www.medscape.com

COMMENTARY

What Happens to Patients After They Leave the ICU

Aaron B. Holley, MD

June 08, 2017

Joblessness and Lost Earnings After ARDS in a 1-Year National Multicenter Study

Kamdar BB, Huang M, Dinglas VD, et al; National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome Network
Am J Respir Crit Care Med. 2017 Apr 27. [Epub ahead of print]

Background

When designing a study in the intensive care unit (ICU) and choosing an outcome of interest, "hard" data points are popular. Think ventilator and ICU days or survival to hospital discharge. None of these are open to interpretation, and all three can be tracked. They're also appealing to ICU physicians who don't see their patients after they leave the unit. We're in the business of survival and recovery. Extubations and ward transfers make us feel like we're doing our job.

But what happens to our patients after they leave the ICU? A new study published online in the *American Journal of Critical Care Medicine* (*AJRCCM*) tracked outcomes at 6 and 12 months post ICU admission for acute respiratory distress syndrome (ARDS).[1] The measures of interest were employment and return to work, along with lost earnings and healthcare coverage. The report was part of the ARDS network (ARDSNet) long-term outcome study (ALTOS) and included data from four different ARDSNet clinical trials. For those unfamiliar, the ARDSNet has published several seminal papers on ARDS management.[2-4]

The Study

Not surprisingly, the socioeconomic burden from ARDS is high. The major findings from the study are as follows:

- Among those previously employed (n=386), 49% and 44% were unemployed at 6 and 12 months, respectively.
- Among those who did return to work after 12 months, 111 (43%) never returned to previous levels (in hours per week), 69 (27%) reported reduced effectiveness, and 62 (24%) ultimately lost their jobs.
- Among survivors who were left unemployed or disabled, there was a shift from private insurance (40% to 30%) to Medicaid/Medicare (33% to 49%).

As a whole, the population was reasonably young. The mean age was 45 (±13) years, and only 14 (4%) were over age 65 years.

Viewpoint

Why is this study important, and what are the takeaways? First, it's part of the growing literature on post ICU ARDS outcomes published by the ARDSNet[5] and others.[6-8] Intensivists need to pay close attention because our day-to-day experiences offer little insight into longer-term, patient-centered outcomes. Information on the post-ICU experience might drive our clinical decision-making and family counseling sessions in new directions. Ignoring it can lead to damaging biases. As a hypothetical example, if neuromuscular blockade improves survival but leads to permanent disabilities and post-ICU posttraumatic stress disorder, we may be less likely to use it.

Second, at 12 months, most ARDS survivors suffer lingering effects from their illness. It's notable that very few of the patients studied were at retirement age (assuming 65 years old is a reasonable estimate), yet the majority was working less or not at all. The insurance burden shifted from private to public. In short, ARDS is an expensive disease with economic effects on the patient and society.

Lastly, socioeconomic data are critical for measuring the impact of disease. The data quantify the true burden to the

patient, which helps hospital systems and policy makers to prioritize the use of limited resources. Data should drive decision-making at the individual physician level as well. We need more data, so the *AJRCCM* paper[1] is a welcome addition to the literature. In summary, the ARDSNet continues to do important work.

Abstract

References

1. Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342:1301-1308. Abstract

2. Yoshida T, Torsani V, Gomes S, et al. Spontaneous effort causes occult pendelluft during mechanical ventilation. Am J Respir Crit Care Med. 2013;188:1420-1427. Abstract

3. Cressoni M, Cadringher P, Chiurazzi C, et al. Lung inhomogeneity in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med. 2014;189:149-158. Abstract

4. Loring SH, Topulos GP, Hubmayr RD. Transpulmonary pressure: the importance of precise definitions and limiting assumptions. Am J Respir Crit Care Med. 2016;194:1452-1457. Abstract

5. Akoumianaki E, Maggiore SM, Valenza F, et al; PLUG Working Group (Acute Respiratory Failure Section of the European Society of Intensive Care Medicine). The application of esophageal pressure measurement in patients with respiratory failure. Am J Respir Crit Care Med. 2014;189:520-531. Abstract

6. Yoshida T, Fujino Y, Amato MB, Kavanagh BP. Fifty years of research in ARDS. Spontaneous breathing during mechanical ventilation. Risks, mechanisms, and management. Am J Respir Crit Care Med. 2017;195:985-992. Abstract

7. Gonzalez M, Arroliga AC, Frutos-Vivar F, et al. Airway pressure release ventilation versus assist-control ventilation: a comparative propensity score and international cohort study. Intensive Care Med. 2010;36:817-827. Abstract

8. Herridge MS, Tansey CM, Matté A, et al; Canadian Critical Care Trials Group. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med. 2011;364:1293-1304. Abstract

Cite this article: What Happens to Patients After They Leave the ICU - *Medscape* - Jun 08, 2017.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

Joblessness and Lost Earnings after ARDS in a 1-Year National Multicenter Study

Biren B. Kamdar, MD, MBA, MHS*[,1], Minxuan Huang, ScM*[,2,3], Victor D. Dinglas, MPH[2,3], Elizabeth Colantuoni, PhD[2,4], Till M. von Wachter, PhD[5], Ramona O. Hopkins, PhD[6,7,8], and Dale M. Needham, FCPA, MD, PhD[2,3,9], with the National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome Network

* Contributed equally as co-first authors

1. Division of Pulmonary and Critical Care Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA
2. Outcomes after Critical Illness and Surgery (OACIS) Group, Johns Hopkins University, Baltimore, MD
3. Division of Pulmonary and Critical Care Medicine, Johns Hopkins University, Baltimore, MD
4. Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
5. Department of Economics, University of California, Los Angeles (UCLA), Los Angeles, CA
6. Department of Medicine, Pulmonary and Critical Care Division, Intermountain Medical Center, Murray, UT
7. Center for Humanizing Critical Care, Intermountain Healthcare, Murray, UT
8. Psychology Department and Neuroscience Center, Brigham Young University, Provo, UT
9. Department of Physical Medicine and Rehabilitation, Johns Hopkins University, Baltimore, MD

Address for correspondence:
Dale M. Needham, FCPA, MD, PhD
Division of Pulmonary and Critical Care Medicine, Johns Hopkins University
1830 E Monument Street, 5th floor, Baltimore, MD, 21205, USA
Tel: 410-955-3467; Email address: dale.needham@jhmi.edu

Author Contributions: MH and BK had full access to all of the data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis. All authors developed the study concept and design. MH and BK conducted the statistical analysis, and all authors have interpreted the data. BK, MH, and DMN drafted the article, and all authors have provided critical revisions for important intellectual content. This study was supervised by DMN. All authors have read and approved the final article.

