

ONLINE DATA SUPPLEMENT

**Return to Work After Critical Illness:
A Systematic Review and Meta-Analysis**

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RESULTS

Subgroup Analyses

In subgroup analyses of studies only including discrete follow-up time points, we observed no significant return to work differences, stratified by follow-up time point, when comparing non-ARDS versus ARDS survivors ($p=0.09$; **eTable 3**); this difference was significant when non-discrete time points were included ($p=0.03$; **eTable 4**). Next, there were no significant regional differences in return to work, stratified by follow-up time point, when comparing Europe, North America, and Australia and including only discrete follow-up time point studies ($p=0.38$; **eTable 3**), or all studies ($p=0.32$; **eTable 4**). When evaluating return to work by mode of employment assessment, significant between-group differences were noted when comparing in-person versus telephone interview versus mailed questionnaire ($p=0.03$ across modes), in-person versus telephone ($p=0.02$), in-person versus mail ($p=0.04$) and telephone versus mail ($p=0.01$; **eTable 3**); similar trends were seen when all studies were included (**eTable 4**). Finally, no between-group differences were observed when evaluating studies based on enrollment start ($p=0.15$) or end ($p=0.08$) dates (1978-1990, 1991-2000, 2001-2010, 2011-2015).

Sensitivity Analyses

In sensitivity analyses, no significant return to work differences were observed when employment evaluations occurred during a time of recession ($p=0.94$), when excluding studies without defined time points ($p=0.65$), when excluding three studies[4, 36, 59] performed as longitudinal follow-up within a randomized trial ($p=0.20$), four studies[21, 50, 58, 60] enrolling patients as part of a multi-disciplinary ICU survivor clinic

($p=0.72$), the intervention arm of one study[58] involving a return to work rehabilitation program ($p=0.15$), or when excluding a national-database-based study[62] accounting for 58% (5,762 of 10,015) of previously employed survivors ($p=0.09$).

Secondary Outcomes

Secondary outcomes related to return to work after critical illness included worsening of employment status, change in occupation, job loss after return to work, receipt of disability benefits, co-occurring psychological outcomes, and lost earnings. Among survivors returning to work, 10 studies[4, 14, 17, 20, 48, 52, 53, 55, 61, 62] found 5-84% reported working less or subsequently retired, four studies[4, 23, 51, 61] found 17-66% changed occupations, and three [5, 32, 62] found 20-36% subsequently incurred job loss. Twelve studies[4, 20, 24, 25, 37, 39, 40, 51, 52, 59, 61, 64] reported that 5-77% of previously-employed survivors did not return to work due to illness or poor health, while six[4, 5, 14, 29, 41, 62] found 10-89% received new disability benefits and 13[4, 5, 16, 18, 26, 38-40, 44, 51, 54, 62, 63] found that 4-28% were newly retired. Three studies[4, 5, 62] estimated lost earnings for previously employed survivors, totaling €1482 to US \$26,949 at 12 months and \$180,221 at 60 months after critical illness. These lost earnings were accrued by 71% of 12 month and 77% of 60 month survivors [4, 5]. Finally, two studies reported changes in healthcare coverage among previously employed survivors, observing declines in private healthcare coverage of 14% and 33% at 12 and 60 month follow-up, respectively, and a concomitant rise of 16% and 37% in government-funded (Medicare/Medicaid) coverage[4, 5].

eTable 1: Search Strategy: February 14, 2018

Database	Search terms and strategy	Results
Pubmed	(intensive care[tiab] OR "intensive care"[MeSH Terms] OR intensive therapy[tiab] OR high dependency[tiab] OR critical care[tiab] OR "critical care"[MeSH Terms] OR intermediate care[tiab] OR step-up care[tiab] OR step-down care[tiab] OR respiratory distress syndrome[tiab] OR acute lung injury[tiab]) AND (outcome measure[tiab] OR "outcome assessment (health care)"[MeSH Terms] OR follow-up[tiab] OR "follow-up studies"[MeSH Terms] OR health status[tiab] OR "health status"[MeSH Terms] OR functional status[tiab] OR clinical outcome[tiab]) AND (organ failure[tiab] OR "multiple organ failure"[MeSH Terms] OR organ dysfunction[tiab] OR sequelae[tiab] OR quality of life[tiab] OR "quality of life"[MeSH Terms] OR impairment[tiab] OR morbidity[tiab] OR "morbidity"[MeSH Terms]) NOT (animals[mh] NOT humans[mh]) Limits: 1970 – present	10,343
Embase	('intensive care'/exp OR 'intensive care':ti,ab OR 'intensive therapy':ti,ab OR 'high dependency':ti,ab OR 'critical care':ti,ab OR 'critical care':ti,ab OR 'intermediate care':ti,ab OR 'step-up care':ti,ab OR 'step-down care':ti,ab OR 'respiratory distress syndrome':ti,ab OR 'acute lung injury':ti,ab) AND ('outcome measure':ti,ab OR 'outcome assessment'/exp OR 'follow up':ti,ab OR 'follow up'/exp OR 'health status':ti,ab OR 'health status'/de OR 'functional status':ti,ab OR 'clinical outcome':ti,ab) AND ('organ failure':ti,ab OR 'multiple organ failure'/exp OR 'organ dysfunction':ti,ab OR 'multiple organ failure':ti,ab OR 'sequelae':ti,ab OR 'quality of life'/exp OR 'quality of life':ti,ab OR 'impairment':ti,ab OR 'morbidity':ti,ab OR 'morbidity'/exp) NOT ('animal'/exp NOT ('animal'/exp AND 'human'/exp)) Limits: 1970 – present	26,658
CINAHL	(MH "intensive care units+" OR "intensive care" OR "intensive therapy" OR "high dependency" OR MH "critical care" OR "critical care" OR "intermediate care" OR "step-up care" OR "step-down care" OR "respiratory distress syndrome" OR "acute lung injury") AND ("outcome measure" OR MH "outcome assessment" OR "follow up" OR MH "prospective studies" OR MH "health status" OR "health status" OR "functional status" OR "clinical outcome") AND ("organ failure" OR "multiple organ failure" OR "organ dysfunction" OR MH "multiple organ dysfunction syndrome" OR "sequelae" OR "quality of life" OR MH "quality of life" OR "impairment" OR "morbidity" OR MH "morbidity")	3,195
PsycINFO	(DE "intensive care" OR "intensive care" OR "intensive therapy" OR "high dependency" OR "critical care" OR "intermediate care" OR "step-up care" OR "step-down care" OR "respiratory distress syndrome" OR "acute lung injury") AND ("outcome measure" OR "outcome assessment" OR "follow up" OR DE "Followup Studies" OR "health status" OR "functional status" OR "clinical outcome") AND ("organ failure" OR "multiple organ failure" OR "organ dysfunction" OR "sequelae" OR "quality of life" OR DE "quality of life" OR "impairment" OR DE morbidity OR "morbidity")	338
Cochrane Library	('Intensive Care Units' [MeSH Terms] OR 'Critical Care' [MeSH Terms] OR "intensive care":ti,ab,kw or "intensive therapy":ti,ab,kw or "high dependency":ti,ab,kw or "critical care":ti,ab,kw or "intermediate care":ti,ab,kw or "step-up care":ti,ab,kw or "step-down care":ti,ab,kw or "respiratory distress syndrome":ti,ab,kw or "acute lung injury":ti,ab,kw) AND ('Outcome Assessment (Health care)' [MeSH Terms] OR 'Health status' [MeSH Terms] OR "outcome measure":ti,ab,kw or "follow-up":ti,ab,kw or "health status":ti,ab,kw or "functional status":ti,ab,kw or "clinical outcome":ti,ab,kw) AND 'Multiple Organ Failure' [MeSH Terms] OR 'Morbidity' [MeSH Terms] OR 'Quality of Life' [MeSH Terms] OR "organ failure":ti,ab,kw or "organ dysfunction":ti,ab,kw or "sequelae":ti,ab,kw or "quality of life":ti,ab,kw or "impairment":ti,ab,kw or "morbidity":ti,ab,kw	1,443

