OR "SARS-CoV 2"[TW] OR "SARS Coronavirus 2"[TW] OR "MERS-CoV"[TW])	Frailty or frail or clinical frailty scale or CFS	Mechanical ventilation or Invasive ventilation

Supplementary Table 2: Summary characteristics of the studies that reported frail patients with COVID-19 related mortality, who were admitted to ICU.

Author Country	**Setting**	**Study period** (DD/MM/YY)	**Sample size Proportion female (%)**	**Age, mean (SD)**	**Proportion Caucasian (%)**	**Frailty measure; Proportion frail**	**COVID-19 Diagnosis**	**Overall Cohort Mortality rate**	**Number of patients admitted to ICU, n (%)**	**NOS grading**
Studies Included for Individual patient data meta-analysis										
Aliberti (1) Brazil	COVID special hospital	30/03/20 to 7/07/20	1830 43%	66 (11)	N/R	CFS 25%	RT-PCR	37%	1141 (62.3%)	7 (fair)
Apea (2) UK	5 Acute hospitals	1/1/20 to 13/05/20	1737	59 (Asian) 64 (Black)	40%	831 had CFS 51.9%	RT-PCR	33%	95 (11.4%)	8 (good)
De Smet (3) Belgium	General hospital	12/03/20 to 30/04/20	81 59%	70.3 (20.1)	100%	CFS 79.5%	RT-PCR	23.5%	7 (8.6%)	6 (poor)
Koduri (4) UK	Acute hospital	20/02/20 to 07/05/20	500 40%	69.3 (17.4)	87.6%	CFS 42.9%	RT-PCR	38.6%	65 (13%)	6 (poor)
Lim (5) Singapore	National Centre of Infectious Disease	23/01/20 to 15/04/20	275 46.2%	59.7 (8.9)	N/R	CFS N/R	RT-PCR	N/R	32 (11.6%)	7 (fair)
Marengoni (6) Italy	COVID special hospital	08/03/20 to 14/04/20	165 39%	69.3 (14.5)	N/R	CFS 15.2%	RT-PCR / clinical	25.6%	5 (3%)	7 (fair)
Welch (7) UK, USA, Italy Libya, Egypt, Iraq, Saudi Arabia, Spain, Greece, Sudan, Cyprus Turkey	55 Acute hospitals	01/02/20 to 31/05/20	5711 44.9%	71.7 (18.8)	N/R	CFS 42.8%	RT-PCR	27.9%	650 (11.4%)	8 (good)
Studies not included in this Individual patient data meta-analysis										
Aw (8) UK	Acute hospital	8/03/20 to 30/04/20	677 39%	62.2 (17.4)	35%	CFS 71.3%	RT-PCR	40.4%	37 (5.6%)	6 (fair)
Brill (9) UK	Acute hospital	Until April 25th 2020	450 40%	70.3 (20)	59%	CFS	RT-PCR	38%	56 (12%)	7 (fair)
Chinnadurai (10) UK	Acute hospital	23/03/20 to 30/04/20	215 38%	72.0 (16.4)	87%	CFS 51.2%	RT-PCR	40%	24 (11.2%)	7 (fair)
Fagard (11) Belgium	Acute hospital	16/03/20 to 16/05/20	105 47.6%	81.7 (8.3)	N/R	CFS 59%	RT-PCR	13.3%	18 (17.1%)	7 (fair)

Hoek (12) Netherlands	Acute hospital	27/02/20 to 30/04/20	23 22%	60.7 (15.0)	61%	CFS ~22%	RT-PCR	21.7%	5 (21.7%)	4 (poor)
Kokosz-Bargiel (13) Poland	Acute hospital and ICU	10/03/20 to 10/06/20	67 31%	62.4 (10.4)	N/R	CFS 55%	RT-PCR	55.2%	32 (47.8%)	5 (poor)
Owen (14) UK	Acute hospital	23/01/20 to 13/03/20	301 44%	68.7 (15.6)	N/R	CFS 43.8%	RT-PCR / clinical	42.9%	13 (4.3%)	6 (poor)
Poco (15) Brazil	COVID special hospital	01/03/20 to 31/05/20	711 43%	66 (11)	N/R	CFS 25%	clinical	37%	159 (22.4%)	7 (fair)
Tehrani (16) Sweden	Acute hospital	05/03/20 to 28/04/20	255 41%	66.0 (17.0)	N/R	CFS 50%	RT-PCR	27.5%	132 (51.8%)	7 (fair)

ICU – intensive care unit, NOS – Newcastle-Ottawa Quality Assessment Score, N/R – not reported, RT-PCR – reversed transcriptase polymerized chain reaction
NOS study quality –
Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

Supplementary Table 3: Studies included in the individual patient data meta-analysis.

		Patients included in the study			Patients admitted to ICU		
		Overall	**Non-frail**	**Frail**	**Overall**	**Non-frail**	**Frail**
1.	Aliberti (1)^	1830	1336	494	1141^ (62.3%)	874 (47.8%)	266^ (53.8%)
2.	Welch (7)*	5711	2640	2441	650 (11.4%)	554 (21%)	91 (4.1%)
3.	Apea (2)**	831	400	431	95 (11.4%)	74 (18.5%)	21 (4.9%)
4.	Koduri (4)	437	284	216	65 (14.9%)	22 (7.7%)	7 (3.2%)
5.	Lim (17)	275	261	14	32 (11.6%)	29 (11.1%)	3 (21.4%)
6.	De Smet (3)	83	17	66	9 (10.8%)	3 (17.6%)	6 (9.1%)
7.	Marengoni (6)***	165	137	28	11 (3%)	11 7.1%)	0 (0%)
Total		9332	5075	3690	**2003^ (21.4%)**	**1613 (31.7%)**	**388 (10.5%)**

^ 2 patients with CFS score of 9 were excluded; 2001 patients were included in the final analysis.
* CFS scores missing in 630 patients.
** Total of 1700 patients with HFRS. Only 831 patients had CFS scores documented.
*** Although there were 11 patients admitted to ICU, the hospital outcome data was available in 5 patients.

Supplementary Table 4: Demographics of Patients with COVID-19 admitted to ICU based on whether the patients survived or died. Data are summarized according to distribution if normal (Mean [SD]), non-normal (Median [IQR]), Categorical and Binary (Number [%]).

