

ORIGINAL RESEARCH

Return to work after critical illness: a systematic review and meta-analysis

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ABSTRACT

Background Survivors of critical illness often experience poor outcomes after hospitalisation, including delayed return to work, which carries substantial economic consequences.

Objective To conduct a systematic review and meta-analysis of return to work after critical illness.

Methods We searched PubMed, Embase, PsycINFO, CINAHL and Cochrane Library from 1970 to February 2018. Data were extracted, in duplicate, and random-effects meta-regression used to obtain pooled estimates.

Results Fifty-two studies evaluated return to work in 10 015 previously employed survivors of critical illness, over a median (IQR) follow-up of 12 (6.25–38.5) months. By 1–3, 12 and 42–60 months' follow-up, pooled return to work prevalence (95% CI) was 36% (23% to 49%), 60% (50% to 69%) and 68% (51% to 85%), respectively ($\tau^2=0.55$, $I^2=87\%$, $p=0.03$).

No significant difference was observed based on diagnosis (acute respiratory distress syndrome (ARDS) vs non-ARDS) or region (Europe vs North America vs Australia/New Zealand), but was observed when comparing mode of employment evaluation (in-person vs telephone vs mail). Following return to work, 20%–36% of survivors experienced job loss, 17%–66% occupation change and 5%–84% worsening employment status (eg, fewer work hours). Potential risk factors for delayed return to work include pre-existing comorbidities and post-hospital impairments (eg, mental health).

Conclusion Approximately two-thirds, two-fifths and one-third of previously employed intensive care unit survivors are jobless up to 3, 12 and 60 months following hospital discharge. Survivors returning to work often experience job loss, occupation change or worse employment status. Interventions should be designed and evaluated to reduce the burden of this common and important problem for survivors of critical illness.

Trial registration number PROSPERO CRD42018093135.

INTRODUCTION

Rising intensive care unit (ICU) utilisation and improvements in critical care medicine have resulted in an ever-expanding population of survivors of critical illness.^{1,2} Following ICU hospitalisation, these survivors often experience the 'post-intensive care syndrome', a constellation of physical, cognitive and mental health impairments

Key messages**What is the key question?**

► Among previously employed survivors of critical illness, what proportion return to work following intensive care unit (ICU) hospitalisation?

What is the bottom line?

► One to 3, 6, 12, 18 to 36, and 42 to 60 months following ICU hospitalisation, previously employed survivors had a pooled return to work prevalence (95% CI) of 36% (23% to 49%), 64% (52% to 75%), 60% (50% to 69%), 63% (44% to 82%) and 68% (51% to 85%).

Why read on?

► No substantial differences in return to work were observed when stratified by diagnosis (acute respiratory distress syndrome (ARDS) vs non-ARDS) or region (Europe vs North America vs Australia/New Zealand); however, there were significant differences when comparing mode of employment evaluation (in-person vs telephone vs mail). In addition, survivors who returned to work commonly experienced adverse work-related outcomes, including changes in occupation, worsening employment status (eg, fewer work hours) and subsequent job loss.

which contribute to disability and poor quality of life.² Delayed return to work is common after critical illness and is likely a consequence of post-ICU impairments, carrying substantial financial consequences for patients, their families and society.³

Despite burgeoning interest in post-ICU outcomes, there remains an incomplete understanding of the epidemiology of delayed return to work after critical illness, including longitudinal trends, associated factors and lost earnings. Recent studies in previously employed survivors of critical illness found that 67% and 69% returned to work at 12 and 60 months, respectively, and more than 70% accrued substantial lost earnings.^{4,5} In order to better understand the effects of critical illness on return to work, we conducted a systematic review and meta-analysis of studies evaluating return to work following ICU hospitalisation in survivors of critical illness.



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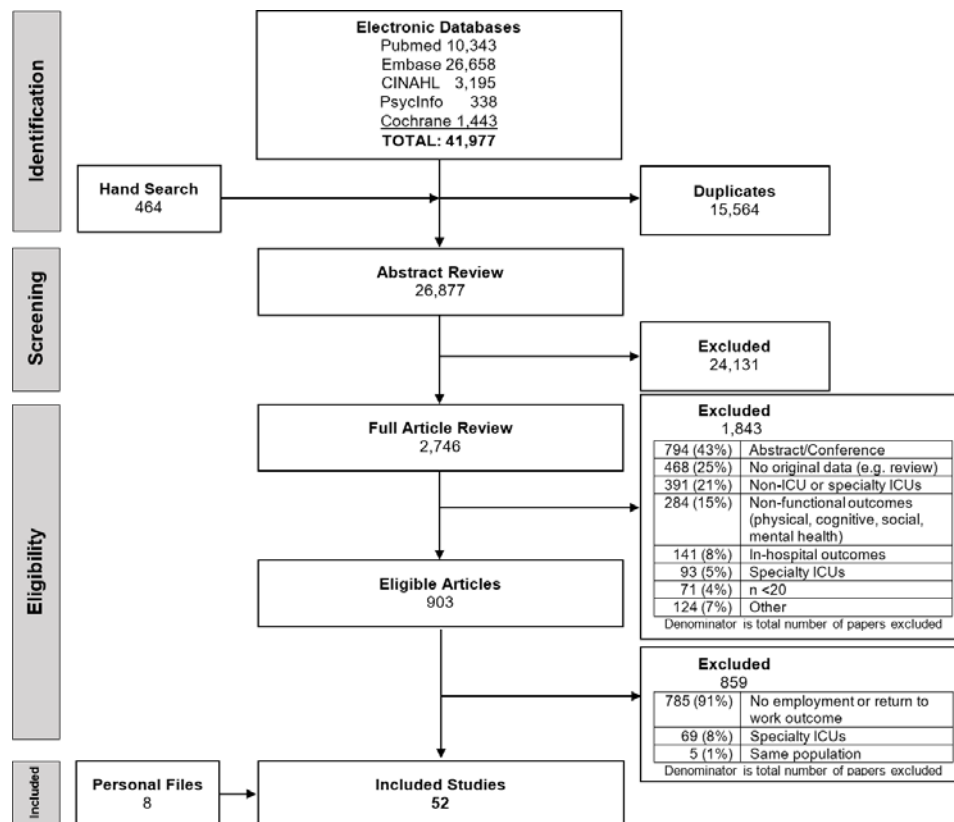


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. ICU, intensive care unit.