eTable 2. Study Characteristics

	All Studies	Disease Category		Region			Employment Evaluation			
		ARDS	Non-ARDS	Europe	North America	Australia/NZ	In-person	Telephone	Mail	Nat'l Database
Studies, n (%)	52	9	43	28	14	8	18	18	15	1
Study Type, n (%)										
Prospective	39 (75%)	7 (78%)	32 (74%)	21 (75%)	11 (79%)	6 (75%)	15 (83%)	12 (67%)	12 (80%)	0 (0%)
Retrospective	13 (25%)	2 (22%)	11 (26%)	7 (25%)	3 (21%)	2 (25%)	3 (17%)	6 (33%)	3 (20%)	1 (100%)
Year of publication, n (%)										
1984-2000	14 (27%)	2 (22%)	12 (28%)	7 (25%)	6 (43%)	1 (13%)	4 (22%)	4 (22%)	6 (40%)	0 (0%)
2001-2010	17 (33%)	1 (11%)	16 (37%)	14 (50%)	2 (14%)	1 (13%)	6 (33%)	4 (22%)	7 (47%)	0 (0%)
2011-2018	21 (40%)	6 (67%)	15 (35%)	7 (25%)	6 (43%)	6 (75%)	8 (44%)	10 (56%)	2 (13%)	1 (100%)
Region, n (%)										
Europe	28 (54%)	2 (22%)	26 (60%)	--	--	--	9 (50%)	6 (33%)	12 (80%)	1 (100%)
North America	14 (27%)	5 (56%)	9 (21%)	--	--	--	5 (28%)	6 (33%)	3 (20%)	0 (0%)
Australia/New Zealand	8 (15%)	1 (11%)	7 (16%)	--	--	--	3 (17%)	5 (28%)	0 (0%)	0 (0%)
Asia	2 (4%)	1 (11%)	1 (2%)	--	--	--	1 (6%)	1 (6%)	0 (0%)	0 (0%)
Disease Category, n (%)										
ARDS	9 (17%)	--	--	2 (7%)	5 (36%)	1 (13%)	5 (28%)	3 (17%)	1 (7%)	0 (0%)
Non-ARDS	43 (83%)	--	--	26 (93%)	9 (64%)	7 (88%)	13 (72%)	15 (83%)	14 (93%)	1 (100%)
Employment Evaluation, n (%)										
In-person Visit	18 (35%)	5 (56%)	13 (30%)	9 (32%)	5 (36%)	3 (38%)	--	--	--	--
Telephone Interview	18 (35%)	3 (33%)	15 (35%)	6 (21%)	6 (43%)	5 (63%)	--	--	--	--
Mailed Questionnaire	15 (29%)	1 (11%)	14 (33%)	12 (43%)	3 (21%)	0 (0%)	--	--	--	--
Total Survivors Enrolled	10,015	694	9,321	7,547	2,007	316	914	2,008	1,331	5,762
Survivors Enrolled per Study, median (IQR)	49 (26, 94)	29 (21, 67)	49 (28, 99)	49 (31, 87)	66 (21, 176)	27 (17, 55)	42 (27, 64)	65 (23, 97)	68 (28, 102)	5,762 (-, -)
Follow-Up Time, median (IQR) ^a	12 (6, 39)	16 (12, 50)	12 (6, 30)	12 (9, 55)	12 (12, 41)	6.25 (6, 14)	12 (6, 12)	14 (12, 30)	12 (6, 41)	79 (-, -)

ARDS = Acute Respiratory Distress Syndrome; NZ = New Zealand

^aOnly including the chronologically last follow-up, for studies that included multiple follow-up time points

eTable 3. Meta-Analysis of Survivors Returning to Work after ICU Hospitalization – studies with discrete follow-up time points^a

Survivor Category	1 to 3 months	6 months	12 months	18 to 36 months	42 to 60 months
All ICU Survivors, no. of studies	9	12	20	4	5
Number of patients	674	1,372	7,889	5,971	295
Proportion, % (95% CI)	36 (23-49)	64 (52-75)	60 (50-69)	63 (44-82)	68 (51-85)
r^2 , I^2 , p -value for heterogeneity	0.55, 87%, 0.03				
Non-ARDS Survivors, no. of studies ^b	9	11	14	3	3
Number of patients	674	986	7,251	5,904	178
Proportion, % (95% CI)	36 (22-49)	65 (53-77)	58 (46-69)	64 (41-86)	57 (32-82)
r^2 , I^2 , p -value for heterogeneity	0.48, 89%, 0.07				
ARDS Survivors, no. of studies ^b	—	1	6	1	2
Number of patients	—	386	638	67	117
Proportion, % (95% CI)	—	55 (22-89)	63 (49-77)	60 (25-94)	82 (65-98)
r^2 , I^2 , p -value for heterogeneity	0.38, 77%, 0.48				
Europe, no. of studies ^c	4	6	11	2	2
Number of patients	293	330	6,524	5,807	149
Proportion, % (95% CI)	34 (12-57)	68 (49-87)	64 (49-78)	65 (34-97)	51 (15-87)
r^2 , I^2 , p -value for heterogeneity	0.85, 88%, 0.82				
North America, no. of studies ^c	4	3	7	2	2
Number of patients	357	826	1,275	164	117
Proportion, % (95% CI)	34 (16-51)	69 (50-89)	56 (41-70)	60 (35-86)	82 (65-99)
r^2 , I^2 , p -value for heterogeneity	0.39, 89%, 0.07				
Australia/New Zealand, no. of studies ^c	1	3	1	—	1
Number of patients	24	216	18	—	29
Proportion, % (95% CI)	50 (11-89)	54 (33-74)	50 (9-91)	—	69 (36-102)
r^2 , I^2 , p -value for heterogeneity	0.48, 90%, 0.87				
In-person follow-up, no. of studies ^d	5	4	8	—	2
Number of patients	407	195	445	—	82
Proportion, % (95% CI)	28 (8-48)	75 (52-97)	65 (47-83)	—	83 (61-106)
r^2 , I^2 , p -value for heterogeneity	1.05, 87%, 0.04				
Telephone follow-up, no. of studies ^d	1	5	7	3	2
Number of patients	67	669	1,442	209	122
Proportion, % (95% CI)	25 (8-43)	53 (44-63)	61 (54-69)	61 (49-73)	74 (61-87)
r^2 , I^2 , p -value for heterogeneity	0.14, 75%, 0.03				
Mail follow-up, no. of studies ^d	3	3	4	—	1
Number of patients	200	508	240	—	91
Proportion, % (95% CI)	53 (35-71)	71 (56-86)	50 (34-66)	—	23 (2-44)
r^2 , I^2 , p -value for heterogeneity	0.30, 77%, 0.10				

ARDS = Acute Respiratory Distress Syndrome; ICU = Intensive Care Unit

^a Includes only studies with discrete follow-up time points. Pooled estimate include only the last follow-up time point from each study. Pooled proportions estimated using random-effects meta-regression; fit via restricted maximum likelihood Knapp-Hartung modification to estimate between-study heterogeneity (r^2). I^2 used to evaluate residual heterogeneity. Adjusted models included a p -value to test the null hypothesis of no differences in pooled proportions across follow-up time. Pooled log-odds coefficients were back-transformed to proportions, and presented with corresponding 95% CIs. Asia (region) and national database (mode of employment evaluation) not listed due to sample size of 1 study per category.

^b $p=0.09$ when comparing non-ARDS and ARDS pooled stratified estimates

^c $p=0.38$ when comparing Europe, North America, and Australia/New Zealand pooled stratified estimates. $p=0.15$ when comparing Europe versus North America, $p=0.64$ Europe versus Australia/New Zealand, and $p=0.23$ North America versus Australia/New Zealand.