Characteristics	**Survivors**	**Non-survivors**	**p-value***
Number	918	1083	-
General Demographics			
Male sex (%)	554 (50.2%)	508 (55.3%)	**0.025**
Age (years) (mean (SD))	67.1 (11.0)	61.4 (11.9)	< **0.001**
Age categories			
- < 50 years	38 (4.1%)	143 (13.2%)	< **0.001**
- 50 – 64.9 years	325 (35.4%)	497 (45.9%)	< **0.001**
- 65 – 74.9 years	351 (38.2%)	315 (38.4%)	< **0.001**
- ≥ 75 years	204 (22.2%)	128 (11.8%)	< **0.001**
Admission source			
- Home	195 (87.8%)	392 (91.8%)	0.12
- 24-hour long-term facility	15 (6.8%)	4 (0.9%)	**0.001**
- Other	12 (5.4%)	31 (7.3%)	0.41
Smoking status			
Current smoker	183 (27.7%)	181 (28.9%)	0.67
Ex or non-smoker	477 (72.3%)	445 (71.2%)	
Documented co-morbidities			
- Hypertension	465 (67.1%)	448 (69.1%)	0.45
- Cardiovascular disease	203 (22.5%)	179 (17.2%)	**0.003**
- Cerebrovascular accident	60 (8.7%)	39 (6.0%)	0.08
- Active cancer	121 (13.6%)	101 (9.7%)	**0.008**
- Chronic respiratory disease**	147 (16.1%)	171 (15.9%)	0.95
- Obesity (BMI ≥30 $kg.m^{-2}$)	215 (26.1%)	363 (38.5%)	< **0.001**
- Chronic kidney disease	130 (19.5%)	82 (13.4%)	**0.004**
- Diabetes mellitus	413 (45.1%)	410 (38.1%)	**0.002**
- Dementia	34 (3.8%)	18 (1.7%)	**0.007**
Charlson comorbidity index (median (IQR))	2 (1, 4)	1 (0, 3)	< **0.001**
Number of co-morbidities ≤ 2	222 (29.6%)	231 (22.6%)	**0.018**
Number of co-morbidities > 2	527 (70.4%)	713 (75.5%)	
Clinical frailty scale (median (IQR))	3 (3, 5)	3 (2, 4)	< **0.001**
Illness severity scores			
APACHE 2 (median (IQR))	14 (6, 23)	14 (9, 23)	0.07
APACHE 3 (median (IQR))	No data	No data	-
SAPS 2 (median (IQR))	38 (24, 56)	41 (30, 57)	**0.006**
SOFA (median (IQR))	7 (5, 12)	8 (5, 12)	0.09
Symptoms, n (%)			
Respiratory	776 (91.2%)	897 (91.4%)	0.93
Sputum	25 (4.1%)	24 (4.5%)	0.77
Fever	474 (55.8%)	630 (64.2%)	< **0.001**
Lethargy / Myalgia	254 (40.5%)	259 (46.8%)	**0.030**
Delirium	98 (11.6%)	100 (10.2%)	0.37
Gastrointestinal	75 (11.9%)	72 (13.0%)	0.60
Symptom time (days)	7 (5, 11)	8 (5, 10)	0.35
Time to ICU (hours)	3 (2, 4)	3 (2, 5)	0.97
Pathology results (first 24hrs), median (IQR)			
Acid base status			
pH	7.36 (0.12)	7.40 (0.09)	< **0.001**
PaO_2 (mmHg)	77 (36)	78 (35)	0.68
$PaCO_2$ (mmHg)	42 (14)	39 (11)	**0.003**
HCO_3 (mmol/l)	23 (5)	24 (4)	< **0.001**
SaO_2	90 (10)	91 (9)	0.87
L-lactate (mmol/l)	13 (7, 18)	9 (2, 15)	< **0.001**

Biochemistry			
CRP	167 (84, 268)	138 (66, 236)	< **0.001**
Urea	54 (18, 102)	26 (7, 55)	< **0.001**
Creatinine	113 (80, 203)	90 (70, 141)	< **0.001**
LDH	501 (384, 666)	431 (321, 547)	< **0.001**
D-dimer	2.36 (1.09, 7.34)	1.37 (0.65, 3.63)	< **0.001**
Troponin	0.03 (0.01, 0.07)	0.02 (0.00, 0.03)	< **0.001**
Haematology			
Neutrophils	8.2 (5.4, 12.6)	7.1 (4.8, 10.5)	< **0.001**
Lymphocytes	0.75 (0.50, 1.10)	0.89 (0.60, 1.20)	< **0.001**
N-L ratio	10.8 (6.2, 19.0)	8.0 (4.8, 14.3)	< **0.001**
Platelets	203 (146, 278)	221 (165, 306)	< **0.001**
Radiology			
Abnormal CXR	672 (73.2%)	850 (78.5%)	**0.003**
Illness severity scores			
APACHE II	19 (9, 25)	10 (5, 19)	< **0.001**
SAPS 2	47 (30, 62)	31 (24, 47)	< **0.001**
SOFA	9 (6, 13)	6 (4, 9)	< **0.001**
Outcome data			
ICU LOS (days)	11 (6, 19)	10 (5, 19)	0.14
Hospital LOS (days)	13 (8, 21)	19 (12, 32)	< **0.001**
Organ Support			
HFNC	31 (79.5%)	42 (73.7%)	0.63
CPAP	176 (27.0%)	241 (40.4%)	< **0.001**
IMV	609 (66.3%)	405 (37.4%)	< **0.001**
IMV (days)	12 (7, 19)	9 (5, 16)	< **0.001**
Dialysis	311 (45.3%)	98 (15.2%)	< **0.001**
Vasopressors	550 (84.8%)	275 (46.8%)	< **0.001**

SD - standard deviation, IQR - interquartile range, IHD - ischemic heart disease, CVD - cardiovascular disease, COPD - chronic obstructive pulmonary disease, BMI – body mass index, APACHE - Acute Physiology and Chronic Health Evaluation, SAPS - Simplified Acute Physiology Score, SOFA - Sequential Organ Failure Score, PaO_2 - partial pressure of oxygen, $PaCO_2$ - partial pressure of carbon dioxide, SaO_2 - arterial oxygen saturation, CRP - C-reactive protein, WCC - white cell count, N-L - neutrophil-lymphocyte ratio, LDH - lactate dehydrogenase, CXR - chest X-ray

* Some of the results will be statistically significant because of the large sample size but may not be clinically significant.

** COPD and/or asthma

Supplementary Table 5: Multivariable analysis: Outcome variable is hospital mortality.

Variable	Initial model		Final model	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**
Age	1.06 (1.04, 1.08)	< **0.001**	1.06 (1.04, 1.08)	< **0.001**
Hypertension	0.62 (0.44, 0.89)	**0.006**	0.64 (0.46, 0.89)	**0.008**
Diabetes Mellitus	1.12 (0.82, 1.53)	0.46	-	-
APACHE-2[#]	0.99 (0.97, 1.02)	0.81	-	-
SOFA[#] (n=1165)	1.04 (0.98, 1.11)	0.17	1.05 (1.01, 1.09)	**0.024**
IMV (n=1014)	3.74 (2.36, 5.92)	< **0.001**	3.87 (2.47, 6.06)	< **0.001**
Dialysis (n=409)	3.75 (2.62, 5.33)	< **0.001**	3.95 (2.79, 5.60)	< **0.001**
Vasopressors (n=815)	3.32 (2.27, 4.87)	< **0.001**	3.19 (2.19, 4.64)	< **0.001**
pH	0.40 (0.06, 2.79)	0.36	-	-
Lactate	1.03 (1.01, 1.05)	**0.013**	1.03 (1.01, 1.05)	**0.008**
CFS Level				
1	1.00	Reference Level	1.00	Reference Level
2	1.41 (0.63, 3.15)	0.63	1.45 (0.66, 3.19)	0.36
3	1.47 (0.68, 3.15)	0.33	1.50 (0.71, 3.19)	0.29
4	2.99 (1.32, 6.77)	**0.008**	3.26 (1.46, 7.29)	**0.004**
5	3.54 (1.48, 8.47)	**0.004**	3.86 (1.63, 9.13)	**0.002**
6	3.44 (1.35, 8.80)	**0.010**	3.67 (1.46, 9.23)	**0.006**
7	4.52 (1.64, 12.41)	**0.003**	4.73 (1.73, 12.90)	**0.002**
8	8.85 (1.26, 62.18)	**0.028**	16.56 (2.82, 120.04)	**0.005**

APACHE - Acute Physiology and Chronic Health Evaluation, SOFA - Sequential Organ Failure Score, IMV - invasive mechanical ventilation, CFS - clinical frailty scale
[#]on day 1

Supplementary Table 6: Univariate analysis (grouped by publication). Dependent variable was hospital death.