Funding/Support: Dr. Kamdar is currently supported by a Career Development Award from the UCLA Clinical and Translational Science Institute (CTSI) (NIH-National Center for Advancing Translational Science (NCATS) UCLA UL1TR000124 & UL1TR001881). National Heart, Lung and Blood Institute funded this follow-up study (N01HR56170, R01HL091760 and 3R01HL091760-02S1) and the ARDS Network trials (contracts HHSN268200536165C to HHSN268200536176C and HHSN268200536179C).

Running head (50 characters max): Joblessness and Lost Earnings After ARDS

Subject category: 4.06 ICU Management/Outcome; 4.02 ALI/ARDS: Diagnosis and Clinical Issues

Word count (excluding abstract, references, acknowledgement, and legends)**:** 3,130

At a Glance Commentary

Scientific Knowledge on the Subject: Survivors of acute respiratory distress syndrome (ARDS) commonly experience joblessness. However, there are little data regarding the timing of return to work after ARDS, and associated risk factors, lost earnings, and changes in healthcare coverage.

What This Study Adds to the Field: Of 386 previously-employed ARDS patients, 379 (98%) survived to 12-month follow-up, with 166 (44%) of these survivors jobless at 12-months. Accounting for competing risks of death and retirement, half of enrolled and previously-employed survivors returned to work by 13 weeks after hospital discharge, with 68% ever returning to work by 12 months. Factors associated with delayed return to work were longer hospitalization and older age among non-white survivors. Over 12-month follow-up, 274 (71%) non-retired survivors accrued lost earnings, averaging nearly $27,000, or 60% of pre-ARDS annual earnings, with jobless, non-retired survivors experiencing a large shift from private health insurance to government-funded healthcare coverage.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

ABSTRACT

Rationale: Following acute respiratory distress syndrome (ARDS), joblessness is common, but poorly understood.

Objectives: To evaluate the timing of return to work following ARDS, and associated risk factors, lost earnings, and changes in healthcare coverage

Methods: Over 12-month longitudinal follow-up, ARDS survivors from 43 U.S. ARDSNet hospitals provided employment and healthcare coverage data via structured telephone interviews. Factors associated with the timing of return to work were assessed using Fine and Gray regression analysis. Lost earnings were estimated using Bureau of Labor Statistics data.

Measurements and Main Results: Of 922 consenting survivors, 386(42%) were employed prior to ARDS (56% male; mean±SD age: 45±13 years), with 7 dying by 12-month follow-up. Of 379 previously-employed 12-month survivors, 166(44%) were jobless at 12-month follow-up. Accounting for competing risks of death and retirement, half of enrolled and previously-employed survivors returned to work by 13 weeks after hospital discharge, with 68% ever returning by 12 months. Delays in return to work were associated with longer hospitalization and older age among non-white survivors. Over 12-month follow-up, 274(71%) survivors accrued lost earnings, averaging $26,949±$22,447 (60% of pre-ARDS annual earnings). Jobless survivors experienced a 14% (95%CI 5%-22%, p=0.002) absolute decrease in private health insurance (from 44% pre-ARDS) and a 16% (95%CI 7%-24%, p<0.001) absolute increase in Medicare and Medicaid (from 33%).

Conclusions: At 12 months after ARDS, nearly one-half of previously-employed survivors were jobless. Post-ARDS joblessness is associated with readily identifiable patient and hospital variables, and accompanied by substantial lost earnings and a shift toward government-funded healthcare coverage.

Word Count: 250

Keywords: Employment; Intensive Care Unit; Income; Health Insurance

INTRODUCTION

Survivors of acute respiratory distress syndrome (ARDS) frequently experience long-term physical, cognitive and mental health impairments after discharge from the intensive care unit (ICU) (1-7). Such impairments contribute to joblessness, with only half of ARDS survivors employed one year later (2, 8), which can have an important economic impact on patients, families, employers, and society (9).

To date, no study has performed a longitudinal evaluation of joblessness following ARDS, including evaluation of associated lost earnings and shifts in healthcare coverage. Such research is needed to help inform survivors and their families, identify at-risk populations, and tailor interventions to prevent joblessness after ARDS. Additionally, these data are important to more completely understand the economic impact of ARDS. Hence, via a national, multicenter prospective study of ARDS survivors over 12-month follow-up, this research aimed to evaluate [1] employment status and joblessness after ARDS, [2] patient- and hospital-related factors associated with the timing of return to work, [3] estimated lost earnings, and [4] changes in healthcare coverage.

METHODS

Study Population

This evaluation was conducted as part of the ARDS Network (ARDSNet) Long-Term Outcome Study (ALTOS), a national multicenter prospective study longitudinally evaluating survivors 6 and 12 months after ARDS. ALTOS participants were enrolled from four recent ARDSNet clinical trials evaluating ICU-based therapies for ARDS (10-

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

13). Between 2006 and late 2014, patients were enrolled from 43 ARDSNet hospitals within 48 hours of ARDS onset and 72 hours of initiation of mechanical ventilation, and followed for 12 months thereafter. ARDSNet exclusion criteria have been described previously, and include pre-existing severe malnutrition, lung, liver, or neuromuscular diseases; or limitations in life support at time of study eligibility (10-13). Participants were further excluded from longitudinal follow-up in ALTOS if they were <18 years old, non-English speaking, homeless or had potential cognitive impairment prior to admission (as per review of medical records or patient/proxy report). The study was approved by the institutional review boards at all participating hospitals. Informed consent was obtained from the patient or a proxy when the patient was incapable of consent.