^d $p=0.03$ when comparing in-person, telephone, and mail follow-up pooled stratified estimates. $p=0.02$ when comparing in-person versus telephone, $p=0.04$ in-person versus mail, $p=0.01$ telephone versus mail stratified estimates.

eTable 4. Meta-Analysis of Survivors Returning to Work after ICU Hospitalization – all studies^a					
Survivor Category	1 to 3 months	6 months	12 months	18 to 36 months	42 to 176 months
All ICU Survivors, no. of studies	10	13	20	10	13
Number of patients	723	1,386	7,889	6,193	6,369
Proportion, % (95% CI)	35 (24-47)	62 (52-73)	59 (51-68)	61 (49-73)	68 (59-78)
r^2 , I^2 , p -value for heterogeneity	0.47, 86%, <0.001				
Non-ARDS Survivors, no. of studies ^b	10	12	14	8	9
Number of patients	723	1000	7,251	6,111	6,218
Proportion, % (95% CI)	36 (22-49)	65 (53-77)	58 (46-69)	64 (41-86)	57 (32-82)
r^2 , I^2 , p -value for heterogeneity	0.61, 88%, 0.06				
ARDS Survivors, no. of studies ^b	—	1	6	2	4
Number of patients	—	386	638	82	151
Proportion, % (95% CI)	—	55 (27-84)	62 (50-75)	57 (33-81)	75 (61-89)
r^2 , I^2 , p -value for heterogeneity	0.25, 69%, 0.47				
Europe, no. of studies ^c	5	6	11	5	8
Number of patients	342	330	6,524	5,930	6,193
Proportion, % (95% CI)	34 (16-52)	67 (49-84)	64 (51-77)	63 (44-82)	67 (53-82)
r^2 , I^2 , p -value for heterogeneity	0.69, 89%, 0.10				
North America, no. of studies ^c	4	3	7	3	4
Number of patients	357	826	1,275	175	147
Proportion, % (95% CI)	34 (16-51)	69 (50-88)	56 (42-69)	57 (34-80)	71 (53-88)
r^2 , I^2 , p -value for heterogeneity	0.47, 87%, 0.11				
Australia/New Zealand, no. of studies ^c	1	4	1	1	1
Number of patients	24	230	18	15	29
Proportion, % (95% CI)	50 (14-86)	52 (35-69)	50 (12-88)	53 (14-92)	69 (38-99)
r^2 , I^2 , p -value for heterogeneity	0.37, 86%, 0.90				
In-person follow-up, no. of studies ^d	6	5	8	—	4
Number of patients	456	209	445	—	140
Proportion, % (95% CI)	29 (12-46)	69 (48-90)	65 (48-82)	—	79 (61-96)
r^2 , I^2 , p -value for heterogeneity	0.83, 85%, 0.02				
Telephone follow-up, no. of studies ^d	1	5	7	6	4
Number of patients	67	669	1,442	308	162
Proportion, % (95% CI)	25 (9-42)	53 (44-63)	62 (54-69)	60 (51-69)	71 (60-81)
r^2 , I^2 , p -value for heterogeneity	0.12, 68%, 0.02				
Mail follow-up, no. of studies ^d	3	3	4	3	4
Number of patients	200	508	240	123	305
Proportion, % (95% CI)	55 (29-81)	72 (51-94)	50 (27-73)	61 (36-86)	54 (32-77)
r^2 , I^2 , p -value for heterogeneity	0.74, 89%, 0.72				

ARDS = Acute Respiratory Distress Syndrome; ICU = Intensive Care Unit

^a Includes all 52 studies in the systematic review. Pooled estimates include only the chronologically latest follow-up time point from each study. For studies providing return to work estimates over a range, rather than discrete follow-up time points, we used the chronologically latest value for follow-up time reported in the study. Pooled proportions estimated using random-effects meta-regression; fit via restricted maximum likelihood Knapp-Hartung modification to estimate between-study heterogeneity (r^2). I^2 used to evaluate residual heterogeneity. Adjusted models included a p -value to test the null hypothesis of no differences in pooled proportions across follow-up time. Pooled log-odds coefficients were back-transformed to proportions, and presented with corresponding 95% CIs. Asia (region, $n=2$ studies) and national database (mode of employment evaluation, $n=1$ study) not listed due to lack of studies for meta-regression.

^b $p=0.03$ when comparing non-ARDS and ARDS pooled stratified estimates.

^c $p=0.32$ when comparing Europe, North America, and Australia/New Zealand pooled stratified estimates. $p=0.08$ when comparing Europe versus North America, $p=0.37$ Europe versus Australia/New Zealand, and $p=0.37$ North America versus Australia/New Zealand.

^d $p=0.05$ when comparing in-person, telephone, and mail follow-up pooled stratified estimates. $p=0.004$ when comparing in-person versus telephone, $p=0.048$ in-person versus mail, $p=0.33$ telephone versus mail pooled stratified estimates.