Variable	Odds ratio	p-value
Age	1.04	< 0.001
Gender	1.05	0.58
Admitted from Home	0.64	0.11
Admitted from Nursing Home	7.66	< 0.001
Admitted from Other	0.73	0.37
Smoker	0.91	0.47
≤ 2 Comorbidities	0.90	0.37
> 2 Comorbidities	1.03	0.82
Hypertension	0.88	0.29
Cardiovascular disease	1.23	0.08
Stroke	1.46	0.08
Active cancer	1.37	0.030
COPD / Asthma	1.17	0.21
Obesity	0.61	< 0.001
Chronic kidney disease	1.57	0.003
Diabetes mellitus	1.23	0.026
Dementia	2.01	0.020
Charlson Comorbidity Index	1.12	< 0.001
Clinical Frailty Score	1.30	< 0.001
Respiratory symptoms	0.85	0.34
Sputum production	0.90	0.73
Fever	0.81	0.032
Lethargy / Myalgia	0.77	0.029
Delirium	1.13	0.41
Gastrointestinal symptoms	0.91	0.58
Symptom time (days)	0.99	0.48
Time to ICU	0.96	0.023
pH	0.021	< 0.001
PaO2 (mmHg)	1.000	0.76
PaCO2 (mmHg)	1.012	0.004
HCO3 (mmol/L)	0.948	< 0.001
SaO2	0.998	0.80
L-lactate (mmol/L)	1.036	< 0.001
CRP	1.001	0.011
Urea	1.011	< 0.001
Creatinine	1.011	< 0.001
LDH	1.001	< 0.001
D-dimer (x1000)	1.000	< 0.001
Troponin	1.001	0.015
Neutrophils	1.036	< 0.001
Lymphocytes	0.768	0.002
N-L ratio	1.000	0.14
Platelets	0.998	< 0.001
Abnormal CXR	0.677	0.002
APACHE II	1.070	< 0.001
SAPS 2	1.042	< 0.001
SOFA	1.169	< 0.001
HFNC	1.384	0.51
CPAP	0.538	< 0.001
IMV	4.295	< 0.001
IMV (days)	1.022	0.001
Dialysis	4.661	< 0.001
Vasopressors	6.505	< 0.001

ICU LOS (days)	0.999	0.79
Hospital LOS (days)	0.964	< 0.001

SD - standard deviation, IQR - interquartile range, IHD - ischemic heart disease, CVD - cardiovascular disease, COPD - chronic obstructive pulmonary disease, BMI – body mass index, APACHE - Acute Physiology and Chronic Health Evaluation, SAPS - Simplified Acute Physiology Score, SOFA - Sequential Organ Failure Score, PaO_2 - partial pressure of oxygen, $PaCO_2$ - partial pressure of carbon dioxide, SaO_2 - arterial oxygen saturation, CRP - C-reactive protein, WCC - white cell count, N-L - neutrophil-lymphocyte ratio, LDH - lactate dehydrogenase, CXR - chest X-ray

[*] Some of the results will be statistically significant because of the large sample size but may not be clinically significant.

[**] COPD and/or asthma

Supplementary Table 7: Demographics, and comorbidities, based on Clinical Frailty Scale status.

Clinical Frailty Scale	***CFS-1***	***CFS-2***	***CFS-3***	***CFS-4***	***CFS-5***	***CFS-6***	***CFS-7***	***CFS-8***
Number of patients, n	***193***	***450***	***669***	***301***	***180***	***124***	***70***	***14***
Age, mean (SD)	*56.8 (13.1)*	*58.9 (11.5)*	*64.4 (9.8)*	*67.2 (10.1)*	*70.4 (11.1)*	*69.9 (11.8)*	*70.6 (12.1)*	*68.7 (18.4)*
APACHE 2 score mean (SD)	*12.8 (9.6)*	*14.8 (9.7)*	*15.5 (9.5)*	*14.5 (8.8)*	*16.3 (8.3)*	*15.0 (9.5)*	*15.1 (8.7)*	*22.8 (8.4)*
SAPS-2 score, mean (SD)	*38.4 (17.3)*	*40.9 (18.1)*	*41.5 (18.0)*	*39.8 (17.1)*	*44.6 (16.5)*	*42.0 (17.7)*	*41.5 (17.9)*	*59.2 (20.5)*
Chronic Respiratory disease, n (%)	*24 (12.7%)*	*62 (14%)*	*94 (14.1%)*	*71 (23.6%)*	*32 (17.8%)*	*23 (18.5%)*	*10 (14.3%)*	*2 (12.5%)*
Chronic Cardiovascular disease, n (%)	*11 (6.0%)*	*43 (10·1%)*	*101 (15.4%)*	*86 (29.0%)*	*70 (39.1%)*	*39 (31.5%)*	*27 (38.6%)*	*5 (35.7%)*
Hypertension, n (%)	*33 (44.6%)*	*143 (61.1%)*	*341 (67.1%)*	*176 (77.5%)*	*105 (76.6%)*	*69 (77.5%)*	*38 (61.5%)*	*8 (61.5%)*
Diabetes Mellitus, n (%)	*45 (23.8%)*	*152 (34.2%)*	*283 (42.4%)*	*163 (54.2%)*	*84 (46.7%)*	*58 (46.8%)*	*32 (45.7%)*	*6 (42.8%)*
Chronic renal failure, n (%)	*4 (6.6%)*	*14 (6.7%)*	*61 (12.5%)*	*55 (24.9%)*	*37 (27%)*	*24 (27.3%)*	*15 (25.4%)*	*2 (14.3%)*
Obesity, n (%)	*40 (27.2%)*	*136 (36.2%)*	*208 (34.3%)*	*112 (39.6%)*	*41 (24.7%)*	*26 (23.6%)*	*13 (20%)*	*2 (12.5%)*
Active Cancer, n (%)	*10 (5.7%)*	*15 (3.6%)*	*56 (8.6%)*	*52 (17.6%)*	*40 (22.2%)*	*28 (22.8%)*	*15 (21.4%)*	*6 (42.8%)*
Dementia, n (%)	*0 (0)*	*1 (0.2%)*	*5 (0.8%)*	*5 (1.7%)*	*9 (5%)*	*13 (10.6%)*	*14 (20%)*	*5 (31.3%)*
Stroke, n (%)	*2 (2.7%)*	*8 (3.4%)*	*22 (4.3%)*	*14 (6.2%)*	*23 (16.8%)*	*14 (15.7%)*	*15 (25.4%)*	*1 (7.1%)*

APACHE = Acute Physiology and Chronic Health Evaluation, SAPS = simplified acute physiology score, SD = standard deviation.