Baseline Patient- and Critical Illness-Related Exposure Variables

Baseline patient-related exposure variables included age, gender, race, body mass index, and pre-existing comorbidity (specifically, diabetes mellitus, cardiovascular disease, chronic pulmonary disease, and alcohol misuse). Alcohol misuse was defined by zones 3 and 4 from the Alcohol Use Disorders Identification Test (AUDIT), indicating alcohol consumption exceeding recommended limits (14). Hospital-related exposures were grouped into 3 categories: [1] baseline intensive care data: admission to a medical (vs. surgical) ICU, Acute Physiology and Chronic Health Evaluation (APACHE) III score, and ARDS risk factor of sepsis (vs. non-sepsis); [2] daily ICU data: organ failure status (maximum organ failure score, derived from the daily Brussels organ failure score for cardiovascular, pulmonary, coagulation, renal, and hepatic systems (15)), and average daily PaO_2/FiO_2 ratio; [3] other ICU data: duration of mechanical ventilation, ICU and

hospital length of stay, and discharge location (home with unassisted breathing vs. other).

Measures of Employment and Return to Work

Data were collected at 6- and 12-month follow-up, via structured interviews using a self-report employment instrument that was similar to prior research (16). Data collection included current employment status (e.g., full-time, part-time, unemployed, disabled, retired, or paid sick leave), type of residence, hours working per week, timing of return to work (reported as weeks to return to work after hospital discharge), perceived effectiveness at work (0 to 100% scale), and major change in occupation (defined as a change in United States Bureau of Labor Statistics occupational profile [www.bls.gov/oes/current/oes_stru.htm]). Employment status prior to ARDS was collected retrospectively during follow-up interview. Data were obtained from patients (94% of assessments) or from proxies when patients were unable to complete the interview (6%), via telephone (98%) or in-person or mail (2%).

Estimated Lost Earnings and Healthcare Coverage

Lost earnings, evaluated as a measure of lost work capacity, were estimated for all survivors who were employed prior to ARDS. In the primary analysis (described below) and *post-hoc* sensitivity analyses (see below and Online Data Supplement), estimated lost earnings after ARDS were defined as the difference between estimated and potential earnings. In the primary analysis, estimated earnings were calculated for each survivor using age- and sex-matched weekly wage data from the US Bureau of Labor Statistics (www.bls.gov), as done in prior research (17). Next, BLS.gov weekly wages were divided by 40 hours per week to determine hourly wages, and

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

subsequently multiplied by patient-reported hours working per week. Similarly, estimated potential earnings were calculated by multiplying estimated hourly wages by the number of hours working prior to hospitalization. All weekly wages were multiplied by 50 weeks to derive annual estimates. Patients reporting unemployment or disability status were assumed to incur lost earnings, while those who were retired or dead were assumed to incur no lost earnings. All earnings data were scaled to 2016 US dollars using the US consumer price index (www.bls.gov/cpi). In *post-hoc* sensitivity analyses, different methods were used to calculate lost wages, including imputing wages based on sex and self-reported occupation; considering full- and part-time employment as 40 and 20 hours per week, respectively; and excluding survivors who were retired and/or ≥65 years of age (see details in Online Data Supplement).

Healthcare coverage data were collected as part of the structured interviews at 6- and 12-month follow-up, with pre-hospitalization data collected during the follow-up interview. Healthcare coverage was categorized into private insurance, Medicaid, Medicare (which included dually-eligible Medicare and Medicaid beneficiaries, for which Medicare is the primary payer (18)), and no coverage. For patients <65 years old surviving to 12-month follow-up and reporting healthcare coverage data, changes in healthcare coverage from pre-hospitalization to 12-month follow-up were computed using a multinomial logistic regression model with the main effect of time and a robust variance estimate for patient level-clustering of healthcare coverage status.

Quality of Life

Six and 12 months after ARDS, survivors' health-related quality of life status was evaluated using the EQ-5D and Medical Outcomes Study Short-Form 36 version 2 (SF-36).

Statistical Analysis

We used survival analysis methods to evaluate the primary outcome of the timing of return to work after hospital discharge among patients who were employed prior to ARDS. Prior to returning to work, patients may experience one of two competing risks: retirement or death. Patients who neither returned to work nor experienced either competing risk were censored at 52 weeks. With retirement and death treated as competing risks, the timing of returning to work was explored using cumulative incidence functions, including stratification by age and race (19); additionally, Fine and Gray regression models were used to evaluate the association of baseline patient- and hospital-related exposure variables with return to work, with hazard ratios <1 indicating longer time to return to work (20). Separate bivariable regression models evaluated the association of each exposure variable (individual independent variables) with the timing of return to work (dependent variable), and all exposure variables with a bivariable association of $p<0.20$ were included in the multivariable regression model. Pairwise statistical interactions were assessed in the multivariable model for pre-selected demographic (age, sex, race, BMI) and ICU (cardiovascular disease, diabetes, APACHE III score, hospital length of stay) variables. A significant statistical interaction was noted between age and race, and therefore included in the final multivariable model. *Post-hoc* sensitivity analyses were performed to evaluate for potential effects of age-related changes in employment, and to evaluate a full multivariable model that

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

included all exposure variables, rather than variable selection based on bivariable associations (Online Data Supplement).

The linearity of each exposure variable was confirmed using locally weighted scatterplot smoothing (LOWESS) of Martingale residuals from the regression models. A Schoenfeld residual plot for each variable confirmed no violation of the proportional hazards assumption (21). Multicollinearity was assessed using variance inflation factors (VIF), with multicollinearity (defined as VIF ≥10) demonstrated between mechanical ventilation duration, ICU length of stay, and hospital length of stay, with the latter variable retained in the final model.

A two-sided $p<0.05$ denoted statistical significance. All statistical analyses were performed using STATA 13.1 (College Station, TX).