eTable 5. Factors Associated with Return to Work After Critical Illness

Author, Year	Outcome	Factors Potentially Associated With RTW Outcome ^a	Factors Potentially Not Associated with RTW Outcome ^a	Other covariates
McHugh et al. 1994[19]	Ever RTW at 12 months	Univariable factors: Lower health and lung-related sickness impact profile (SIP) scores	Univariable: Severity of lung injury, forced vital capacity, DLco	—
Longo et al. 2007[36]	Ever RTW at 1 and 7 months	Receipt (versus no receipt) of activated protein C, in the setting of sepsis (90% vs. 64% at 1 month, 100% vs. 73% at 7 months, $p=0.096$ for trend)	—	Age
Myhren et al. 2010[43]	Ever RTW at 12 months	Male sex (OR=3.00, $p<0.05$), higher education (OR=2.07, $p<0.05$), optimism (OR=1.13, $p<0.05$), medical (vs. surgical or trauma) disease category (OR=2.90, $p<0.05$)	—	Age, mechanical ventilation
Herridge et al. 2011[44, 66, 67] ^b	Never RTW	22mo (range 6 to 48mo): Multivariable: Moderate to severe (versus minimal to mild) depression (OR=0.20, $p=0.006$)	60mo: Univariable: Moderate to severe (versus minimal or mild) depression (OR=0.23, $p=0.12$)	—
Quasim et al. 2015[51]	Ever RTW up to 29 months	Univariable factors (all $p<0.05$): EQ-5D Tool: Better health, improved mobility, fewer problems with usual activities or self-care, less pain, less depression/anxiety;	Univariable factors (all $p>0.05$): Age, APACHE II, ICU/hospital length of stay, predicted hospital mortality	—
Reid et al. 2016[54]	Ever RTW at 12 months	Univariable: Augmented (1.5 kcal/mL, versus routine 1.0 kcal/mL) enteral nutrition ($p=0.02$)	—	—
Norman et al. 2016[55]	Interim decrease in employment level at 3 and 12 months	Severity of illness (Sequential Organ Failure Assessment [SOFA] Score; OR=2.36-2.56, $p=0.01$ -0.024), physical health status (Short Form [SF]-36 Physical component; OR=0.30-0.33, $p=0.001$ -0.003), years of education (OR=0.55-0.62, $p=0.03$ -0.04) at 3 months	Days of delirium (OR=0.80, $p=0.43$), cognitive function (RBANS global; OR=1.17, $p=0.66$), depression (OR=1.20-1.24, $p=0.53$ -0.61) at 3 months Days of delirium (OR=0.99, $p=0.96$), cognitive function (RBANS global; OR=0.49, $p=0.07$), depression (OR=1.44-1.61, $p=0.18$ -0.31), physical health status (SF-36 Physical component; OR=0.59-0.61, $p=0.12$), years of education (OR=0.86-1.10, $p=0.47$ -0.70) at 12m	Marital status
Kamdar et al. 2017[4]	Ever RTW at 12 months	Univariable factors: Female (HR 0.76, $p=0.033$), White (HR=1.46, $p=0.033$), Age, per 10 (0.86, $p=0.001$), Cardiovascular disease (HR=0.75, $p=0.027$), Diabetes (HR=0.63, $p=0.013$), Ventilation duration, per week (HR=0.79, $p<0.001$), ICU LOS, per week (HR=0.79, $p<0.001$), Hospital LOS, per week (HR=0.80, $p<0.001$), Discharge to home with unassisted breathing (HR=3.6, $p=0.021$). Multivariable factors: Nonwhite, per 10 year (HR 0.68, $p=0.001$) and Hospital LOS (HR=0.81, $p<0.001$)	Univariable factors: APACHE III, per 20 (HR=0.91, $p=0.059$), Sepsis as ARDS risk factor (HR=0.91, $p=0.456$), Maximum Organ failure score (HR=0.87, $p=0.051$), PaO ₂ /FiO ₂ (HR=0.99, $p=0.238$), Multivariable factors: Female (HR=0.81, $p=0.136$), White per 10yr (HR=0.91, $p=0.114$), Cardiovascular disease (HR=1.16, $p=0.351$), Diabetes (HR=0.79, $p=0.212$), APACHE III, per 20 (HR=1.01, $p=0.841$), Maximum organ failure score (HR=0.94, $p=0.411$), Discharge to home with unassisted breathing (HR=1.65, $p=0.418$)	BMI, Chronic pulmonary disease, alcohol misuse, Admission to medical ICU
Kamdar et al. 2018[5]	Ever RTW at 60 months	Charlson Comorbidity Index, per point (HR=0.77, $p=0.04$), mechanical ventilation, per day ≤ 5 days (HR=0.67, $p<0.001$), discharge to rehabilitation or other healthcare facility (HR=0.49, $p=0.03$)	Mechanical ventilation, per day >5 days (HR=1.02, $p=0.20$)	Age, Functional Comorbidity Index
Hodgson et al. 2018[61]	Never RTW at 6 months	Multivariable factors: Major trauma admission category (OR=8.83, $p=0.0006$), lower GCS score (OR=0.86, $p=0.03$), longer hospital LOS, per day (OR=1.05, $p=0.004$) Univariable factors (all $p<0.05$): Discharge home, Age, GCS, Hospital LOS, Global function and disability (WHODAS II), cognitive function (TICS), anxiety (HADS), depression (HADS), post-traumatic stress (Impact of Event Scale-Revised [IES-R]), health status (EQ5D-5LTM)	Univariable factors (all $p>0.05$): Male gender, APACHE II, APACHE III, history of anxiety/depression, divorced, renal replacement therapy, days of mechanical ventilation, ICU LOS	—
Riddersholm et al. 2018[62]	Never RTW from hospitalization (2005-2014) to January 31, 2017	Longer ICU length of stay (HR not reported) and receipt of mechanical ventilation (HR=0.70) or any one, two, or three (vs. zero; HR=0.74, 0.79, and 0.77, respectively) organ support therapies (renal replacement therapy, cardiovascular support, and/or mechanical ventilation)	Simplified Acute Physiology Score (SAPS) II, receipt of only renal replacement therapy (HR=1.16) or cardiovascular support (HR=0.96)	Age, sex, education level, cohabiting status, COPD, diabetes, anxiety/depression, heart disease, kidney disease, cancer, year of ICU admission

RTW = Return to Work; OR = Odds Ratio, HR = Hazard Ratio; EQ-5D = EuroQuality of Life Group Quality of Life Tool; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status, m=month, ICU = Intensive Care Unit; LOS = length of stay. ARDS = Acute Respiratory Distress Syndrome, GCS = Glasgow coma scale, WHODAS II = WHO Disability Assessment Schedule 2.0 COPD = Chronic obstructive pulmonary disease. HADS = Hospital Anxiety and Depression Scale. TICS = Telephone Interview for Cognitive Status

^a Based on authors' interpretation of study findings. *P*-values included when available. 95% confidence intervals omitted. Multivariable results provided unless otherwise noted.

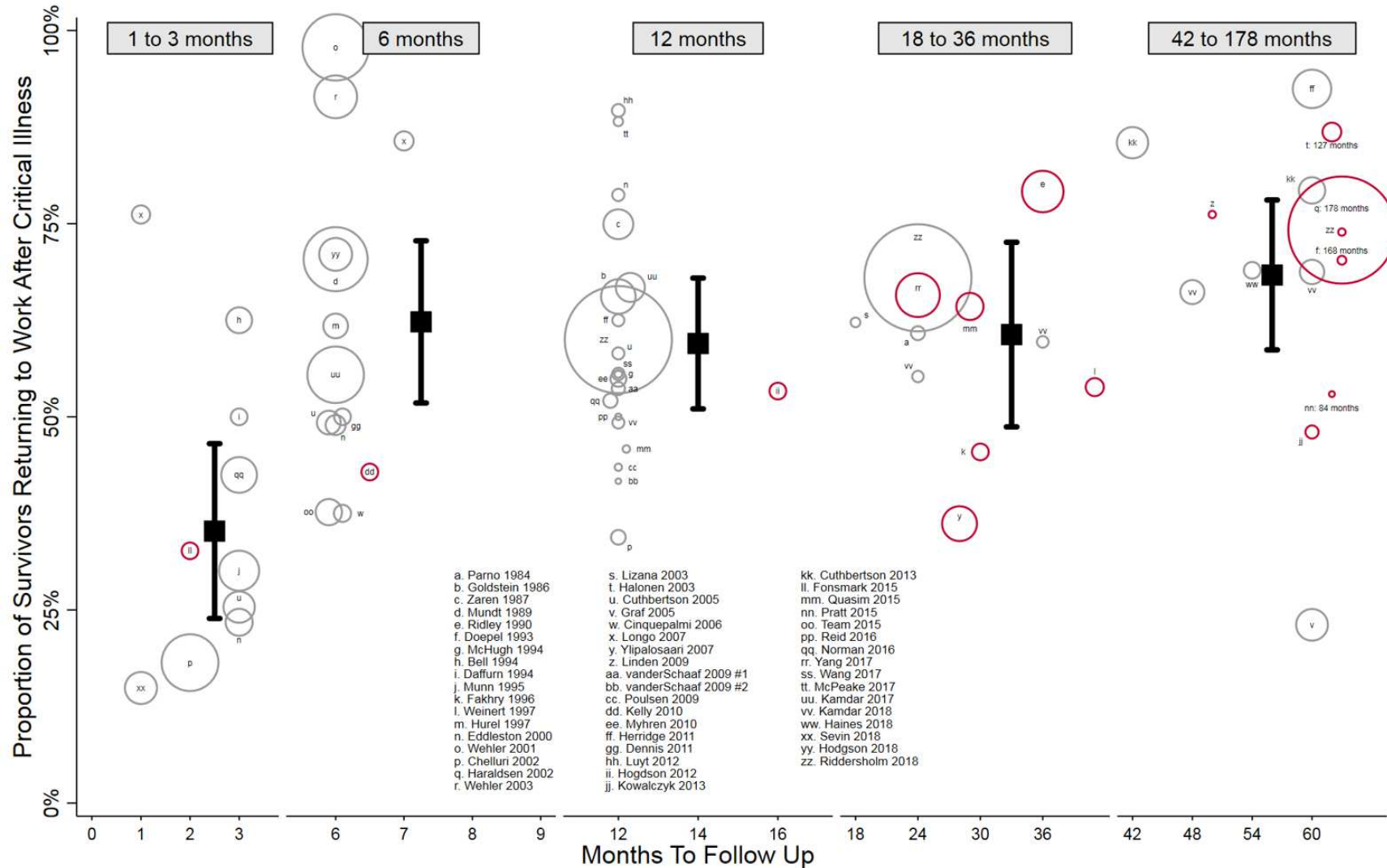
^b Associated factors from this cohort study reported in a separate publication (Adhikari NKJ et al. *CHEST* 2011)[67]