Supplementary Table 8: Unadjusted secondary outcomes.

Variable	Non-frail	Frail	p-value
Length of stay, (median (IQR))			
- ICU length of stay	11 (5, 20)	8 (4, 16)	< **0.001**
- Hospital length of stay	16 (10, 28)	13 (8, 23)	< **0.001**
- ICU Occupied bed-days (x1000)	21.4 (84.3%)	4.0 (15.7%)	< **0.001**
Organ support, n (%)			
- Noninvasive ventilation	344 (35%)	73 (27%)	**0.011**
- Mechanical ventilation	815 (51%)	199 (51%)	**0.787**
- Mechanical ventilation (days), (median (IQR))	11 (6, 18)	9 (5, 16)	**0.012**
- Continuous renal replacement therapy	335 (32%)	74 (25%)	**0.026**
- Vasopressors	653 (68%)	172 (63%)	0.19
Discharge destination, n (%)			
- Home	726 (45%)	89 (23%)	< **0.001**
- Rehabilitation	568 (35%)	90 (23%)	< **0.001**
- 24-hour long-term facility	24 (1.5%)	9 (2.3%)	0.17
- Other	119 (15%)	47 (25%)	**0.001**

ICU - intensive care unit, IQR - interquartile range

Supplementary Table 9: Organ support and discharge destination based on Clinical Frailty Scale.

Clinical Frailty Scale	***CFS-1***	***CFS-2***	***CFS-3***	***CFS-4***	***CFS-5***	***CFS-6***	***CFS-7***	***CFS-8***
Number of patients, n	***193***	***450***	***669***	***301***	***180***	***124***	***70***	***14***
Mechanical Ventilation, n/N (%)	*54/193 (28.0%)*	*199/450 (44.2%)*	*391/669 (58.5%)*	*171/301 (56.8%)*	*94/180 (52.2%)*	*64/124 (51.6%)*	*31/70 (44.4%)*	*10/14 (71.4%)*
Mechanical ventilation days, Mean (SD)	*13.8 (12.2)*	*15.1 (12.8)*	*14.4 (11.1)*	*12.5 (10.1)*	*12.2 (10.2)*	*12.8 (10.0)*	*10.2 (7.8)*	*10.6 (11.9)*
Non-invasive ventilation, n/N (%)	*34/72 (47.2%)*	*88/222 (39.6%)*	*153/476 (32.1%)*	*69/207 (33.3%)*	*36/126 (28.6%)*	*28/81 (34.6%)*	*8/51 (15.7%)*	*1/14 (7.7%)*
Renal replacement therapy, n/N (%)	*25/74 (33.8%)*	*70/233 (30%)*	*170/506 (33.6%)*	*70/227 (30.8%)*	*36/136 (26.5%)*	*25/87 (28.7%)*	*12/56 (21.4%)*	*1/13 (7.7%)*
Vasopressor infusion, n/N (%)	*41/68 (60.3%)*	*158/216 (73.2%)*	*324/475 (68.2%)*	*130/207 (62.8%)*	*79/126 (62.7%)*	*58/81 (71.6%)*	*28/51 (54.9%)*	*7/13 (53.9%)*
Died, n (%)	*53 (27.5%)*	*165 (36.7%)*	*295 (44.1%)*	*161 (53.5%)*	*109 (60.6%)*	*80 (64.5%)*	*43 (61.4%)*	*12 (8%)*
Home, n (%)*	*110 (570%)*	*232 (51.6%)*	*281 (42.0%)*	*103 (34.2%)*	*45 (25%)*	*29 (23.4%)*	*15 (21.4%)*	*0 (0)*
24-hour long-term facility, n (%)*	*2 (1.0%)*	*2 (0.4%)*	*15 (2.2%)*	*5 (1.7%)*	*2 (1.1%)*	*4 (3.2%)*	*3 (4.3%)*	*0 (0)*
Rehabilitation, n (%)*	*117 (60.6%)*	*215 (47.8%)*	*162 (24.2%)*	*46 (15.3%)*	*43 (23.9%)*	*35 (28.2%)*	*11 (15.7%)*	*1 (7.1%)*
Other, n (%)*	*28 (14.5%)*	*51 (11.3%)*	*78 (11.6%)*	*32 (10.6%)*	*24 (13.3%)*	*11 (8.9%)*	*9 (12.9%)*	*2 (14.3%)*

* Some of the entries are double counted

Supplementary Table 10: Duration of mechanical ventilation (secondary outcome; adjusted for age, chronic respiratory disease, chronic kidney disease, ischemic heart disease, admission source and APACHE 2 score), for patients among survivors and non-survivors who died after ICU by CFS.

Clinical frailty scale	Number of patients	Duration of Mechanical Ventilation among ICU survivors (days)		Duration of Mechanical Ventilation among those dying after ICU (days)	
		Unadjusted geometric mean (95%-CI)	Adjusted geometric mean^ (95%-CI)	Unadjusted geometric mean (95%-CI)	Adjusted geometric mean^^ (95%-CI)
1	193	6.7 (4.5, 10.1)	9.5 (8.3, 10.7)	16.8 (13.1, 15.6)	15.7 (14.3, 17.1)
2	450	10.2 (8.9, 12.0)	8.5 (7.7, 9.4)	13.1 (11.0, 15.6)	14.7 (13.5, 15.9)
3	669	7.8 (6.6, 9.4)	7.6 (6.9, 8.2)	12.1 (10.7, 13.8)	13.8 (12.7, 14.8)
4	301	7.8 (6.6, 9.4)	6.6 (5.9, 7.2)	11.8 (9.6, 14.6)	12.8 (11.7, 13.8)
5	180	7.5 (5.6, 10.0)	5.6 (4.8, 6.4)	10.6 (8.6, 13.2)	11.8 (10.7, 13.0)
6	124	8.2 (6.2, 11.0)	4.6 (3.6, 5.7)	11.3 (7.9, 16.0)	10.8 (9.5, 12.2)
7*	70	7.9** (5.2, 12.0)	3.6** (2.3, 5.0)	7.3** (4.6, 11.6)	9.9** (8.2, 11.5)
8*	14				

ICU - intensive care unit, 95%-CI - 95% confidence interval

* Note: Due to small sample numbers, CFS 7 & 8 were combined for duration of mechanical ventilation

^ Dichotomous comparison: non-frail vs. frail adjusted geometric mean for mechanical ventilation in survivors = 7.7 (7.0, 8.3) vs. 4.6 (3.5, 5.7); p<0.001

^^ Dichotomous comparison: non-frail vs. frail adjusted geometric mean for mechanical ventilation in non-survivors = 13.9 (12.8, 15.0) vs. 10.8 (9.5, 12.3); p<0.001