METHODS

Search strategy and selection criteria

The conduct and reporting of this meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.⁶ This meta-analysis protocol was registered on PROSPERO (accessible at www.crd.york.ac.uk; ID=CRD42018093135). This meta-analysis only involved the return to work outcome detailed in the PROSPERO protocol.

This systematic review and meta-analysis assessed studies that evaluated return to work following ICU hospitalisation in survivors of critical illness, specifically focusing on return to work prevalence over time and associated patient and clinical variables. To identify eligible studies, we searched five electronic databases (PubMed, Embase, PsycINFO, CINAHL and Cochrane Library) from 1 January 1970 to 14 February 2018, with no language restrictions. As prior studies may have evaluated return to work as one of several post-ICU outcomes, without including work-related terms (eg, 'employment') in the title, abstract or keywords, a broad search was performed, using keywords 'intensive care', 'outcome assessment' and 'follow-up' to capture articles with any assessment of any post-discharge outcomes in survivors of critical illness (full search strategy in online data supplement).⁷ To identify eligible studies, we also conducted a hand search of reference lists of relevant articles, along with a search of personal files.

Our inclusion criteria included primary research studies that (1) enrolled adult survivors (≥ 16 years old) of critical illness, and (2) performed a patient-level evaluation of return to work after hospital discharge. We excluded studies enrolling fewer than 50% ICU patients and with fewer than 20 patients for follow-up. Our aim was to evaluate return to work in general ICU survivors (ie, hospitalised in medical or surgical ICUs); hence, we

excluded studies that primarily included patients from specialty ICUs (eg, cardiac surgery, neurological/neurosurgical or trauma ICU). We excluded abstracts and dissertations not published in peer-reviewed journals.

Trained reviewers screened, in duplicate, titles and abstracts, followed by full-text articles, using DistillerSR (2014 Evidence Partners, Ottawa, Canada). All screening conflicts were resolved by consensus.

Data analysis

Two independent reviewers (from among KDS, MRS, RH, RS, KFD) abstracted data from each eligible article, with conflicts resolved by an independent researcher (RS, KDS, KFD or BBK). Data collected from each eligible study included author, journal, publication year, country, start date, end date, study design, study location, sample size, patient demographics, sample size of patients working before ICU hospitalisation, work status during follow-up, predictors of return to work and secondary outcomes related to employment, such as estimated lost earnings.

Our primary analysis involved estimating the proportion of previously employed survivors reporting return to work after critical illness. First, regarding post-ICU follow-up, prior outcome studies often use 1, 3, 6 and 12 months' follow-up time points. In addition, some studies we identified evaluated survivors beyond 12 months, and we determined that 18 to 36 and 42 to 60 months were logical cut points based on the data. Next, for studies reporting proportions of previously employed ICU survivors returning to work, we calculated log odds of return to work at each follow-up time point. Random-effects meta-regression of the log odds was then used to estimate pooled proportions of return to work as a function of follow-up time (categorical: 1

Table 1 Summary of 52 studies included in review

Author year (country)	Study design, location, population studied, employment instrument*	Enrolment: sample size and demographics	Employed before ICU, % (n/N)	Post-ICU return to work outcome
Parno <i>et al</i> 1984 (USA) ¹³	Prospective, medical–surgical ICU, any patient, mailed questionnaire	n=217; mean age (SD)=55 (4.6)	45% (97/216)	61% (59/97) returned to work at 24 m
Goldstein <i>et al</i> 1986 (USA) ¹⁴	Prospective, medical and cardiac ICU, any patient, mail/telephone interview	n=2213; mean age=64 to 65†	30% (656/2213)	65% (360/549) returned to work at 12 m
Zaren and Hedstrand 1987 (Sweden) ¹⁵	Prospective, general ICU, age ≤64 years, telephone interview	n=717; mean age (SD)=50 (19), 44% female	65% (339/518)	75% (254/339) returned to work at 12 m
Mundt <i>et al</i> 1989 (USA) ¹⁶	Retrospective, medical–surgical ICU, any patient, mailed questionnaire	n=887; mean age (SD)=59 (18), 43% female	47% (419/887)	70% (295/419) returned to work at 6 m