eTable 6: Risk of bias of individual studies

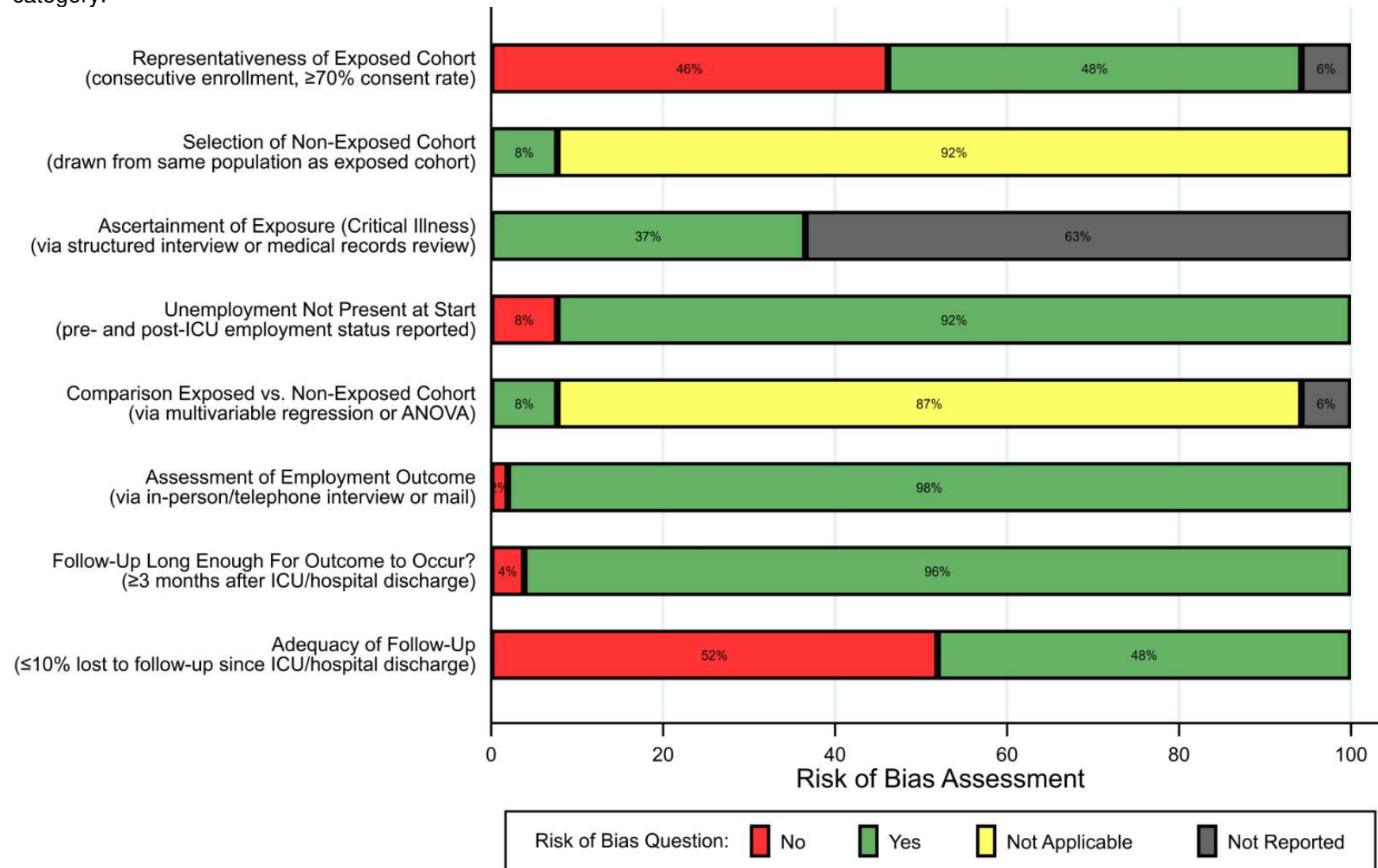
Cohort studies	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure(s)	Demonstration that unemployment was not present at the start	Comparability of exposed vs non-exposed cohort	Assessment of outcome	Follow-up enough for outcome to occur?	Adequacy of follow-up
Parno 1984	-	N/A	NR	-	N/A	+	+	-
Goldstein 1986	-	N/A	NR	+	N/A	+	+	-
Zaren 1987	+	N/A	NR	+	N/A	+	+	+
Mundt 1989	-	N/A	NR	+	N/A	+	+	-
Ridley 1990	+	N/A	NR	+	N/A	+	+	+
Doepel 1993	+	N/A	+	+	N/A	+	+	+
McHugh 1994	-	N/A	NR	-	N/A	+	+	+
Bell 1994	+	N/A	NR	+	N/A	+	+	+
Daffurn 1994	+	N/A	NR	+	N/A	+	+	-
Munn 1995	-	N/A	NR	+	N/A	+	+	-
Fakhry 1996	-	N/A	NR	+	N/A	+	+	-
Weinert 1997	NR	N/A	NR	+	N/A	+	+	-
Hurel 1997	+	N/A	NR	+	N/A	+	+	-
Eddleston 2000	-	N/A	NR	+	N/A	+	+	+
Wehler 2001	-	N/A	NR	+	N/A	+	+	+
Chelluri 2002 & 2004	+	N/A	+	+	N/A	+	-	-
Haraldsen 2002	-	N/A	+	+	NR	+	+	-
Wehler 2003	-	N/A	NR	+	N/A	+	+	+
Lizana 2003	-	N/A	NR	+	N/A	+	+	-
Halonen 2003	+	N/A	NR	+	N/A	+	+	-
Cuthbertson 2005	-	N/A	NR	+	N/A	+	+	-
Graf 2005	+	N/A	NR	+	N/A	+	+	+
Cinquelpalmi 2006	+	N/A	NR	+	N/A	+	+	+
Longo 2007	-	+	+	+	+	+	+	-
Ylipalosaari 2007	+	N/A	NR	+	N/A	+	+	-
Linden 2009	+	N/A	+	+	N/A	+	+	+
van der Schaaf 2009	-	N/A	NR	+	N/A	+	+	-
van der Schaaf 2009	+	N/A	+	+	N/A	+	+	-
Poulsen 2009	+	N/A	+	+	N/A	+	+	-
Kelly 2010	-	N/A	NR	+	NR	+	+	-
Myhren 2010	+	N/A	NR	+	N/A	+	+	-
Herridge 2011	+	N/A	+	+	N/A	+	+	-
Dennis 2011	-	N/A	NR	+	N/A	+	+	+
Luyt 2012	-	+	+	+	+	+	+	-
Hodgson 2012	+	N/A	+	-	N/A	+	+	+
Kowalczyk 2013	-	N/A	NR	-	NR	+	+	-
Cuthbertson 2013	-	N/A	+	+	N/A	+	+	+

Fonsmark 2015	-	N/A	NR	+	N/A	+	-	+
Quasim 2015	-	N/A	NR	+	N/A	+	+	-
Pratt 2015	+	N/A	+	+	N/A	+	+	+
Team 2015	+	N/A	+	+	N/A	+	+	-
Reid 2016	NR	+	+	+	+	+	+	-
Norman 2016	+	N/A	+	+	N/A	+	+	-
Yang 2017	-	N/A	NR	-	N/A	+	+	+
Wang 2017	+	N/A	+	-	N/A	+	+	+
McPeake 2017	-	+	+	+	+	+	+	+
Kamdar 2017	+	N/A	+	+	N/A	+	+	+
Kamdar 2018	NR	N/A	+	+	N/A	+	+	+
Haines 2018	+	N/A	NR	+	N/A	+	+	+
Sevin 2018	-	N/A	NR	+	N/A	+	-	+
Hodgson 2018	+	N/A	NR	+	N/A	+	+	+
Riddersholm 2018	+	N/A	NR	+	N/A	-	+	+