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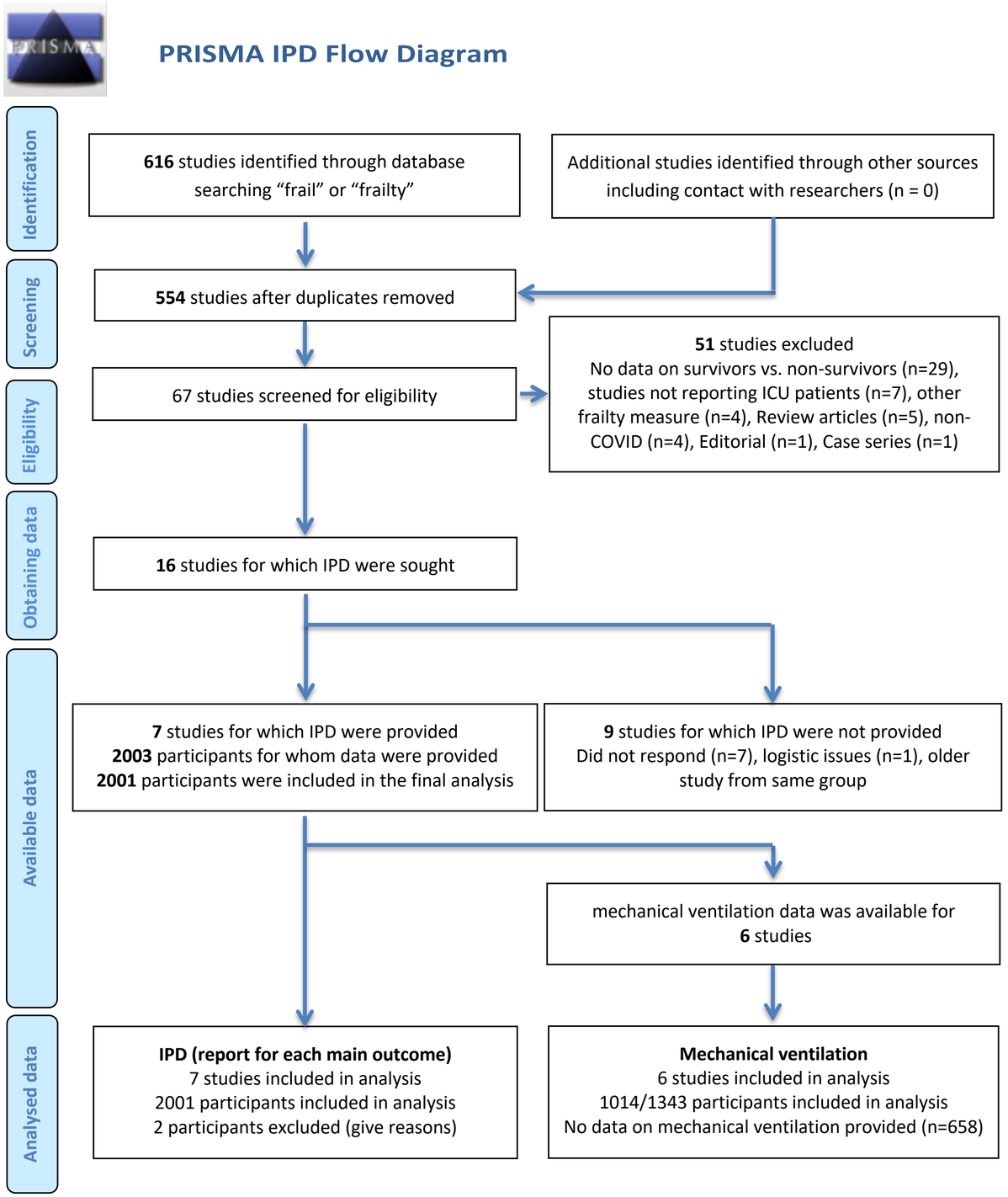
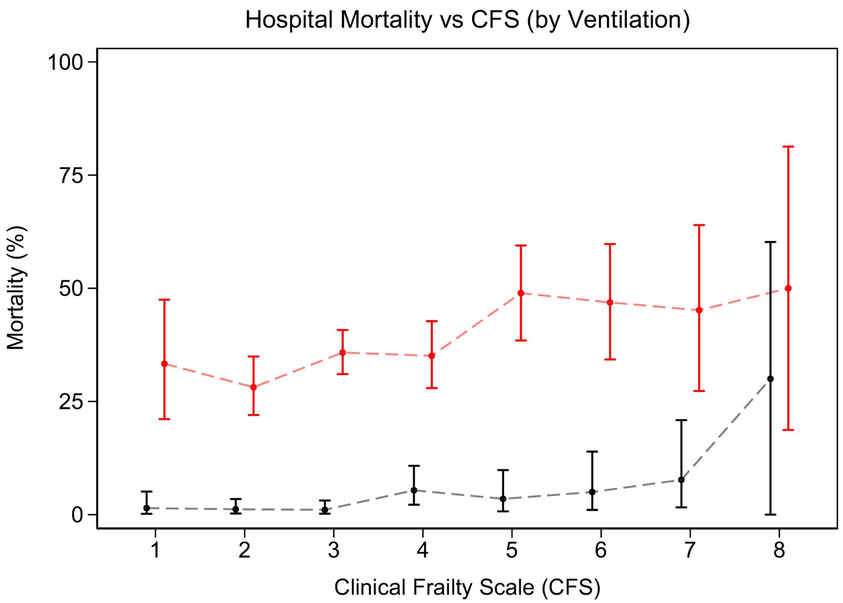
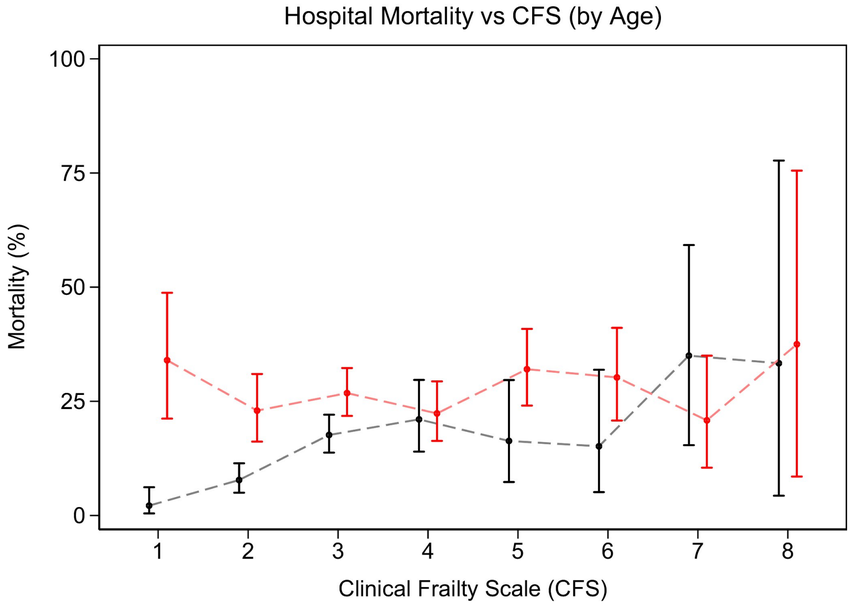
Supplementary Figure 1:

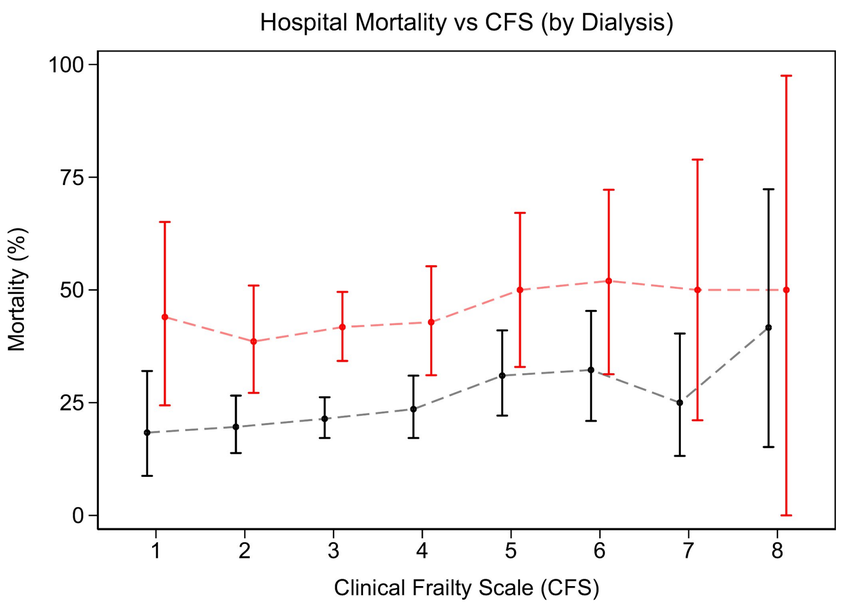


The PRISMA IPD flow diagram

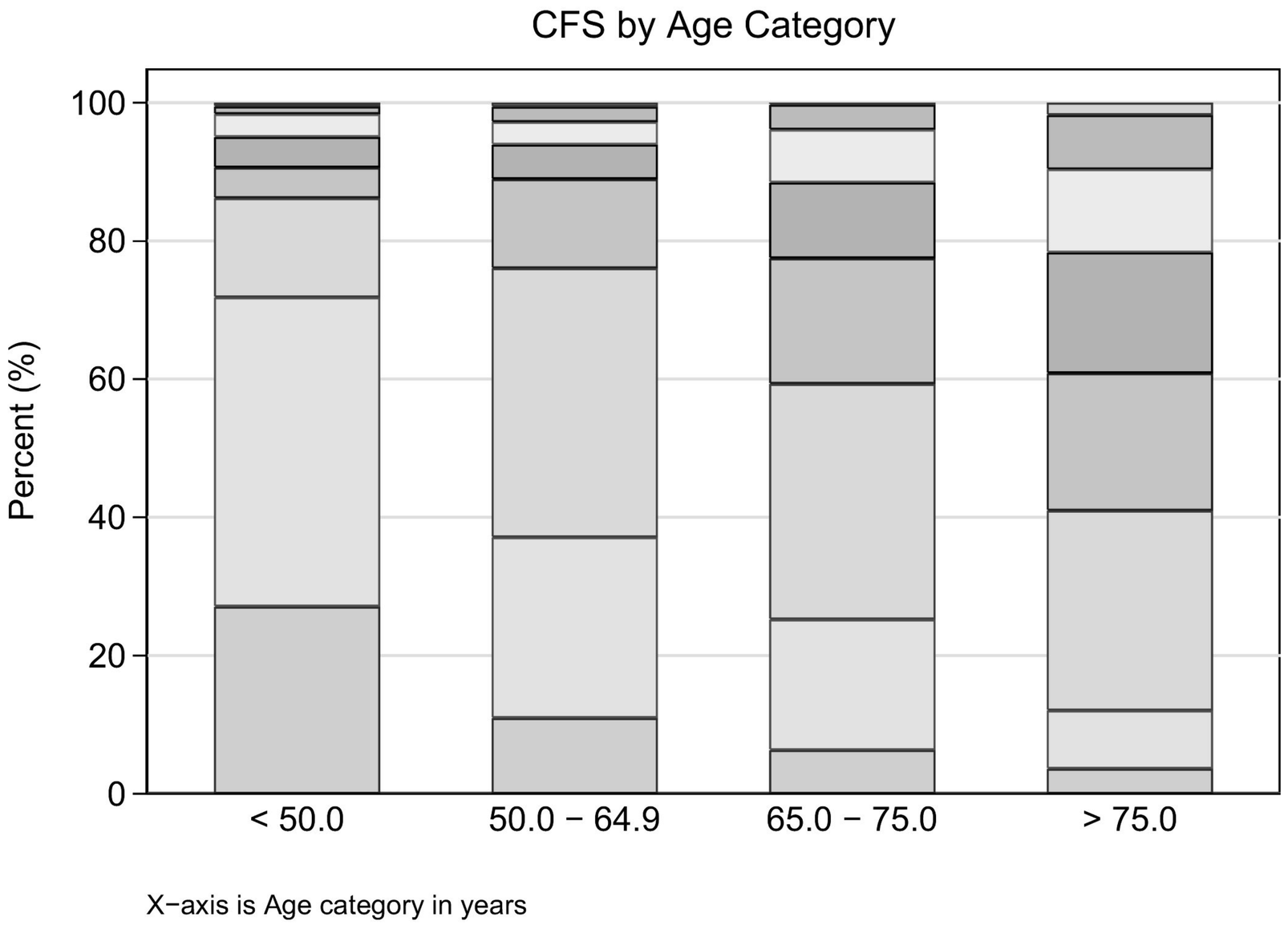
Supplementary Figure 2: Hospital mortality vs CFS categorises based on patient's age (panel a), MV (panel a), and need for renal replacement therapy (panel c).