Ridley and Wallace 1990 (UK) ¹⁷	Prospective, general ICU, any patient, mailed questionnaire	n=156	35% (48/136)	79% (38/48) returned to work between 12 and 36 m
Doepel <i>et al</i> 1993 (Finland) ¹⁸	Retrospective, general ICU, severe acute pancreatitis, in-person interview	n=37; mean age (range)=49 (26 to 90), 32% female	84% (31/37)	70% (26/37) returned to work at mean 74 m (range 12 to 168 m)
McHugh <i>et al</i> 1994 (USA) ¹⁹	Prospective, multiple ICU, ARDS requiring intubation, in-person interview	n=37; mean age=41, 38% female	73% (27/37)	56% (15/27) returned to work at 12 m
Bell and Turpin 1994 (UK) ²⁰	Prospective case–control, general and cardiac ICU, any patient, mailed questionnaire	n=172; mean age=54 to 63, 39% female†	42%‡ (66/156)§	63% (35/56) returned to work at 3 m†‡§###
Daffurn <i>et al</i> 1994 (Australia) ²¹	Prospective, general ICU, present >48 hours, clinic visit	n=54; mean age (SD)=51 (18)	44% (24/54)	50% (12/24) returned to work at 3 m
Munn <i>et al</i> 1995 (UK) ²²	Prospective, general ICU, any patient, mailed questionnaire	n=504	59% (123/207)	30% (37/123) returned to work at 3 m
Fakhry <i>et al</i> 1996 (USA) ²³	Retrospective, surgical ICU, present in ICU >14 days, mail/telephone interview	n=39; mean age=53, 31% female	58% (11/19)	45% (5/11) returned to work at mean 18 m (range 4 to 30 m)
Weinert <i>et al</i> 1997 (USA) ²⁴	Prospective, general ICU, acute lung injury, mailed questionnaire	n=24; mean age (SD)=40 (12), 33% female	54% (13/24)	54% (7/13) returned to work at median 15 m (range 6 to 41 m)
Hurel <i>et al</i> 1997 (France) ²⁵	Prospective, medical–surgical ICU, any patient, mailed questionnaire	n=223; mean age (SD)=52 (18), 44% female	30% (68/223)	62% (42/68) returned to work at 6 m
Eddleston <i>et al</i> 2000 (UK) ²⁶	Prospective, general ICU, any patient, in-person questionnaire	n=143; mean age (SD)=49 (12), 48% female	33% (47/143)	23% (11/47) returned to work at 3 m 49% (23/47) returned to work at 6 m 79% (37/47) returned to work at 12 m
Wehler <i>et al</i> 2001 (Germany) ²⁷	Prospective, medical ICU, present in ICU >24 hours, telephone interview	n=185; mean age (SD)=56 (18), 44% female	25% (46/185)	98% (45/46) returned to work at 6 m
Chelluri <i>et al</i> 2002 and 2004 (USA) ^{28,29}	Prospective, multiple ICU¶, intubated >48 hours, in-person interview	n=817; mean age (SD)=60 (19), 46% female	23% (176/772)	18% (32/176) returned to work at 2 m 34% (32/93) returned to work at 12 m
Haraldsen and Andersson 2002 (Sweden) ³⁰	Retrospective, surgical ICU, abdominal sepsis, mail/telephone interview	n=49; median age=67	47% (23/49)	74% (17/23) returned to work at median 72 m (range 24 to 178 m)
Wehler <i>et al</i> 2003 (Germany) ³¹	Prospective, medical ICU, present in ICU >24 hours, telephone interview	n=318; mean age (SD)=57 (17), 42% female	32% (102/318)§	91% (64/70) returned to work at 6 m
Garcia Lizana <i>et al</i> 2003 (Belgium) ³²	Prospective, medical–surgical ICU, any patient, telephone interview	n=96; median (IQR) age=60 (42–75), 36% female	47% (45/96)	62% (28/45) returned to work at 18 m
Halonon <i>et al</i> 2003 (Finland) ³³	Retrospective, surgical and general ICU, severe pancreatitis, mailed questionnaire	n=145; mean age=44, 17% female	68% (99/145)	87% (86/99) returned to work at median 66 m (range 19 to 127 m)
Cuthbertson <i>et al</i> 2005 (UK) ³⁴	Prospective, general ICU, any patient, telephone interview	n=300; median age=61, 41% female	39% (67/173)	25% (17/67) returned to work at 3 m 49% (33/67) returned to work at 6 m 58% (39/67) returned to work at 12 m
Graf <i>et al.</i> 2005 (Germany) ³⁵	Prospective, medical ICU, present >24 hours, mailed questionnaire	n=173; mean age (SD)=61 (13), 25% female	53% (91/173)	23% (21/91) returned to work at 60 m
Cinquelpalmi <i>et al</i> 2006 (Italy) ³⁶	Prospective, surgical ICU, pancreatic necrosis surgery, clinic visit	n=35; mean age (SD)=55 (11), 29% female	100% (32/32)	38% (12/32) returned to work at 6 m
Longo <i>et al</i> 2007 (Canada) ³⁷	Prospective (post-RCT), general ICU, severe sepsis, mailed questionnaire	n=98; mean age (SD)=60 (17), 48% female	21% (21/98)**	76% (16/21) returned to work at 1 m 86% (18/21) returned to work at 7 m
Ylipalosaari <i>et al</i> 2007 (Finland) ³⁸	Prospective, general ICU, present in ICU >48 hours, mailed (80%) and telephone (20%) questionnaire	n=142; median (IQR) age=57 (43–69), 39% female	33% (47/142)	36% (17/47) returned to work at median 24 m (IQR 21–28 m)§
Linden <i>et al</i> 2009 (Sweden) ³⁹	Retrospective, general ICU, ARDS requiring ECMO, in-person questionnaire	n=21; mean age=40, 43% female	100% (21/21)	76% (16/21) returned to work at mean 26 m (range 12 to 50 m)