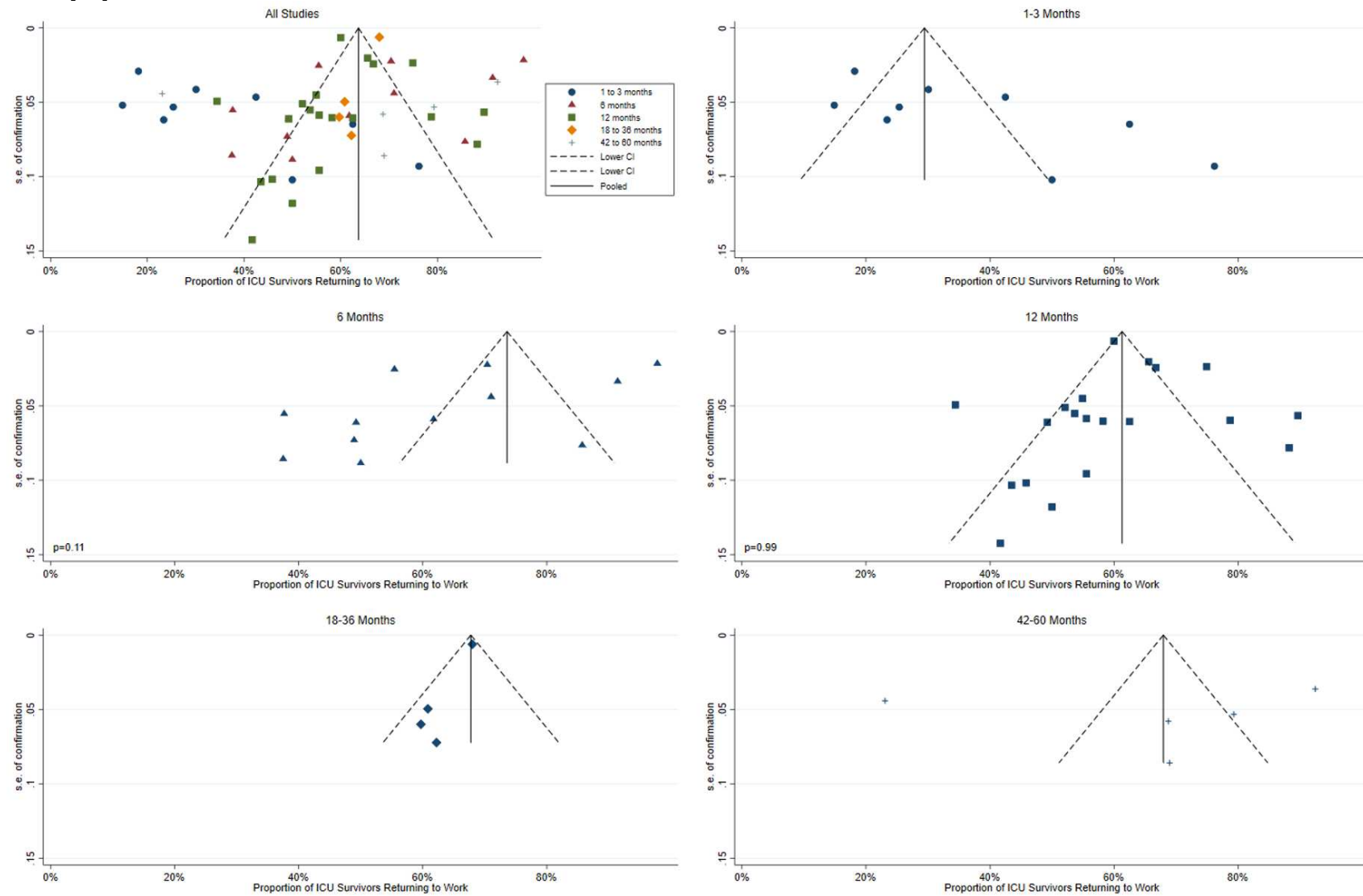
eFigure 1. Proportion of survivors returning to work after critical illness, including all 52 studies. Black squares represent pooled proportions (with 95% confidence intervals) by that time point: 35% (24-47%) by 1 to 3 months, 62% (52-73%) by 6 months, 59% (51-68%) by 12 months, 61% (49-73%) by 18 to 36 months, and 68% (59-78%) by 42 to 60 months. For studies reporting non-discrete follow-up times, we used the chronologically latest reported time to follow-up. For the 3 pairs of estimates falling within the same follow-up strata, only the latest estimate was included. Gray and red bubbles represent point estimates from studies with discrete and non-discrete follow-up time points, respectively, with bubble size corresponding to study sample size. Pooled estimates calculated using random effects meta-regression.



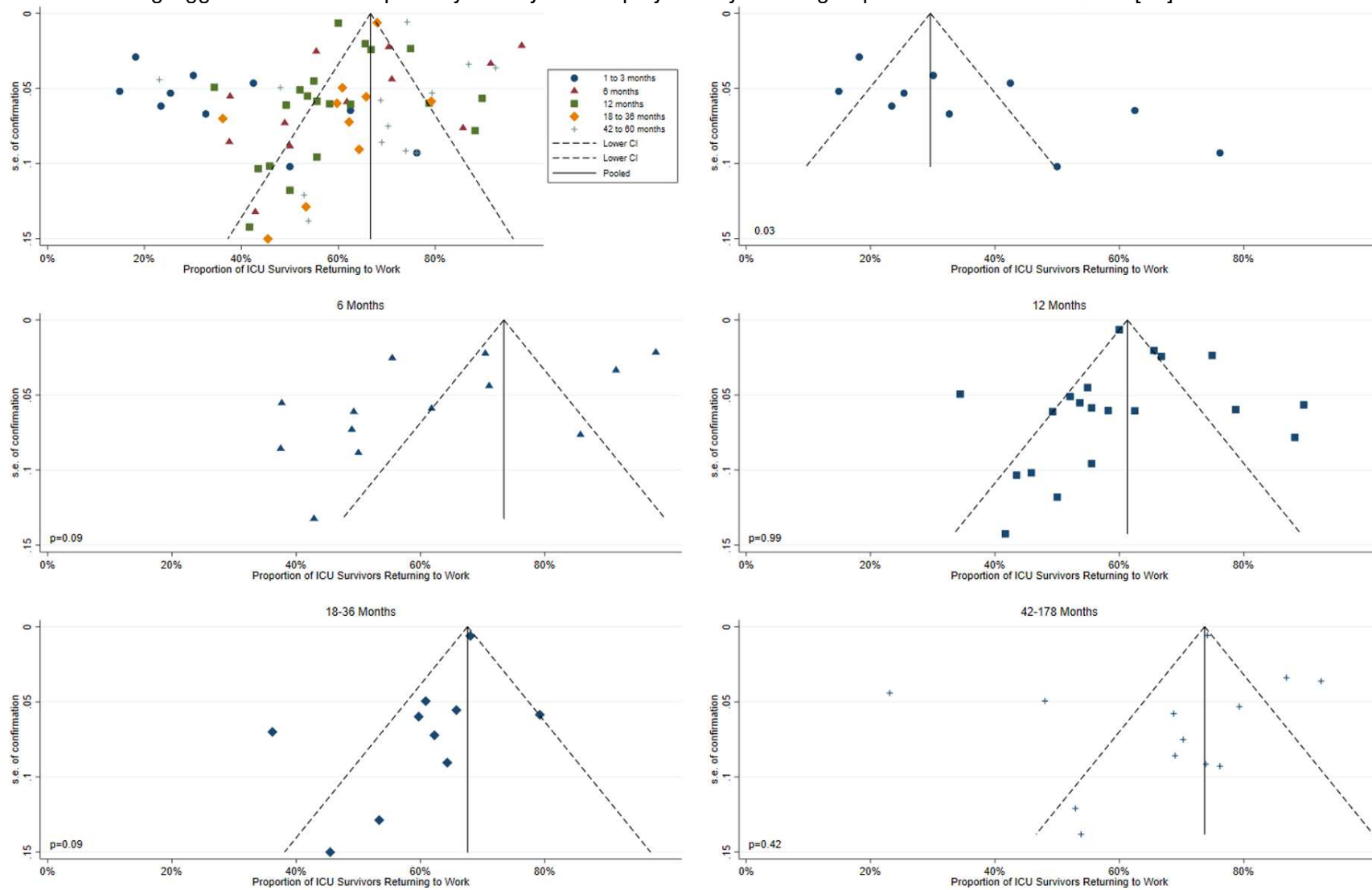
eFigure 2: Risk of Bias Assessment for 52 included studies. Bar labels represent proportion of studies falling under each question category.



eFigure 3: Funnel plots for meta-analysis of return to work in previously employed survivors of critical illness – studies with discrete follow-up time points. *P*-value calculated using Egger test for funnel plot asymmetry and displayed only for subgroups with 10 or more studies[12].



eFigure 4: Funnel plots for meta-analysis of return to work in previously employed survivors of critical illness – all studies. *P*-value calculated using Egger test for funnel plot asymmetry and displayed only for subgroups with 10 or more studies[12].