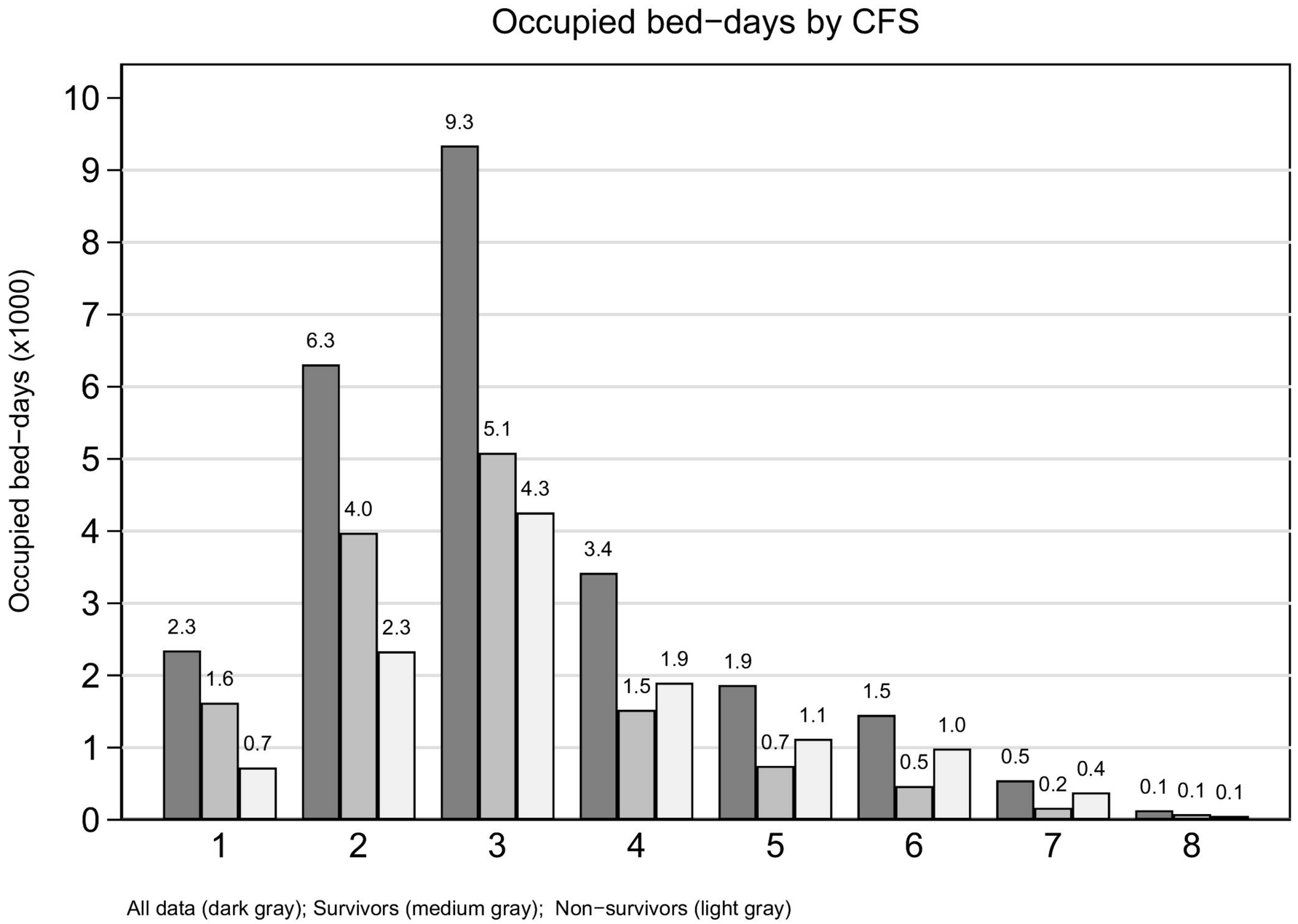




Supplementary Figure 3: CFS categories are denoted by the different stacked starting with CFS 1 at the bottom up to CFS 8 at the top.



Supplementary Figure 4: Total ICU bed-days stratified by Clinical Frailty Scale (CFS) comparing survivors and non-survivors.



Supplementary Figure 5: Heat map demonstrating the number of patients by individual CFS category who received mechanical ventilation (top panel). Heat map demonstrating the number of patients by individual CFS category who received mechanical ventilation amongst survivors and non-survivors (bottom panels).

	CFS 1	CFS 2	CFS 3	CFS 4	CFS 5	CFS 6	CFS 7	CFS 8
<50 years	4	5	1	0	0	0	0	0
50-59 years	14	67	118	34	12	10	9	1
60-69 years	18	70	154	74	31	21	10	3
70-79 years	13	47	97	47	31	22	8	2
≥80 years	4	6	21	16	20	11	4	4

ICU Survivors

	CFS 1	CFS 2	CFS 3	CFS 4	CFS 5	CFS 6	CFS 7	CFS 8
<60 years								
Total patients	13	58	121	31	9	12	6	1
>2 comorbidities	2	16	41	13	5	4	2	1
Mean ICU LOS	**12.1 (4.2)**	**14.5 (10.7)**	**15.9 (11.9)**	**11.9 (8.7)**	**19.6 (24.0)**	**13.8 (10.9)**	**7.0 (0.7)**	**1.0**
60-69.9 years								
Total patients	19	54	139	61	35	14	10	3
>2 comorbidities	4	11	55	35	22	9	5	3
Mean ICU LOS	**10.8 (2.6)**	**16.3 (7.5)**	**16.7 (14.4)**	**14.7 (8.7)**	**11.0 (8.0)**	**16.6 (18.5)**	**8.4 (1.5)**	**26.3 (24)**
70-79.9 years								
Total patients	8	35	66	46	20	17	13	2
>2 comorbidities	1	10	21	33	12	8	9	0
Mean ICU LOS	**13.4**	**18.0 (6.5)**	**16.6 (10.6)**	**11.2 (11.5)**	**11.7 (11.6)**	**8.1 (3.8)**	**10.0 (7.9)**	**2.0**
80-89.9 years								
Total patients	1	2	16	15	22	9	8	1
>2 comorbidities	0	1	7	12	15	4	4	0
Mean ICU LOS	**2.0**	**7.5**	**13.6 (16.4)**	**8.4 (5.1)**	**7.4 (3.6)**	**7.5 (17.2)**	**3.9 (5.9)**	**13.0**
90-100 years								
Total patients	0	0	2	1	1	1	2	1
>2 comorbidities	0	0	1	1	1	1	1	0
Mean ICU LOS	*	*	**6.5**	**9.0**	**1.0**	**0.0**	**5.5**	**6.0**

ICU non-survivors

	CFS 1	CFS 2	CFS 3	CFS 4	CFS 5	CFS 6	CFS 7	CFS 8
<60 years								
Total patients	2	16	28	13	5	1	6	1
>2 comorbidities	0	2	14	6	3	0	1	0
Mean ICU LOS	**29.5**	**18.5 (5.7)**	**13.0 (6.5)**	**13.8 (8.4)**	**16.0 (13.0)**	**42.0**	**12.7**	**3.0**
60-69.9 years								
Total patients	5	25	52	29	11	12	4	1
>2 comorbidities	1	7	16	15	5	8	2	0
Mean ICU LOS	**22.8**	**15.7 (11.5)**	**16.8 (15.3)**	**16.1 (13.0)**	**17.1 (4.8)**	**18.6 (13.8)**	**9.3 (9.2)**	**6.0**
70-79.9 years								
Total patients	9	12	49	15	20	11	3	1
>2 comorbidities	5	3	19	8	8	6	3	1
Mean ICU LOS	**12.9 (7.2)**	**14.4 (22.7)**	**17.1 (22.1)**	**17.1 (5.6)**	**15.4 (6.7)**	**15.3 (8.3)**	**10.3 (6.0)**	**9.0**
80-89.9 years								
Total patients	4	6	12	10	11	8	4	1
>2 comorbidities	3	0	3	6	6	5	2	1
Mean ICU LOS	**18.0 (4.2)**	**20.2 (5.7)**	**10.0 (4.7)**	**7.3 (3.1)**	**8.6 (3.2)**	**10.5 (9.0)**	**12.7 (9.2)**	**5.0**
90-100 years								
Total patients	0	0	2	0	2	1	0	1
>2 comorbidities	0	0	0	0	1	1	0	1
Mean ICU LOS	*	*	**2.0**	*	**5.5**	**5.0**	*	**3.0**

PRISMA-IPD Checklist of items to include when reporting a systematic review and meta-analysis of individual participant data (IPD)