Continued

Table 1 Continued

Author year (country)	Study design, location, population studied, employment instrument*	Enrolment: sample size and demographics	Employed before ICU, % (n/N)	Post-ICU return to work outcome
van der Schaaf <i>et al</i> 2009 (Netherlands) ⁴⁰	Cross-sectional, general ICU, present in ICU >48 hours, mailed questionnaire	n=255; mean age (SD)=59 (17), 34% female	33% (82/251)	54% (44/82) returned to work at 12 m
van der Schaaf <i>et al</i> 2009 (Netherlands) ⁴¹	Prospective, medical–surgical ICU, receiving MV >48 hours, mailed questionnaire	n=30; mean age (SD)=57 (16), 40% female	40% (12/30)	42% (5/12) returned to work at 12 m
Poulsen <i>et al</i> 2009 (Denmark) ⁴²	Retrospective, general ICU, septic shock, telephone interview	n=70; median (IQR) age=59 (46–67), 21% female	33% (23/70)	43% (10/23) returned to work at 12 m
Kelly and McKinley 2010 (Australia) ⁴³	Retrospective, general ICU, present in ICU >48 hours, clinic/phone interview	n=39; mean age (SD)=60 (16), 41% female	36% (14/39)	43% (6/14) returned to work at mean 3.5 m (range 1 to 7 m)
Myhren <i>et al</i> 2010 (Norway) ⁴⁴	Prospective, general ICU, present in ICU >24 hours, mailed questionnaire	n=194; mean age (SD)=49 (15), 40% female	63% (122/194)	55% (67/122) returned to work at 12 m††
Herridge <i>et al</i> 2011 (Canada)‡‡ ⁴⁵	Prospective, medical–surgical ICU, ARDS requiring MV, clinic or home visit	n=83; median (IQR) age=45 (36–56), 45% female	77% (64/83)	63% (40/64) returned to work at 12 m 92% (49/53) returned to work at 60 m
Dennis <i>et al</i> 2011 (Australia) ⁴⁶	Prospective, medical–surgical ICU, present in ICU >48 hours, telephone interview	n=77; mean age (SD)=54 (18), 42% female	45% (32/71)	50% (16/32) returned to work at 6 m
Luyt <i>et al</i> 2012 (France) ⁶³	Prospective case–control, general ICU, H1N1 influenza with ARDS, in-person questionnaire	n=37, median (IQR) age 39 (32–49), 51% female§§	78% (29/37)	90% (26 of 29) returned to work at 12 m
Hodgson <i>et al</i> 2012 (Australia) ⁴⁷	Retrospective, general ICU, ARDS requiring ECMO, telephone interview	n=21; mean age (SD)=36 (12), 52% female	100% (15/15)	53% (8/15) working at median 8.4 m (range 6 to 16 m)
Kowalczyk <i>et al</i> 2013 (Poland) ⁴⁸	Cross-sectional, general ICU, present in ICU >24 hours, mailed questionnaire	n=186; mean age (SD)=48 (19), 42.5% female	55% (102/185)	48% (49/102) returned to work at 12–60 m
Cuthbertson <i>et al</i> 2013 (Scotland) ⁴⁹	Prospective, adult ICU, severe sepsis, telephone interview	n=439; median age=58 (45, 67), 47% female	73% (62/85)	85% (53/62) returned to work at 42 m¶¶¶ 79% (46/58) returned to work at 60 m¶¶¶
Fonsmark and Nielsen 2015 (Denmark) ⁵⁰	Prospective, medical–surgical ICU, present in ICU >4 days and in hospital >10 days, in-person interview	n=101; median (IQR) age=60 (49–66), 39% female	49% (49/101)	33% (16/49) returned to work at ≥2 m
Quasim <i>et al</i> 2015 (UK) ⁵¹	Prospective, general ICU, any patient, mailed questionnaire	N=75§§§	54% (28/52)	46% (11/24) returned to work at 12 m**** 64% (18/28) returned to work at median 27 m (range 24 to 29 m)
Pratt <i>et al</i> 2015 (USA) ⁵²	Retrospective, ICU, 90 day survivors of severe shock, telephone interview	n=76; mean age (SD)=55 (17), 47% female	47% (17/36)	53% (9/17) returned to work at mean±SD 60±16 m (range 36 to 84 m)
Team Study 2015 (AUS and NZ) ⁵³	Prospective, ICU, requiring MV >48 hours, telephone interview	n=192; mean age (SD)=58 (16), 39% female	64% (77/120)	38% (29/77) returned to work at 6 m
Reid <i>et al</i> 2016 (Australia) ⁵⁴	Prospective, general ICU, any patient requiring MV, telephone interview	n=39; mean age (SD)=56 (2), 23% female	51% (18/35)†††	50% (9/18) returned to work at 12 m
Norman <i>et al</i> 2016 (USA) ⁵⁵	Prospective, medical–surgical ICU, respiratory failure or cardiogenic shock or septic shock, questionnaire	n=113; median (IQR) age=53 (44–60), 39% female	26% (115/446)	42% (48/113) returned to work at 3 m 52% (49/94) returned to work at 12 m§
Yang <i>et al</i> 2017 (China) ⁵⁶	Retrospective, general ICU, severe pancreatitis for >14 days, telephone interview	n=214; median (IQR) age=45 (38–52), 34% female	34% (73/214)‡‡‡	66% (48/73) returned to work at median 17 m (IQR 10–24 m)§§§
Wang <i>et al</i> 2017 (China) ⁵⁷	Prospective, general ICU, severe ARDS, in-person interview	n=72; mean age (SD)=42 (15), 29% female¶¶¶¶	100% (72/72)	56% (40/72) returned to work at 12 m
McPeake <i>et al</i> 2017 (Scotland) ⁵⁸	Prospective, medical–surgical ICU, level 3 stay×72 hours or level 2 stay×14 days and age <65, **** clinic visit	n=40; median (IQR) age=51 (43–57), 38% female	43% (17/40)	88% (15/17) returned to work at 12 m
Kamdar <i>et al</i> 2017 (USA)†††† ⁴	Prospective (post-RCT), medical or surgical ICU, ARDS, telephone interview	n=825; mean age=45 to 54, 52% female	47% (386/825)	55% (214/386) ever returned to work at 6 m 67% (253/379) ever returned to work at 12 m
Kamdar <i>et al</i> 2018 (USA) ⁵	Prospective, medical or surgical ICU, ARDS, telephone interview	n=138; median age=46 to 49, 46% female	49% (67/138)	49% (33/67) ever returned to work at 12 m 55% (37/67) ever returned to work at 24 m 60% (40/67) ever returned to work at 36 m 66% (43/65) ever returned to work at 48 m 69% (44/64) ever returned to work at 60 m
Haines <i>et al</i> 2018 (Australia) ⁵⁹	Prospective (post-RCT), mixed ICU, present in ICU >5 days, in-person questionnaire	n=56; mean age (SD)=59 (14), 39% female	52% (29/56)	69% (20/29) returned to work at 54 m
Sevin <i>et al</i> 2018 (USA) ⁶⁰	Prospective, medical ICU, at risk for post intensive care syndrome, in-person interview	n=62; median (IQR) age=50 (36–57), 45% female	76% (47/62)	15% (7/47) returned to work at 1 m
Hodgson <i>et al</i> 2018 (Australia) ⁶¹	Prospective, general ICU, >24 hours MV, telephone interview	n=107; mean age=47 to 53, 27% female	41% (107/262)	71% (76/107) returned to work at 6 m

Continued

Table 1 Continued

Author year (country)	Study design, location, population studied, employment instrument*	Enrolment: sample size and demographics	Employed before ICU, % (n/N)	Post-ICU return to work outcome
Riddersholm <i>et al</i> 2018 (Denmark) ⁶²	Retrospective, ICU, present in ICU >72 hours and working prior to admission, country database	n=5762; median (IQR) age=50 (38–58), 36% female	100% (5762/5762)	60% (3457/5762) ever returned to work at 12 m§ 68% (3918/5762) ever returned to work at 24 m§ 74% (4274/5762) ever returned to work over median 6.4 years (95% CI 6.1 to 6.6 years)

*Cohort studies unless noted otherwise.

†Mean/median age not provided for total population. Study provided mean/median for groups within total population.

‡Proportion estimated from bar graph.

§Numerator not provided. Calculated using other available data.

¶Medical, neurological, trauma, surgical ICU.

**Merged two populations: patients receiving Activated Protein C (APC) and no APC.

††Includes patients returning to school.

‡‡Study involved two secondary analyses evaluating risk factors for RTW.^{65 66}

§§Included baseline data specifically for previously employed survivors.

¶¶Included 25 of 62 (40%) and 24 of 58 (41%) of 42 m and 60 m survivors reporting "1 work less" compared with pre-ICU.

***Data published in another study.⁵⁸

†††Merged from two populations: patients receiving 1 vs 1.5 kcal/mL enteral nutrition.

‡‡‡Merged from two populations: patients with and without persistent inflammation-immunosuppression and catabolism syndrome after severe acute pancreatitis.

§§§Denominator not provided; calculated using other available data.

¶¶¶Merged from two populations: patients receiving and not receiving ECMO.

****Levels refers to the UK Intensive Care Society definition of ICU patients.

††††Evaluation of cohort of previously employed ARDS survivors. Two previously published studies (Needham *et al*⁷³ and Dinglas *et al*⁷⁴) reported return to work from subgroups from the same parent cohort.