RESULTS

Patient characteristics and employment status

Among 922 survivors who consented for follow-up, 386 (42%) reported full- or part-time employment before ARDS (Figure 1). These 386 enrolled and previously-employed survivors were 44% female, and 82% white, with a mean±SD age of 45±13 years and APACHE III score of 83±26 (Table 1). Fourteen (4%) of these survivors were ≧65 years old. A total of 299 (77%) had sepsis as an ARDS risk factor. These enrolled and previously-employed survivors had a mean duration of mechanical ventilation of 11±10 days and hospital length of stay (LOS) of 22±16 days. As compared to survivors who were not employed before ARDS, previously-employed survivors were younger,

predominantly male, and had fewer baseline comorbidities, with similar values across their ICU variables.

Return to Work after ARDS

Among previously-employed surviving patients at 6- and 12-month follow-up, 189 of 386 (49%) and 166 of 379 (44%), respectively, were jobless (Figure 1). Accounting for competing risks of death and retirement, half of enrolled and previously-employed survivors returned to work by 13 weeks after hospital discharge, with 68% ever returning by 12 months. When stratified by age (at the median: 48 years) and race (non-white vs. white), the 12-month cumulative incidence of returning to work was 76% and 32% among non-white survivors <48 and ≥48 years old, respectively, and 79% and 64% for white survivors <48 and ≥48 years old (Figure 2). Among the 257 eligible and previously-employed survivors ever returning to work, 111 (43%) never returned to their previous hours worked, 69 (27%) reported reduced effectiveness at work (mean±SD self-reported effectiveness score: 77%±22%), and 62 (24%) subsequently lost their jobs during 12-month follow-up. Finally, of these 257 survivors, 62 of 215 (29%) previously full-time workers and 17 of 42 (40%) previously part-time workers experienced a major occupation change. Those surviving workers with vs. without a major occupation change worked fewer hours per week after ARDS (31 of 59 [53%] vs. 51 of 127 [40%], p=0.11) at 12-month follow-up.

Among the 166 survivors who were jobless 12 months after ARDS, 72 (43%) were unemployed, 76 (46%) receiving disability, 3 (2%) on paid sick leave, and 15 (9%) retired. The majority of these survivors (98%) were living at home, while 3 (2%) were hospitalized and 1 (1%) at a nursing home. Of 72 unemployed survivors, 41 (57%) were

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

unable to work due to other health-related issues, while 16 (22%) were actively looking for work, 5 (7%) laid-off, 6 (8%) in school, 2 (3%) were in a healthcare facility, and 2 (3%) homemakers.

In the multivariable Fine and Gray regression model, longer hospital length of stay was associated with longer time to return to work (hazard ratio [HR] 0.81 per week [95% confidence interval (CI), 0.74-0.88]; P<0.001) (Table 2). Older non-white survivors also were estimated to have a longer time to return to work (hazard ratio [HR], 0.68 per 10-year increase [95% confidence interval (CI), 0.54-0.84]; P=0.001), whereas, among white survivors, age was not significantly associated with return to work (HR 0.91 [95% CI, 0.81-1.02]; P=0.114). In all *post-hoc* sensitivity analyses, there were no important differences in results (Tables E1-E3 in Online Data Supplement).

Estimated Lost Earnings after ARDS

Over 12-month follow-up, 274 (71%) of non-retired survivors accrued lost earnings, totaling an estimated $7,384,062 and averaging $26,949±22,447, representing 60% of their estimated pre-ARDS annual income ($44,784). When averaged across all previously-employed ARDS survivors (N = 386), mean estimated lost earnings totaled $19,130±22,522. All *post-hoc* sensitivity analyses demonstrated results similar to the primary analysis (Online Data Supplement).

Healthcare Coverage after ARDS

Among survivors who were unemployed or disabled, there was a marked decline in private health insurance (44% to 30%; difference = -14%, 95% CI -22% to -5%, p=0.002) and a concomitant rise in Medicare and Medicaid (33% to 49%, difference = 16%, 95% CI 7% to 24%, p<0.001) coverage, with little change in those with no

healthcare coverage (23% to 21%, difference = -2%, 95% CI -10% to 7%, p=0.67) (Figure 3). Conversely, previously employed survivors who were working exhibited little change from pre-ARDS baseline in private health insurance (78% to 79%, difference = 1%, 95% CI -3% to 6%, p=0.59), Medicare and Medicaid (10% to 12%, difference = 2%, 95% CI -3% to 7%, p=0.41), and no coverage (12% to 9%, difference = -3%, 95% CI -8% to 1%, p=0.16).

Quality of Life

Survivors who never vs. ever returned to work by 6- or 12-month follow-up consistently reported worse health-related quality of life (Table E4, Online Data Supplement).

DISCUSSION

In this multicenter, prospective longitudinal study of 386 ARDS survivors employed prior to hospitalization, nearly one-half were jobless at 12-month follow-up, and among those who returned to work, one-fourth became jobless during the follow-up period. Older, non-white survivors, and those experiencing longer hospitalization experienced significantly greater delays in return to work. Additionally, 71% of previously-employed, non-retired survivors incurred lost earnings, averaging nearly $27,000 in lost earnings over 12 months, representing nearly two-thirds of their pre-ARDS annual income. Moreover, jobless, non-retired survivors experienced a marked shift from private to government-funded healthcare coverage.

In our multi-center national study, 42% (386 of 922) of survivors were employed prior to hospitalization, similar to a prior single-center U.S. ARDS study (54%) (22) and consistent with the 23-58% employment rates reported in other U.S. ICU survivor

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

studies (23-28). We found that 68% of enrolled, previously-employed, and non-retired survivors returned to work within 12 months of ARDS, which was higher than the 48-56% reported in 2 smaller (N=82 and 27) single-center North American ARDS studies (8, 29) and the 49-58% reported in international studies (N=67 to 363) involving ICU survivors without ARDS (28, 30-32). These differences may be due to a national, multicenter design, a relatively young mean age (49 years old), and patient recruitment as part of trials with multiple exclusion criteria.