References

- 1 Elliott D, Davidson JE, Harvey MA, Bemis-Dougherty A, Hopkins RO, Iwashyna TJ, *et al.* Exploring the scope of post-intensive care syndrome therapy and care: engagement of non-critical care providers and survivors in a second stakeholders meeting. *CritCare Med* 2014;42:2518-26.
- 2 Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, *et al.* Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. *CritCare Med* 2012;40:502-9.
- 3 Coopersmith CM, Wunsch H, Fink MP, Linde-Zwirble WT, Olsen KM, Sommers MS, *et al.* A comparison of critical care research funding and the financial burden of critical illness in the United States. *CritCare Med* 2012;40:1072-9.
- 4 Kamdar BB, Huang M, Dinglas VD, Colantuoni E, von Wachter TM, Hopkins RO, *et al.* Joblessness and Lost Earnings after Acute Respiratory Distress Syndrome in a 1-Year National Multicenter Study. *Am J Respir Crit Care Med* 2017;196:1012-20.
- 5 Kamdar BB, Sepulveda KA, Chong A, Lord RK, Dinglas VD, Mendez-Tellez PA, *et al.* Return to work and lost earnings after acute respiratory distress syndrome: a 5-year prospective, longitudinal study of long-term survivors. *Thorax* 2018;73:125-33.
- 6 Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epi* 2009;62:1006-12.
- 7 Turnbull AE, Rabiee A, Davis WE, Nasser MF, Venna VR, Lolitha R, *et al.* Outcome Measurement in ICU Survivorship Research From 1970 to 2013: A Scoping Review of 425 Publications. *Crit Care Med* 2016;44:1267-77.
- 8 Cornell JE, Mulrow CD, Localio R, Stack CB, Meibohm AR, Guallar E, *et al.* Random-effects meta-analysis of inconsistent effects: a time for change. *Ann Intern Med* 2014;160:267-70.
- 9 Feveile H, Olsen O, Hogh A. A randomized trial of mailed questionnaires versus telephone interviews: response patterns in a survey. *BMC medical research methodology* 2007;7:27.

- 10 Wells G, Shea B, O'connell D, Peterson J, Welch V, Losos M, *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa (ON): Ottawa Hospital Research Institute; 2009. 2016.
- 11 Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *Bmj* 1997;315:629-34.
- 12 Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, *et al.* Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *Bmj* 2011;343:d4002.
- 13 Parno JR, Teres D, Lemeshow S, Brown RB, Avrunin JS. Two-year outcome of adult intensive care patients. *Med Care* 1984;22:167-76.
- 14 Goldstein RL, Campion EW, Thibault GE, Mulley AG, Skinner E. Functional outcomes following medical intensive care. *Crit Care Med* 1986;14:783-8.
- 15 Zaren B, Hedstrand U. Quality of life among long-term survivors of intensive care. *CritCare Med* 1987;15:743-7.
- 16 Mundt DJ, Gage RW, Lemeshow S, Pastides H, Teres D, Avrunin JS. Intensive care unit patient follow-up. Mortality, functional status, and return to work at six months. *Arch Intern Med* 1989;149:68-72.
- 17 Ridley SA, Wallace PG. Quality of life after intensive care. *Anaesthesia* 1990;45:808-13.
- 18 Doepel M, Eriksson J, Halme L, Kumpulainen T, Hockerstedt K. Good long-term results in patients surviving severe acute pancreatitis. *The British journal of surgery* 1993;80:1583-6.
- 19 McHugh LG, Milberg JA, Whitcomb ME, Schoene RB, Maunder RJ, Hudson LD. Recovery of function in survivors of the acute respiratory distress syndrome. *Am J Respir Crit Care Med* 1994;150:90-4.
- 20 Bell D, Turpin K. Quality of life at three months following admission to intensive and coronary care units. *Clin Intensive Care* 1994;5:276-81.
- 21 Daffurn K, Bishop GF, Hillman KM, Bauman A. Problems following discharge after intensive care. *Intensive Crit Care Nurs* 1994;10:244-51.
- 22 Munn J, Willatts SM, Tooley MA. Health and activity after intensive care. *Anaesthesia* 1995;50:1017-21.

- 23 Fakhry SM, Kercher KW, Rutledge R. Survival, quality of life, and charges in critically ill surgical patients requiring prolonged ICU stays. *J Trauma* 1996;41:999-1007.
- 24 Weinert CR, Gross CR, Kangas JR, Bury CL, Marinelli WA. Health-related quality of life after acute lung injury. *Am J Respir Crit Care Med* 1997;156:1120-8.
- 25 Hurel D, Loirat P, Saulnier F, Nicolas F, Brivet F. Quality of life 6 months after intensive care: results of a prospective multicenter study using a generic health status scale and a satisfaction scale. *Intensive Care Med* 1997;23:331-7.
- 26 Eddleston JM, White P, Guthrie E. Survival, morbidity, and quality of life after discharge from intensive care. *Crit Care Med* 2000;28:2293-9.
- 27 Wehler M, Martus P, Geise A, Bost A, Mueller A, Hahn EG, *et al.* Changes in quality of life after medical intensive care. *Intensive Care Med* 2001;27:154-9.
- 28 Quality of Life After Mechanized Ventilation in the Elderly Study I. 2-month mortality and functional status of critically ill adult patients receiving prolonged mechanical ventilation. *Chest* 2002;121:549-58.
- 29 Haraldsen P, Andersson R. Quality of life, morbidity, and mortality after surgical intensive care: a follow-up study of patients treated for abdominal sepsis in the surgical intensive care unit. *Eur J Surg Suppl* 2003:23-7.
- 30 Wehler M, Geise A, Hadzionerovic D, Aljukic E, Reulbach U, Hahn EG, *et al.* Health-related quality of life of patients with multiple organ dysfunction: individual changes and comparison with normative population. *Crit Care Med* 2003;31:1094-101.
- 31 Garcia Lizana F, Peres Bota D, De Cubber M, Vincent JL. Long-term outcome in ICU patients: what about quality of life? *Intensive Care Med* 2003;29:1286-93.
- 32 Halonen KI, Pettila V, Leppaniemi AK, Kemppainen EA, Puolakkainen PA, Haapiainen RK. Long-term health-related quality of life in survivors of severe acute pancreatitis. *Intensive Care Med* 2003;29:782-6.
- 33 Cuthbertson BH, Scott J, Strachan M, Kilonzo M, Vale L. Quality of life before and after intensive care. *Anaesthesia* 2005;60:332-9.
- 34 Graf J, Wagner J, Graf C, Koch K-C, Janssens U. Five-year survival, quality of life, and individual costs of 303 consecutive medical intensive care patients—A cost-utility analysis. *CritCare Med* 2005;33:547-55.