‡‡‡‡Full-time workers who returned to full-time work.

ARDS, acute respiratory distress syndrome; d, days; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; m, months; MV, mechanical ventilation; RCT, randomised controlled trial; RTW, return to work.

to 3, 6, 12, 18 to 36, 42 to 60 months); this model was fit via a restricted maximum-likelihood Knapp-Hartung modification to estimate between-study heterogeneity (τ^2), given a small number of studies available at each follow-up time.⁸ Pooled log odds estimates were back-transformed to proportions and presented with corresponding 95% CIs. An I^2 statistic estimated residual heterogeneity and a p value calculated to test the null hypothesis of no differences in pooled proportions across follow-up time.

Our primary analysis included only studies evaluating return to work at the defined follow-up time points. For studies with multiple data within a follow-up time points (eg, 24 and 36 months), we included only the data most distant from ICU discharge as some studies reported rising employment rates over time. Subgroup analyses were conducted evaluating factors that are thought to influence return to work: (1) ICU admission diagnosis category, specifically acute respiratory distress syndrome (ARDS) versus non-ARDS (other diagnoses (ie, sepsis) were infrequent and, as such, further subgroup analyses were not conducted); (2) geographical region (Europe vs North America vs Australia/New Zealand); (3) mode of employment evaluation (in-person vs telephone interview vs mailed questionnaire), to account for possible reporting differences.⁹ In addition, to evaluate for temporal trends in employment, a subgroup analysis was conducted involving enrolment dates (pre-1990, 1991–2000, 2001–2010, 2011–current). These subgroup analyses were conducted by including the main term for subgroup (categorical) and an interaction of the subgroup and follow-up time categories. We were unable to evaluate other variables of interest including survivors' age, severity of illness and length of stay with return to work, as the majority of studies did not report these variables for the subpopulation that was previously employed. Sensitivity analyses involved (1) including studies with non-discrete follow-up times, using the chronologically latest value for follow-up time reported in the study (ie, third quartile if median (IQR) reported and maximum if median (range) reported); and (2) extending the primary analysis model

to include an indicator of whether the employment data were collected during periods of global economic downturn (ie, 2008 to 2010) to further evaluate for temporal trends in employment.

Risk of bias was independently assessed by two reviewers (from among KDS and/or MRS and/or RH or KDS and/or RS and/or KFD), using the Newcastle-Ottawa Scale¹⁰ for observational studies, including those conducted as longitudinal follow-up of randomised controlled trials. Disagreements were resolved by consensus. Publication bias was assessed visually using funnel plots and quantitatively using the Egger statistical test.^{11 12 12} A two-sided p value <0.05 was considered statistically significant. All analyses were performed using STATA V.15.1 (StataCorp, College Station, Texas, USA).

RESULTS

Our search yielded 41 977 articles; after removal of duplicates, 26 877 abstracts were reviewed, of which 2754 were reviewed as full text. After excluding 2689 articles and adding 8 articles from personal files, 73 potential citations were identified. Among these articles, 52 unique studies evaluated return to work in previously employed ICU survivors (figure 1, table 1, online supplementary eTable 2).^{4 5 13–63} These studies included 13 retrospective^{16 18 23 30 33 39 42 43 47 48 52 56 62} and 39 prospective^{4 5 13–15 17 19–22 24–28 30–32 34–38 40 41 44–46 49–51 53–55 57–61 63} cohort studies, of which three were longitudinal follow-up within a randomised trial.^{4 37 59} Eleven (21%) studies included more than one follow-up time point after discharge.^{4 5 26 28 29 34 37 45 49 51 55 62} Fourteen (27%) studies were published between 1984 and 2000, 17 (33%) from 2001 to 2010, and 21 (40%) from 2011 to 2018. Eleven studies conducted employment assessments during either the first (2000–2004) or second (2008–2010) global economic downturns occurring during the publication period.^{4 32 36 46–48 50–52 55 63 64} Twenty-eight (54%) studies were conducted in Europe,^{15 17 18 20 22 25–27 30–36 38–42 44 48–51 58 62 63} 14 (27%) in North America,^{4 5 13 14 16 19 23 24 28 29 37 45 52 55 60 60} 8 (15%) in Australia/

New Zealand^{21 43 46 47 53 54 59 61} and 2 (4%) in Asia.^{56 57} Nine studies (17%) evaluated return to work in survivors of ARDS.^{45 19 24 39 45 47 57 63} Employment evaluation occurred via in-person visit in 18 (35%) studies,^{18 19 21 26–29 31 36 39 43 45 50 55 57–60 63} telephone interview in 18 (35%) studies,^{4 5 13–15 23 30 32 34 42 46 47 49 52–54 56 61} mailed questionnaire in 15 (29%) studies^{16 17 20 22 24 25 33 35 37 38 40 41 44 48 51} and national database in 1 study.⁶² The majority of studies used ‘had returned to work’, ‘back to work’, ‘working’ or multiple phrases to describe survivors’ post-ICU employment status, and did not report the specific employment question(s) used, the timing of return to work or status of survivors who had not returned to work (ie, retirement, unemployment, disability). Three studies differentiated whether previously employed survivors were currently working or had ever returned to worked at the time of post-ICU follow-up.^{4 5 62} Eleven (21%) studies evaluated factors associated with return to work.^{4 5 19 37 44 45 51 54 55 61 62 65 66} Notably, four (8%) studies enrolled patients who were seen in a multidisciplinary ICU survivor clinic,^{21 50 58 60} of which one evaluated an intervention to improve return to work.⁵⁸

The included studies evaluated return to work in 10015 (median 48.5, IQR 25.5–94, range=11 to 5762) previously employed ICU survivors, with a median maximum follow-up time of 12 (IQR 6.25–38.5, range=1 to 178) months. Five (10%) studies reported a median time to return to work, ranging from 10 to 29 weeks.^{4 5 30 57 62 63} Six (12%) studies provided demographic and/or ICU data specifically for the previously employed survivor subcohort.^{4 5 51 55 57 61–63} In addition, four (8%) studies

documented death, loss to follow-up and participation refusal specifically among previously employed survivors, with rates of 3% (20 of 631), 6% (36 of 631) and 1% (6 of 631), respectively, across longitudinal follow-up.^{4 5 55 56} In risk of bias evaluation of the 52 observational studies, 46% did not have adequate representativeness of the exposed cohort, and 52% did not have adequate follow-up (online supplementary eTable 6, eFigure 2). The funnel plots and Egger tests did not support evidence of publication bias, based on follow-up time point category (online supplementary eFigures 3 and 4).