Notably, of the ARDS survivors who returned to work (N=257), 43% (n=111) never returned to their previous hours worked, 31% (n=79) experienced a major occupation change, 27% (n=69) reported reduced effectiveness at work, and 24% (n=62) subsequently lost their jobs, demonstrating that return to work after ARDS may fall short of previous levels or be short-lived. Among previously employed survivors not returning to work during 12-month follow-up, 58% were receiving disability, suggesting functional impairments as a contributor to unemployment. Prior post-ARDS research has suggested that impairments in memory and attention may contribute to delayed return to work (33), with survivors also reporting that fatigue and weakness (34) contributed to joblessness. Additionally, depressive symptoms have been associated with unemployment 2 years after ARDS (35). Conversely, a recent study demonstrated no independent association of cognitive and physical function with 12-month post-ICU employment status in critical illness survivors (28). Notably, we found that survivors who never returned to work by 6 and 12 months reported worse quality of life, although the directionality of this cross-sectional association is unknown. Additional longitudinal

studies are needed to explore the associations of post-ICU impairments with return to work and impact on quality of life.

Additionally, we demonstrated that white patients of different ages had similar timing of return to work, while older (vs. younger) non-white patients experienced longer delays in returning to work. The reason for this racial difference is unclear, but may be due to differences in type of work (i.e., office vs. manual work), socioeconomic status and/or access to rehabilitation services. Additionally, longer hospital length of stay was associated with delayed return to work, regardless of age and race, potentially due to worse physical impairments occurring with longer hospitalization (36, 37). Future studies should evaluate the efficacy and cost-effectiveness of targeting occupational rehabilitation interventions toward these at-risk patient groups to reduce delays in returning to work after ARDS.

To our knowledge, this analysis was the first to evaluate lost earnings and changes in healthcare coverage after ARDS. We demonstrated that 71% of non-retired survivors accrued lost earnings over 12-month follow-up, averaging $26,949 – representing nearly two-thirds of estimated pre-ARDS annual earnings. These lost earnings totals were substantial, and comparable to traumatic brain injury and stroke (38, 39). Additionally, over 12 months, jobless, non-retired survivors experienced a substantial decline in private insurance and rise in government-funded healthcare coverage, an important finding given the substantial healthcare utilization of ARDS survivors (40, 41).

Strengths of this study include its national, multicenter longitudinal design, relatively large sample size, high participant retention rate (>94%), and evaluation of

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

patient- and hospital-related risk factors, estimated lost earnings and shifts in healthcare coverage. However, this study has potential limitations. First, similar to most studies in the field (42), employment status was determined via self-report. However, sensitivity analyses did not materially change the primary results; nonetheless, the true magnitude of any measurement error if not known. Second, lost earnings were calculated based on estimated, rather than actual, earnings. However, our analysis was conducted using a national ARDS survivor cohort, estimating lost earnings using age- and sex-matched Bureau of Labor Statistics data. Hence, these results may be more nationally representative; thus, enhancing generalizability. Additionally, since we focused on earnings as a measure of lost work capacity, our calculation did not account for disability benefits and other sources of disposable income (i.e., personal or retirement savings) which may have offset the financial hardship created by lost earnings (43). Moreover, we did not consider lost earnings while patients were hospitalized, lost earnings accrued by informal caregivers, costs of ongoing medical care, and other economic and non-economic issues associated with patient and informal caregiver joblessness (44). Third, there may be other important variables, not included in this study, which may be associated with joblessness after ARDS, including baseline physical and cognitive function and potential ICU-related variables (e.g., delirium), along with expected declines in employment potential with age. However, a sensitivity analysis adjusting for advancing age did not change our overall results, and in a recent study, neither baseline neurocognitive function nor delirium in the ICU was associated with 12-month employment status (28). Further studies are needed to evaluate the association of post-discharge factors and post-ARDS employment. Fourth, our study

population included relatively young ARDS survivors and findings may not generalize to all ICU populations. However, enrollment from 43 sites and comparability of results with prior literature help support generalizability. Finally, as an observational cohort study, we could not assess the causality of ARDS with joblessness.

In conclusion, in this multicenter longitudinal study, we found that nearly one-half of previously-employed survivors were jobless at 12-month post-ARDS follow-up, with older, non-white survivors and those with longer a hospital stay having a greater risk of delayed return to work. Jobless, non-retired survivors also accrued substantial lost earnings, amounting to two-thirds of their pre-ARDS earnings, and experienced a substantial decline in private healthcare coverage and rise in Medicare and Medicaid. These findings highlight the major economic consequences of joblessness after ARDS and identify at-risk groups for future evaluation of occupational rehabilitation interventions.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

ACKNOWLEDGEMENTS

We thank all of the patients and their proxies who participated in this study. We thank Caroline Chessare, Mardee Merrill, Mariela Pinedo, Kyle Schneck, Stacey Schoonmaker, Kristin Sepulveda, Marcella Shrout, Cassie Wicken, Melissa McCullough, Jonathan Gellar, Elizabeth Vayda, Gita Byraiah, Laura Methvin, Vanessa Stan, Shirani Rajan, Cassie Wicken, Meg Shanahan, Elizabeth Baer, and Anita Chandra who assisted with data collection; and Lin Chen, William Flickinger, Christopher Mayhew, and Bharat Kamdar who assisted with data management. We also thank Akshay S. Desai, MD, MPH, and Jennifer L. Martin, PhD for their thoughtful review of a draft of the manuscript.