- 35 Cinquepalmi L, Boni L, Dionigi G, Rovera F, Diurni M, Benevento A, *et al.* Long-term results and quality of life of patients undergoing sequential surgical treatment for severe acute pancreatitis complicated by infected pancreatic necrosis. *Surg Infect (Larchmt)* 2006;7 Suppl 2:S113-6.
- 36 Longo CJ, Heyland DK, Fisher HN, Fowler RA, Martin CM, Day AG. A long-term follow-up study investigating health-related quality of life and resource use in survivors of severe sepsis: comparison of recombinant human activated protein C with standard care. *Crit Care* 2007;11:R128.
- 37 Ylipalosaari P, Ala-Kokko TI, Laurila J, Ohtonen P, Syrjala H. Intensive care unit acquired infection has no impact on long-term survival or quality of life: a prospective cohort study. *Crit Care* 2007;11:R35.
- 38 Linden VB, Lidgran MK, Frisen G, Dahlgren P, Frenckner BP, Larsen F. ECMO in ARDS: a long-term follow-up study regarding pulmonary morphology and function and health-related quality of life. *Acta Anaesthesiol Scand* 2009;53:489-95.
- 39 van der Schaaf M, Beelen A, Dongelmans DA, Vroom MB, Nollet F. Functional status after intensive care: a challenge for rehabilitation professionals to improve outcome. *J Rehabil Med* 2009;41:360-6.
- 40 van der Schaaf M, Beelen A, Dongelmans DA, Vroom MB, Nollet F. Poor functional recovery after a critical illness: a longitudinal study. *J Rehabil Med* 2009;41:1041-8.
- 41 Poulsen JB, Moller K, Kehlet H, Perner A. Long-term physical outcome in patients with septic shock. *Acta Anaesthesiol Scand* 2009;53:724-30.
- 42 Kelly MA, McKinley S. Patients' recovery after critical illness at early follow-up. *J Clin Nurs* 2010;19:691-700.
- 43 Myhren H, Ekeberg O, Stokland O. Health-related quality of life and return to work after critical illness in general intensive care unit patients: a 1-year follow-up study. *Crit Care Med* 2010;38:1554-61.
- 44 Herridge MS, Tansey CM, Matte A, Tomlinson G, Diaz-Granados N, Cooper A, *et al.* Functional disability 5 years after acute respiratory distress syndrome. *The New England journal of medicine* 2011;364:1293-304.

- 45 Dennis DM, Hebden-Todd TK, Marsh LJ, Cipriano LJ, Parsons RW. How do Australian ICU survivors fare functionally 6 months after admission? *Critical care and resuscitation : journal of the Australasian Academy of Critical Care Medicine* 2011;13:9-16.
- 46 Luyt CE, Combes A, Becquemin MH, Beigelman-Aubry C, Hatem S, Brun AL, *et al.* Long-term outcomes of pandemic 2009 influenza A(H1N1)-associated severe ARDS. *Chest* 2012;142:583-92.
- 47 Hodgson CL, Hayes K, Everard T, Nichol A, Davies AR, Bailey MJ, *et al.* Long-term quality of life in patients with acute respiratory distress syndrome requiring extracorporeal membrane oxygenation for refractory hypoxaemia. *Crit Care* 2012;16:R202.
- 48 Kowalczyk M, Nestorowicz A, Fijalkowska A, Kwiatosz-Muc M. Emotional sequelae among survivors of critical illness: a long-term retrospective study. *Eur J Anaesthesiol* 2013;30:111-8.
- 49 Cuthbertson BH, Elders A, Hall S, Taylor J, MacLennan G, Mackirdy F, *et al.* Mortality and quality of life in the five years after severe sepsis. *Crit Care* 2013;17:R70.
- 50 Fonsmark L, Rosendahl-Nielsen M. Experience from multidisciplinary follow-up on critically ill patients treated in an intensive care unit. *Dan Med J* 2015;62.
- 51 Quasim T, Brown J, Kinsella J. Employment, social dependency and return to work after intensive care. *J Intensive Care Soc* 2015;16:31-6.
- 52 Pratt CM, Hirshberg EL, Jones JP, Kuttler KG, Lanspa MJ, Wilson EL, *et al.* Long-Term Outcomes After Severe Shock. *Shock* 2015;43:128-32.
- 53 Investigators TS, Hodgson C, Bellomo R, Berney S, Bailey M, Buhr H, *et al.* Early mobilization and recovery in mechanically ventilated patients in the ICU: a bi-national, multi-centre, prospective cohort study. *Crit Care* 2015;19:81.
- 54 Reid DB, Chapple LS, O'Connor SN, Bellomo R, Buhr H, Chapman MJ, *et al.* The effect of augmenting early nutritional energy delivery on quality of life and employment status one year after ICU admission. *Anaesthesia and intensive care* 2016;44:406-12.
- 55 Norman BC, Jackson JC, Graves JA, Girard TD, Pandharipande PP, Brummel NE, *et al.* Employment Outcomes After Critical Illness: An Analysis of the Bringing to

- Light the Risk Factors and Incidence of Neuropsychological Dysfunction in ICU Survivors Cohort. *Crit Care Med* 2016;44:2003-9.
- 56 Yang N, Li B, Ye B, Ke L, Chen F, Lu G, *et al.* The long-term quality of life in patients with persistent inflammation-immunosuppression and catabolism syndrome after severe acute pancreatitis: A retrospective cohort study. *Journal of critical care* 2017;42:101-6.
- 57 Wang ZY, Li T, Wang CT, Xu L, Gao XJ. Assessment of 1-year Outcomes in Survivors of Severe Acute Respiratory Distress Syndrome Receiving Extracorporeal Membrane Oxygenation or Mechanical Ventilation: A Prospective Observational Study. *Chin Med J (Engl)* 2017;130:1161-8.
- 58 McPeake J, Shaw M, Iwashyna TJ, Daniel M, Devine H, Jarvie L, *et al.* Intensive Care Syndrome: Promoting Independence and Return to Employment (InS:PIRE). Early evaluation of a complex intervention. *PLoS one* 2017;12:e0188028.
- 59 Haines KJ, Berney S, Warrillow S, Denehy L. Long-term recovery following critical illness in an Australian cohort. *Journal of Intensive Care* 2018;6.
- 60 Sevin CM, Bloom SL, Jackson JC, Wang L, Ely EW, Stollings JL. Comprehensive care of ICU survivors: Development and implementation of an ICU recovery center. *Journal of critical care* 2018;46:141-8.
- 61 Hodgson CL, Haines KJ, Bailey M, Barrett J, Bellomo R, Bucknall T, *et al.* Predictors of return to work in survivors of critical illness. *Journal of critical care* 2018;48:21-5.
- 62 Riddersholm S, Christensen S, Kragholm K, Christiansen CF, Rasmussen BS. Organ support therapy in the intensive care unit and return to work: a nationwide, register-based cohort study. *Intensive Care Med* 2018;44:418-27.
- 63 Chelluri L, Im KA, Belle SH, Schulz R, Rotondi AJ, Donahoe MP, *et al.* Long-term mortality and quality of life after prolonged mechanical ventilation. *CritCare Med* 2004;32:61-9.
- 64 Needham DM, Dinglas VD, Bienvenu OJ, Colantuoni E, Wozniak AW, Rice TW, *et al.* One year outcomes in patients with acute lung injury randomised to initial trophic or full enteral feeding: prospective follow-up of EDEN randomised trial. *Bmj* 2013;346:f1532.

65 Dinglas VD, Hopkins RO, Wozniak AW, Hough CL, Morris PE, Jackson JC, *et al.* One-year outcomes of rosuvastatin versus placebo in sepsis-associated acute respiratory distress syndrome: prospective follow-up of SAILS randomised trial. *Thorax* 2016;71:401-10.

66 Adhikari NKJ, McAndrews MP, Tansey CM, Matte A, Pinto R, Cheung AM, *et al.* Self-reported symptoms of depression and memory dysfunction in survivors of ARDS. *Chest* 2009;135:678-87.

67 Adhikari NKJ, Tansey CM, McAndrews MP, Matte A, Pinto R, Cheung AM, *et al.* Self-reported depressive symptoms and memory complaints in survivors five years after ARDS. *Chest* 2011;140:1484-93.