When evaluating the 38 studies with discrete follow-up time points, we estimated pooled 1 to 3, 6, 12, 18 to 36, and 42 to 60 months’ return to work prevalence (95% CI) of 36% (23% to 49%), 64% (52% to 75%), 60% (50% to 69%), 63% (44% to 82%) and 68% (51% to 85%), respectively ($\tau^2=0.55$, $I^2=87%$, $p=0.03$) (figure 2, online supplementary eTable 3). These results did not differ substantially ($p=0.65$) when including the 11 studies^{17 23 24 30 33 38 39 43 48 50 51} reporting only non-discrete follow-up time points (online supplementary eTable 4, eFigure 1).

In subgroup analyses of studies only including discrete follow-up time points, significant return to work differences, stratified by follow-up time point, were not observed when comparing disease category (online supplementary eTable 3), region (online supplementary eTable 3) or date of enrolment (online data supplement), but were observed when comparing mode of employment evaluation (online supplementary eTable

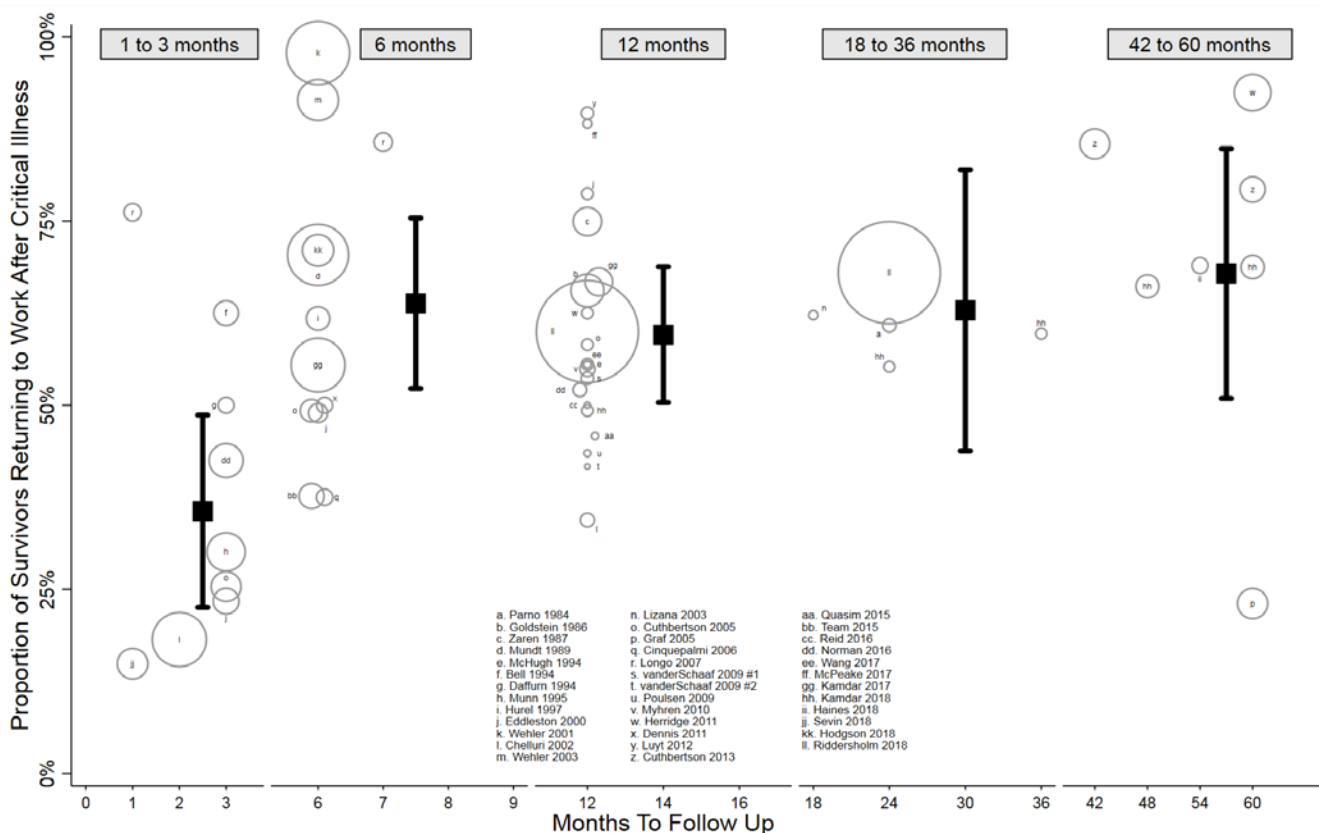


Figure 2 Proportion of survivors returning to work after critical illness, among 38 studies with discrete follow-up time points. Black squares represent pooled proportions (with 95% CIs) by that time point: 36% (23% to 49%) by 1 to 3 months, 64% (52% to 75%) by 6 months, 60% (50% to 69%) by 12 months, 63% (44% to 82%) by 18 to 36 months and 68% (51% to 85%) by 42 to 60 months. Pooled estimates calculated using random-effects meta-regression. For the 3 pairs of estimates falling within the same follow-up stratum, only the final follow-up point estimate was included. Bubbles represent 53 point estimates from the 38 studies, with bubble size corresponding to study sample size.

3). Sensitivity analyses yielded no significant differences (online data supplement). Among secondary outcomes reported, previously employed survivors often received new disability benefits and incurred substantial lost earnings, totalling up to US\$26 949 at 12 months and \$180 221 60 months after critical illness (table 2, online data supplement). In addition, among survivors who returned to work, 5%–84% were working less or subsequently retired, 17%–66% changed occupations and 20%–36% subsequently incurred job loss (table 2, online data supplement).

Eleven studies reported risk factors for delayed return to work after critical illness (table 3, online supplementary eTable 5).^{4 5 19 37 44 45 51 54 55 61 62 65 66} Possible predictors of delayed return to work (ie, >50% of studies demonstrating a similar positive finding) included lower education, pre-existing comorbidities, non-trauma admission, discharge to non-hospital location and mental health impairments following hospital discharge.