Investigators and research staff from National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network sites that participated in this follow-up study: University of Washington, Harborview (*L. Hudson, S. Gundel, C. Hough, M. Neff, K. Sims, A. Ungar, T. Watkins); Baystate Medical Center (*J. Steingrub, M. Tidswell, E. Braden, L. DeSouza, C. Kardos, L. Kozikowski, S. Ouellette); Baylor College of Medicine (K. Guntupalli, V. Bandi, C. Pope, C. Ross); Johns Hopkins University (*R. Brower, H. Fessler, D. Hager, P. Mendez-Tellez, D. Needham, K. Oakjones); Johns Hopkins Bayview Medical Center (J. Sevransky, A. Workneh); University of Maryland (C. Shanholtz, D. Herr, H. Howes, G. Netzer, P. Rock, A. Sampaio, J. Titus); Union Memorial Hospital (P. Sloane, T. Beck, D. Highfield, S. King); Washington Hospital Center (B. Lee, N. Bolouri); Cleveland Clinic Foundation (*H.P. Wiedemann, R.W. Ashton, D.A. Culver, T. Frederick, J.A. Guzman, J.J. Komara Jr, A.J. Reddy); University Hospitals of Cleveland (R. Hejal, M. Andrews, D. Haney); MetroHealth Medical Center (A.F. Connors, S. Lasalvia, J.D. Thornton, E.L. Warren); University of Colorado Hospital, Aurora (*M. Moss, E.L. Burnham, L. Gray, J. Maloney, M. Mealer); Denver Health Medical Center (I. Douglas, K. Overdier, K. Thompson, R. Wolken); Rose Medical Center (S. Frankel, J. McKeehan); Swedish Medical Center (M.L. Warner); Saint Anthony's Hospital (T. Bost, C. Higgins, K. Hodgin); Duke University (*N. MacIntyre, L. Brown, C. Cox, M. Gentile, J. Govert, N. Knudsen); University of North Carolina (S. Carson, L. Chang, S. Choudhury, W. Hall, J. Lanier); Vanderbilt University (*A.P. Wheeler, G.R. Bernard, M. Hays, S. Mogan, T.W. Rice); Wake Forest University (*R.D. Hite, A. Harvey, P.E. Morris, Mary Ragusky); Moses Cone Memorial Hospital (P. Wright, S. Groce, J. McLean, A. Overton); University of Virginia (J. Truwit, K. Enfield, M. Marshall); Intermountain Medical Center (*A. Morris, *C. Grissom, A. Austin, S. Barney, S. Brown, J. Ferguson, H. Gallo, T. Graydon, E. Hirshberg, A. Jephson, N. Kumar, M. Lanspa, R. Miller, D. Murphy, J. Orme, A. Stowe, L. Struck, F. Thomas, D. Ward,); LDS Hospital (P. Bailey, W. Beninati, L. Bezdjian, T. Clemmer, S. Rimkus, R. Tanaka, L. Weaver); McKay Dee Hospital (C. Lawton, D. Hanselman); Utah Valley Regional Medical Center (K. Sundar, W. Alward, C. Bishop, D. Eckley, D. Harris, T. Hill, B. Jensen, K. Ludwig, D. Nielsen, M. Pearce); University of California, San Francisco (*M.A. Matthay, C. Calfee, B. Daniel, M. Eisner, O. Garcia, K. Kordesch, K. Liu, N. Shum, H. Zhou); University of California, San Francisco, Fresno (M.W. Peterson, J. Blaauw, K. Van Gundy); San Francisco General Hospital (R. Kallet, E. Johnson); University of California, Davis (T. Albertson, B. Morrissey, E. Vlastelin);

Louisiana State University Health Sciences Center-New Orleans (*B. deBoisblanc, A. Antoine, D. Charbonnet, J. Hunt, P. Lauto, A. Marr, G. Meyaski, C. Romaine); Earl K. Long Medical Center (S. Brierre, J. Byrne, T. Jagneaux, C. LeBlanc, K. Moreau, C. Thomas); Ochsner Clinic Foundation (S. Jain, D. Taylor, L. Seoane); Our Lady of the Lake Medical Center (C. Hebert, J. Thompson); Tulane Medical Center (F. Simeone, J. Fearon). **Clinical Coordinating Center:** Massachusetts General Hospital and Harvard Medical School (*D. Schoenfeld, N. Dong, M. Guha, E. Hammond, P. Lazar, R. Morse, C. Oldmixon, N. Ringwood, E. Smoot, B.T. Thompson, R. Wilson). **National Heart, Lung and Blood Institute:** A. Harabin, S. Bredow, M. Waclawiw, G. Weinmann. **Data and Safety Monitoring Board:** R. G. Spragg (chair), A. Slutsky, M. Levy, B. Markovitz, E. Petkova, C. Weijer. **Protocol Review Committee:** J. Sznajder (chair), M. Begg, L. Gilbert-McClain E. Israel, J. Lewis, S. McClave, P. Parsons.

*Principal investigator.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

References

1. Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Diaz-Granados N, Al-Saidi F, Cooper AB, Guest CB, Mazer CD, Mehta S, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. *N Engl J Med* 2003;348:683-693.
2. Herridge MS, Tansey CM, Matte A, Tomlinson G, Diaz-Granados N, Cooper A, Guest CB, Mazer CD, Mehta S, Stewart TE, et al. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med* 2011;364:1293-1304.
3. Desai SV, Law TJ, Needham DM. Long-term complications of critical care. *Crit Care Med* 2011;39:371-379.
4. Hopkins RO, Weaver LK, Collingridge D, Parkinson RB, Chan KJ, Orme JF, Jr. Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2005;171:340-347.
5. Huang M, Parker AM, Bienvenu OJ, Dinglas VD, Colantuoni E, Hopkins RO, Needham DM, National Institutes of Health NHL, Blood Institute Acute Respiratory Distress Syndrome N. Psychiatric Symptoms in Acute Respiratory Distress Syndrome Survivors: A 1-Year National Multicenter Study. *Crit Care Med* 2016;44:954-965.
6. Needham DM, Dinglas VD, Morris PE, Jackson JC, Hough CL, Mendez-Tellez PA, Wozniak AW, Colantuoni E, Ely EW, Rice TW, et al. Physical and Cognitive Performance of Patients with Acute Lung Injury 1 Year after Initial Trophic versus Full Enteral Feeding. EDEN Trial Follow-up. *Am J Respir Crit Care Med* 2013;188:567-576.
7. Fan E, Dowdy DW, Colantuoni E, Mendez-Tellez PA, Sevransky JE, Shanholtz C, Himmelfarb CR, Desai SV, Ciesla N, Herridge MS, et al. Physical complications in acute lung injury survivors: a two-year longitudinal prospective study. *Crit Care Med* 2014;42:849-859.
8. 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;150:90-94.