PRISMA-IPD Section/topic	Item No	Checklist item	Reported on page
Title			
Title	1	Identify the report as a systematic review and meta-analysis of individual participant data.	Yes
Abstract			
Structured summary	2	Provide a structured summary including as applicable:	Yes
		Background: state research question and main objectives, with information on participants, interventions, comparators and outcomes.	
		Methods: report eligibility criteria; data sources including dates of last bibliographic search or elicitation, noting that IPD were sought; methods of assessing risk of bias.	
		Results: provide number and type of studies and participants identified and number (%) obtained; summary effect estimates for main outcomes (benefits and harms) with confidence intervals and measures of statistical heterogeneity. Describe the direction and size of summary effects in terms meaningful to those who would put findings into practice.	
		Discussion: state main strengths and limitations of the evidence, general interpretation of the results and any important implications.	
		Other: report primary funding source, registration number and registry name for the systematic review and IPD meta-analysis.	
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Yes
Objectives	4	Provide an explicit statement of the questions being addressed with reference, as applicable, to participants, interventions, comparisons, outcomes and study design (PICOS). Include any hypotheses that relate to particular types of participant-level subgroups.	Yes
Methods			
Protocol and registration	5	Indicate if a protocol exists and where it can be accessed. If available, provide registration information including registration number and registry name. Provide publication details, if applicable.	Yes
Eligibility criteria	6	Specify inclusion and exclusion criteria including those relating to participants, interventions, comparisons, outcomes, study design and characteristics (e.g. years when conducted, required minimum follow-up). Note whether these were applied at the study or individual level i.e. whether eligible participants were included (and ineligible participants excluded) from a study that included a wider population than specified by the review inclusion criteria. The rationale for criteria should be stated.	Yes
Identifying studies -	7	Describe all methods of identifying published and unpublished studies including, as applicable: which bibliographic databases were searched with dates of coverage; details of any hand searching including of conference proceedings; use of study registers	Yes

information sources		and agency or company databases; contact with the original research team and experts in the field; open adverts and surveys. Give the date of last search or elicitation.	
Identifying studies - search	8	Present the full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	**Yes**
Study selection processes	9	State the process for determining which studies were eligible for inclusion.	**Yes**
Data collection processes	10	Describe how IPD were requested, collected and managed, including any processes for querying and confirming data with investigators. If IPD were not sought from any eligible study, the reason for this should be stated (for each such study). If applicable, describe how any studies for which IPD were not available were dealt with. This should include whether, how and what aggregate data were sought or extracted from study reports and publications (such as extracting data independently in duplicate) and any processes for obtaining and confirming these data with investigators.	**Yes**
Data items	11	Describe how the information and variables to be collected were chosen. List and define all study level and participant level data that were sought, including baseline and follow-up information. If applicable, describe methods of standardising or translating variables within the IPD datasets to ensure common scales or measurements across studies.	**Yes**
IPD integrity	A1	Describe what aspects of IPD were subject to data checking (such as sequence generation, data consistency and completeness, baseline imbalance) and how this was done.	**Yes**
Risk of bias assessment in individual studies.	12	Describe methods used to assess risk of bias in the individual studies and whether this was applied separately for each outcome. If applicable, describe how findings of IPD checking were used to inform the assessment. Report if and how risk of bias assessment was used in any data synthesis.	**Yes** **Newcastle Ottawa Scale**
Specification of outcomes and effect measures	13	State all treatment comparisons of interests. State all outcomes addressed and define them in detail. State whether they were pre-specified for the review and, if applicable, whether they were primary/main or secondary/additional outcomes. Give the principal measures of effect (such as risk ratio, hazard ratio, difference in means) used for each outcome.	**Yes**
Synthesis methods	14	Describe the meta-analysis methods used to synthesise IPD. Specify any statistical methods and models used. Issues should include (but are not restricted to): • Use of a one-stage or two-stage approach. • How effect estimates were generated separately within each study and combined across studies (where applicable). • Specification of one-stage models (where applicable) including how clustering of patients within studies was accounted for. • Use of fixed or random effects models and any other model assumptions, such as proportional hazards. • How (summary) survival curves were generated (where applicable). • Methods for quantifying statistical heterogeneity (such as I^2 and τ^2). • How studies providing IPD and not providing IPD were analysed together (where applicable). • How missing data within the IPD were dealt with (where applicable).	**Yes** **No**

Exploration of variation in effects	A2	If applicable, describe any methods used to explore variation in effects by study or participant level characteristics (such as estimation of interactions between effect and covariates). State all participant-level characteristics that were analysed as potential effect modifiers, and whether these were pre-specified.	**Yes**
Risk of bias across studies	15	Specify any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to not obtaining IPD for particular studies, outcomes or other variables.	**No**
Additional analyses	16	Describe methods of any additional analyses, including sensitivity analyses. State which of these were pre-specified.	**Yes All**
Results			
Study selection and IPD obtained	17	Give numbers of studies screened, assessed for eligibility, and included in the systematic review with reasons for exclusions at each stage. Indicate the number of studies and participants for which IPD were sought and for which IPD were obtained. For those studies where IPD were not available, give the numbers of studies and participants for which aggregate data were available. Report reasons for non-availability of IPD. Include a flow diagram.	**Yes**
Study characteristics	18	For each study, present information on key study and participant characteristics (such as description of interventions, numbers of participants, demographic data, unavailability of outcomes, funding source, and if applicable duration of follow-up). Provide (main) citations for each study. Where applicable, also report similar study characteristics for any studies not providing IPD.	**Yes**
IPD integrity	A3	Report any important issues identified in checking IPD or state that there were none.	**Yes**
Risk of bias within studies	19	Present data on risk of bias assessments. If applicable, describe whether data checking led to the up-weighting or down-weighting of these assessments. Consider how any potential bias impacts on the robustness of meta-analysis conclusions.	**Yes**
Results of individual studies	20	For each comparison and for each main outcome (benefit or harm), for each individual study report the number of eligible participants for which data were obtained and show simple summary data for each intervention group (including, where applicable, the number of events), effect estimates and confidence intervals. These may be tabulated or included on a forest plot.	**Yes**
Results of syntheses	21	Present summary effects for each meta-analysis undertaken, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was pre-specified, and report the numbers of studies and participants and, where applicable, the number of events on which it is based.	**No**
		When exploring variation in effects due to patient or study characteristics, present summary interaction estimates for each characteristic examined, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was pre-specified. State whether any interaction is consistent across trials.	
		Provide a description of the direction and size of effect in terms meaningful to those who would put findings into practice.	
Risk of bias across studies	22	Present results of any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to the	**No**

		availability and representativeness of available studies, outcomes or other variables.	
Additional analyses	23	Give results of any additional analyses (e.g. sensitivity analyses). If applicable, this should also include any analyses that incorporate aggregate data for studies that do not have IPD. If applicable, summarise the main meta-analysis results following the inclusion or exclusion of studies for which IPD were not available.	**Yes**
Discussion			
Summary of evidence	24	Summarise the main findings, including the strength of evidence for each main outcome.	**Yes**
Strengths and limitations	25	Discuss any important strengths and limitations of the evidence including the benefits of access to IPD and any limitations arising from IPD that were not available.	**Yes**
Conclusions	26	Provide a general interpretation of the findings in the context of other evidence.	**Yes**
Implications	A4	Consider relevance to key groups (such as policy makers, service providers and service users). Consider implications for future research.	**Yes**
Funding			
Funding	27	Describe sources of funding and other support (such as supply of IPD), and the role in the systematic review of those providing such support.	**Yes** **n/a**

A1 – A3 denote new items that are additional to standard PRISMA items. A4 has been created as a result of re-arranging content of the standard PRISMA statement to suit the way that systematic review IPD meta-analyses are reported.