DISCUSSION

Our systematic review identified 52 studies that evaluated return to work in previously employed survivors of critical illness. Delayed return to work and joblessness are common and persistent issues, with approximately two-thirds, two-fifths and one-third jobless up to 3, 12 and 60 months after ICU hospitalisation. Significant differences in return to work were not observed when evaluated according to ICU admission diagnosis category (ARDS vs non-ARDS) or geographical region but were observed when different modes of employment evaluation (in-person vs telephone vs mail) were used. Previously employed survivors frequently required new disability benefits and accrued substantial lost earnings, and those who did return to work were vulnerable to subsequent job loss, occupation changes and worsening employment status.

As part of growing interest in post-ICU outcomes, we observed an increase in research studies that evaluated return to work following critical illness. Our analysis of 10 015 previously employed survivors demonstrated that 36%, 64%, 60%, 63% and 68% of survivors had reported returning to work by 1 to 3, 6, 12, 18 to 36, and 42 to 60 months' follow-up. Although our review included general medical-surgical survivors and excluded those in neurological intensive care, our return to work rates were similar to or exceeded the rates observed following traumatic brain injury⁶⁷ and stroke.⁶⁸ While our analysis was limited by substantial heterogeneity, in particular timing and modes of employment evaluation, we observed consistent trends in return to work over time, culminating in nearly one-third of survivors having not returned to work up to 60 months after critical illness.

In subgroup and sensitivity analyses, we found few differences in return to work by geographical region or when evaluated during economic downturn, suggesting little influence of societal or economic factors on the findings. In addition, we observed no significant difference based on ICU admission diagnosis (ARDS vs non-ARDS). Lastly, significant return to work differences were observed when comparing different types of follow-up; notably, studies involving mailed questionnaire reported a particularly high return to work prevalence (53%) at 1 to 3 months. Given that 1 to 3 months' response rates by mail were more than 50% lower than in-person/telephone rates (22% vs 48%), it is possible that only survivors who returned to work were able to respond to mailed questionnaires. While death, loss to follow-up and refusal rates were low (1%–6%) in previously employed survivors undergoing serial in-person or telephone evaluations, the majority of studies used return to work

as a secondary outcome and did not report these data. Trials incorporating return to work as a primary outcome could report these data and perform a more detailed investigation of variables preventing or promoting return to work. Future research should consider direct and standardised return to work assessments while determining core data elements and the optimal timing of data collection. In addition, qualitative and quantitative studies could focus on patient-reported reasons for delayed return to work, modelling these factors with variables gathered during the trial.

Notably, despite an overall rise in return to work over time, there was a decline between 6 and 12 months, suggesting that for some individuals, working was short-lived. This observation was supported by two longitudinal studies reporting fixed or declining employment rates with concomitant increase in job loss (8% to 14% increase from 6 to 12 months and 12% to 25% increase from 24 to 60 months),^{4 5} and a national database study of 5762 patients reporting a cumulative incidence of job loss (after return to work) of nearly 50% 3 years after intensive care.⁶² Though no study evaluated risk factors for subsequent job loss after return to work, lasting physical, cognitive and mental health impairments following critical illness may play a role.^{1 2} Several studies suggested an association of joblessness with depression, anxiety and poor quality of life, with improved mental health and quality of life after return to work.^{25 44 45 48 51 61 65 66} Given the cross-sectional nature of these studies, the directionality of associations is unclear. However, there is known a negative impact of depression and anxiety on return to work, particularly when combined with somatic illness.⁶⁹ Longitudinal studies which evaluate the co-occurrence and association of post-ICU impairments, predictors or return to work and their effects are needed. Also needed are trials of interventions to facilitate return to work, for example, specialist-led vocational⁷⁰ or combined cognitive and vocational rehabilitation interventions⁷¹ such as those used in survivors of traumatic brain injury.

From an economic standpoint, we identified six studies reporting that previously employed survivors often received new disability benefits after critical illness, with rates of 20%–27% at 12 months to 59%–89% at 76 months.^{4 5 14 30 42 62} Jobless survivors in the USA also were likely to transition from private to government-provided healthcare coverage,^{4 5} and despite return to work, the majority of non-retired survivors incurred substantial lost earnings that increased over time, totalling up to two-thirds of pre-ICU annual income.^{4 5 62} While these data do not include other financial consequences, such as medical expenses and caregiver costs, they highlight the substantial economic implications that require further investigation.

Finally, four included studies evaluated outcomes as part of novel multidisciplinary outpatient ICU recovery programmes aimed at evaluating and improving impairments common in survivors of critical illness.^{21 50 58 60} Unsurprisingly, at the time of enrolment in these programmes (approximately 1 to 5 months after discharge), survivors commonly exhibited disabling cognitive (up to 64%),⁶⁰ physical (83%)⁵⁰ and mental health (69%)⁶⁰ impairments in addition to low return to work rates (15%–33%). Of these four studies, one included an intense 5-week peer-supported physical and psychological rehabilitation programme, resulting in ICU survivors exhibiting significant improvements in self-efficacy and quality of life metrics at 12-month follow-up, with a return to work rate of 88%.⁵⁸ Adding to this literature, a qualitative review of return to work after injury highlighted workplace-related issues, such as cumbersome administrative processes and a lack