9. Coopersmith CM, Wunsch H, Fink MP, Linde-Zwirble WT, Olsen KM, Sommers MS, Anand KJ, Tchorz KM, Angus DC, Deutschman CS. A comparison of critical care research funding and the financial burden of critical illness in the United States. *Crit Care Med* 2012;40:1072-1079.
10. Matthay MA, Brower RG, Carson S, Douglas IS, Eisner M, Hite D, Holets S, Kallet RH, Liu KD, MacIntyre N, et al. Randomized, placebo-controlled clinical trial of an aerosolized beta(2)-agonist for treatment of acute lung injury. *Am J Respir Crit Care Med* 2011;184:561-568.
11. Rice TW, Wheeler AP, Thompson BT, Steingrub J, Hite RD, Moss M, Morris A, Dong N, Rock P. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. *JAMA* 2012;307:795-803.
12. Rice TW, Wheeler AP, Thompson BT, deBoisblanc BP, Steingrub J, Rock P. Enteral omega-3 fatty acid, gamma-linolenic acid, and antioxidant supplementation in acute lung injury. *JAMA* 2011;306:1574-1581.
13. The Acute Respiratory Distress Syndrome Network. Rosuvastatin for sepsis-associated acute respiratory distress syndrome. *N Engl J Med* 2014;370:2191-2200.
14. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. AUDIT: the Alcohol Use Disorder Identification Test: Guidelines for Use in Primary Care. Second Edition. Geneva: World Health Organization; 2001.
15. Bernard GR. The Brussels Score. *Sepsis* 1997;1:43-44.
16. Radford K, Phillips J, Drummond A, Sach T, Walker M, Tyerman A, Haboubi N, Jones T. Return to work after traumatic brain injury: cohort comparison and economic evaluation. *Brain Inj* 2013;27:507-520.
17. Corso P, Finkelstein E, Miller T, Fiebelkorn I, Zaloshnja E. Incidence and lifetime costs of injuries in the United States. *Inj Prev* 2006;12:212-218.
18. Data book: beneficiaries dually eligible for Medicare and Medicaid. [Web page] May 2016]. Available from: http://medpac.gov/documents/publications/january-2016-medpac-and-macpac-data-book-beneficiaries-dually-eligible-for-medicare-and-medicaid.pdf.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

19. Geskus RB. Cause-specific cumulative incidence estimation and the fine and gray model under both left truncation and right censoring. *Biometrics* 2011;67:39-49.
20. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc* 1999;94:496-509.
21. Schoenfeld D. Partial residuals for the proportional hazards regression model. *Biometrika* 1982;69:239-241.
22. Weinert CR, Gross CR, Kangas JR, Bury CL, Marinelli WA. Health-related quality of life after acute lung injury. *Am J Resp Crit Care Med* 1997;156:1120.
23. Parno JR, Teres D, Lemeshow S, Brown RB, Avrunin JS. Two-year outcome of adult intensive care patients. *Med Care* 1984;22:167-176.
24. Goldstein RL, Campion EW, Thibault GE, Mulley AG, Skinner E. Functional outcomes following medical intensive care. *Crit Care Med* 1986;14:783-788.
25. 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.
26. Fakhry SM, Kercher KW, Rutledge R. Survival, quality of life, and charges in critically III surgical patients requiring prolonged ICU stays. *J Trauma* 1996;41:999-1007.
27. 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;121:549-558.
28. Norman BC, Jackson JC, Graves JA, Girard TD, Pandharipande PP, Brummel NE, Wang L, Thompson JL, Chandrasekhar R, Ely EW. 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;44:2003-2009.
29. Herridge MS, Tansey CM, Matte A, Tomlinson G, Diaz-Granados N, Cooper A, Guest CB, Mazer CD, Mehta S, Stewart TE, et al. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med* 2011;364:1293-1304.
30. Cuthbertson BH, Scott J, Strachan M, Kilonzo M, Vale L. Quality of life before and after intensive care. *Anaesthesia* 2005;60:332-339.

31. McGee HM, Doyle F, Conroy RM, De La Harpe D, Shelley E. Impact of briefly-assessed depression on secondary prevention outcomes after acute coronary syndrome: a one-year longitudinal survey. *BMC Health Serv Res* 2006;6:9.
32. 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;38:1554-1561.
33. Rothenhausler HB, Ehrentraut S, Stoll C, Schelling G, Kapfhammer HP. The relationship between cognitive performance and employment and health status in long-term survivors of the acute respiratory distress syndrome: results of an exploratory study. *Gen Hosp Psychiatry* 2001;23:90-96.
34. Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Diaz-Granados N, Al Saidi F, Cooper AB, Guest CB, Mazer CD, Mehta S, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. *N Engl J Med* 2003;348:683-693.
35. Adhikari NK, McAndrews MP, Tansey CM, Matte A, Pinto R, Cheung AM, Diaz-Granados N, Barr A, Herridge MS. Self-reported symptoms of depression and memory dysfunction in survivors of ARDS. *Chest* 2009;135:678-687.
36. Fan E, Dowdy DW, Colantuoni E, Mendez-Tellez PA, Sevransky JE, Shanholtz C, Himmelfarb CR, Desai SV, Ciesla N, Herridge MS, et al. Physical complications in acute lung injury survivors: a two-year longitudinal prospective study. *Crit Care Med* 2014;42:849-859.
37. Needham DM, Wozniak AW, Hough CL, Morris PE, Dinglas VD, Jackson JC, Mendez-Tellez PA, Shanholtz C, Ely EW, Colantuoni E, et al. Risk factors for physical impairment after acute lung injury in a national, multicenter study. *Am J Respir Crit Care Med* 2014;189:1214-1224.
38. Johnstone B, Mount D, Schopp LH. Financial and vocational outcomes 1 year after traumatic brain injury. *Arch Phys Med Rehabil* 2003;84:238-241.
39. Taylor TN, Davis PH, Torner JC, Holmes J, Meyer JW, Jacobson MF. Lifetime cost of stroke in the United States. *Stroke* 1996;27:1459-1466.
40. Ruhl AP, Lord RK, Panek JA, Colantuoni E, Sepulveda KA, Chong A, Dinglas VD, Shanholtz CB, Pronovost PJ, Steinwachs DM, et al. Health care resource use

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

and costs of two-year survivors of acute lung injury. An observational cohort study. *Ann Am Thorac Soc* 2015;12:392-401.