Table 2 Secondary outcomes associated with return to work after critical illness

Theme	Month	Outcome
Decline in post-ICU employment status	3	17% newly part-time, ²⁰ 15%–23% worse work status ²⁰
	6	4 of 29 (14%), ⁵³ 25 of 107 (23%), ⁶¹ 80 of 190 (42%) ⁴ working less
	12	28 of 549 (5%) ¹⁴ and 85 of 191 (45%) ⁴ working less, 79 of 94 (84%) newly part-time or unemployed ⁵⁵
	36	9 of 39 (23%) worse work status ¹⁷
	60	17% to 33% increase in part-time work ⁵² ; 59% manual vs 45% white-collar workers not RTW ⁴⁸
Occupation change	6	22 of 107 (21%) changed occupation ⁶¹
	12	79 of 257 (31%) changed occupation ⁴
	18	66% changed occupation due to physical limitations caused by illness ²³
	29	3 of 18 (17%) who RTW took on different role due to health issues ⁵¹
Poor work performance	12	69 of 257 (27%) ⁴ reduced effectiveness at work
Job loss after returning to work	12	69 of 257 (27%), ⁴ 1235 of 4274 ever RTW (29%) lost job within 12 months ⁶²
	60	12 of 33 (36%), of whom 6 (50%) lost job due to illness ⁵
	127	17 of 86 (20%) ³³
Illness or poor health affecting return to work	3	5%–11% ²⁰ not RTW due to health
	6	31 of 107 (29%), ⁶¹ 19 of 68 (28%), ²⁵ 41 of 72 (57%) ⁴ not RTW due to health
	12	37 of 251 (15%), ⁴⁰ 6 of 12 (50%), ⁴¹ 82 of 107 (77%) ⁷³ not RTW due to health
	28	26 of 47 (55%) ³⁸ not RTW due to health
	29	6 of 28 (21%) ⁵¹ not RTW due to sickness
	41	6 of 13 (46%) ²⁴ not RTW due to health
	54	5 of 29 (17%) ⁵⁹ not RTW due to health
	84	10 of 17 (59%) ⁵² previously employed had new disability
Receiving new disability benefits	6	57 of 549 (10%), ¹⁴ 56 of 386 (15%) ⁴
	12	76 of 379 (20%), ⁴ 18 of 67 (27%) ⁵
	24	20 of 67 (30%) ⁵
	36	20 of 65 (31%) ⁵
	48	21 of 64 (33%) ⁵
	60	7 of 23 (30%) ³⁰
	72	Pre–post ICU increase from 46 of 70 (66%) to 59 of 70 (84%) ⁴²
	76	Never RTW: 89% ⁶² ; job loss within 1 year of RTW: 59% ⁶²
Newly retired after critical illness	6	30 of 419 (7%), ¹⁶ 14 of 386 (4%) ⁴
	12	15 of 93 (16%), ²⁸ 6 of 82 (7%), ⁴⁰ 1 of 12 (8%), ⁴¹ 5 of 18 (28%), ⁵⁴ 15 of 379 (4%) ⁴
	18	2 of 45 (4%) ³²
	24	2 of 53 (4%), ⁴⁵ 3 of 67 (4%) ⁵
	26	2 of 21 (10%) ³⁹
	27	1 of 28 (4%) ⁵¹
	36	4 of 67 (6%) ⁵
	48	4 of 65 (6%) ⁵
	60	5 of 64 (8%) ⁵
	74	5 of 31 (16%) ¹⁸
Psychological Outcomes	6	111 of 1235 (9%) retired within 1 year of return to work ⁶²
	12	Not RTW: worse disability scores, health status, anxiety, depression, ⁶¹ QOL ²⁵
	29	RTW: higher HRQOL, fewer depression symptoms ⁴⁴
	60	RTW: higher QOL ⁵¹
Lost earnings	12	RTW: lower anxiety, depression scores ⁴⁸
	60	71% accrued lost earnings, mean (SD) US\$26 949 (22 447) (60% of pre-ICU income) ⁴ ; €1482–1513 lower yearly income in non-retired survivors returning to work ⁶²
Change in healthcare coverage	60	77% accrued lost earnings, mean (SD) US\$180 221 (110 285) (55% of pre-ICU income) ⁵
	12	Unemployed/disabled: 14% decline in private insurance, 16% rise in Medicare/Medicaid ⁴
	60	Unemployed/disabled: 33% decline in private insurance, 37% rise in Medicare/Medicaid ⁵

HRQOL, health-related quality of life; ICU, intensive care unit; QOL, quality of life; RTW, return to work.

Table 3 Risk factors for delayed return to work*†

Risk factors	Total number of studies	Studies without any association, n	%		Studies with positive association, n	%
Pre-ICU factors						
Older age	2	1	50		1	50
Sex	3	2	67		1	33
Non-white race	1	1	100		0	0
Lower education	3	1	33		2	67
Divorced	1	1	100		0	0
Chronic non-psychiatric health problems	4	0	0		4	100
Chronic psychiatric problems	1	1	100		0	0
ICU factors						
Non-trauma admission	2	0	0		2	100
Severity of illness	6	3	50		3	50
Longer mechanical ventilation	4	2	50		2	50
Altered level of consciousness	2	1	50		1	50
Dialysis initiation	1	1	100		0	0
Post-ICU factors						
Length of stay	4	2	50		2	50
Discharge to non-home location	3	1	33		2	67
Cognitive impairments	2	1	50		1	50
Functional/physical impairments	4	2	50		2	50
Mental health impairments	5	1	20		4	80
Quality of life impairments	2	0	0		2	100

*Includes all risk factors identified via univariable or multivariable analysis, with $p < 0.05$ denoting significance. Detailed study-by-study findings provided in online supplementary eTable 5.

†Excludes one study (Longo *et al* 2007³⁷) suggesting delayed return to work in patients not receiving activated protein C. ICU, intensive care unit.

of goodwill and trust as perceived barriers to return to work.⁷² Co-ordination with employers, in addition to patient-focused rehabilitation, will be vital to post-ICU programmes aimed at helping survivors return to work.

Strengths of this systematic review include a comprehensive screening strategy that included 41 977 citations and 2754 full texts to help maximise identifying eligible studies. Moreover, we performed meta-regression, along with subgroup and sensitivity analyses, and evaluation of secondary outcomes and factors associated with return to work. Despite these strengths, our review had limitations. First, there was substantial between-study heterogeneity in the meta-analysis that was not eliminated with sensitivity and subgroup analyses. The observational nature of the studies, variable follow-up times and temporal trends may have contributed to this. Population and individual factors may have also contributed, including ICU types, admission diagnoses, pre-existing comorbidities, age, gender, region and pre-ICU occupation. Moreover, the use of non-standardised employment questionnaires with varying definitions of employment and modes of data collection also contributes to heterogeneity. A standardised, detailed data collection research tool for return to work assessment does exist,^{4 5 73 74} which can be used without cost for non-commercial use (see www.improveLTO.com). To address this heterogeneity, we performed a random-effects meta-regression to derive more conservative pooled estimates and excluded studies with non-discrete follow-up time points. Second, due to their cross-sectional, bi-directional nature, the risk factors presented must be interpreted with caution. Future studies

should assist with understanding the temporal nature of these associations. Finally, potentially eligible studies may have been omitted despite a highly sensitive search strategy.

CONCLUSION

This systematic review and meta-analysis demonstrated that delayed return to work is common after critical illness, affecting two-thirds, two-fifths and one-third of previously employed survivors up to 3, 12 and 60 months following hospitalisation. Notably, this meta-analysis was limited by substantial between-study heterogeneity. For survivors who return to work after critical illness, the experience is often accompanied by subsequent job loss, change in occupation and worsening employment status. Potential risk factors for delayed return to work include pre-existing comorbidities along with mental health impairments after critical illness. Future efforts should focus on designing, evaluating and optimising multidisciplinary vocational interventions aimed at helping survivors return to work.

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