41. Ruhl AP, Huang M, Colantuoni E, Lord RK, Dinglas VD, Chong A, Sepulveda KA, Mendez-Tellez PA, Shanholtz CB, Steinwachs DM, et al. Healthcare Resource Use and Costs in Long-Term Survivors of Acute Respiratory Distress Syndrome: A 5-Year Longitudinal Cohort Study. *Crit Care Med* 2017;45:196-204.
42. Dupont J, Sollberger PA, Organisation for Economic Co-operation and Development. Productivity measurement and analysis. Paris: OECD; 2008.
43. Dobkin C, Finkelstein A, Kluender R, Notowidigdo MJ. The economic consequences of hospital admissions: National Bureau of Economic Research; 2016.
44. Cameron JI, Chu LM, Matte A, Tomlinson G, Chan L, Thomas C, Friedrich JO, Mehta S, Lamontagne F, Levasseur M, et al. One-Year Outcomes in Caregivers of Critically Ill Patients. *N Engl J Med* 2016;374:1831-1841.

Table 1. Baseline and intensive care data by return to work status by 12 months after ARDS

Variable[a]	Not employed before ARDS (n=439)	Employed before ARDS (n=386)				
		Total (n=386)	Ever returned to work (n=257)	Never returned to work (n=105)	Retired or Died (n=14)	Missing data (n=10)[b]
Baseline patient data						
Age, mean (SD) year	54 (15)	45 (13)	43 (13)	48 (12)	56 (11)	48 (12)
Age ≥65 years old, N (%)	111 (25)	14 (4)	7 (3)	4 (4)	3 (21)	0 (0)
Female, N (%)	257 (59)	171 (44)	102 (40)	56 (53)	9 (64)	4 (40)
White, N (%)	353 (82)	308 (82)	215 (85)	75 (77)	11 (79)	7 (78)
BMI, mean (SD) kg/m^2	31 (9)	30 (8)	30 (7)	31 (8)	32 (7)	33 (9)
Cardiovascular disease, N (%)[c]	230 (52)	148 (38)	88 (34)	45 (43)	9 (64)	6 (60)
Diabetes, N (%)	127 (29)	67 (17)	35 (14)	27 (26)	1 (7)	4 (40)
Chronic pulmonary disease, N (%)[c]	72 (16)	28 (7)	17 (7)	8 (8)	1 (7)	2 (20)
Alcohol misuse, N (%)[c]	78 (20)	81 (23)	53 (22)	23 (23)	2 (14)	3 (33)
Baseline intensive care data						
Admission to medical ICU, N (%)	274 (62)	206 (53)	136 (53)	58 (55)	7 (50)	5 (50)
APACHE III, mean (SD)	88 (26)	83 (26)	82 (26)	86 (26)	85 (35)	86 (32)
Sepsis as ARDS risk factor, N (%)	357 (81)	299 (77)	194 (75)	84 (80)	13 (93)	8 (80)
Daily intensive care data						
Maximum organ failure, mean (SD)[d]	2 (1)	2 (1)	2 (1)	3 (1)	2 (1)	3 (1)
PaO_2/FiO_2, mean (SD)	200 (72)	208 (80)	207 (76)	210 (87)	211 (88)	207 (61)
Other intensive care data						
Ventilation duration, mean (SD) day	10 (9)	11 (10)	9 (8)	14 (13)	13 (14)	10 (10)
ICU length of stay, mean (SD) day	13 (10)	15 (12)	13 (10)	19 (14)	18 (16)	14 (10)
Hospital length of stay, mean (SD) day	21 (13)	22 (16)	19 (13)	29 (18)	31 (22)	25 (18)
Discharge to home with unassisted breathing, N (%)	408 (93)	373 (97)	253 (98)	96 (91)	14 (100)	10 (100)

Abbreviations: ARDS (acute respiratory distress syndrome), SD (standard deviation), BMI (body mass index), ICU (intensive care unit), APACHE III (Acute Physiology and Chronic Health Evaluation III), PaO2/FiO2 (ratio between partial pressure of oxygen in arterial blood and fraction of inspired oxygen).

[a] Missing data for each variable (N, %): race (12, 3%), BMI (2, 0%), alcohol misuse (65, 8%), APACHE III (24, 3%), maximum organ failure (1, 0%), PaO_2/FiO_2 (29, 4%), ventilation duration (25, 3%), ICU length of stay (6, 1%), hospital length of stay (6, 1%).

[b] Did not report return to work status within 12-month follow-up period.

[c] Cardiovascular and chronic pulmonary disease status was measured as part of the APACHE III questionnaire. Alcohol misuse was defined by zone 3 and 4 from the Alcohol Use Disorders Identification Test (AUDIT), which indicates alcohol consumption exceeded recommended limits.

[d] Maximum number of organ failures during ICU stay, using the Brussels scoring system (15) for the following five organ systems (with definition of organ failure): cardiac (systolic blood pressure ≤90 mmHg or use of vasopressor), pulmonary (PaO2/FiO2 ratio ≤300), coagulation (platelets ≤80 x 10^9/L), renal (creatinine ≥2.0 mg/dL) and hepatic (bilirubin ≥2.0 mg/dL).

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

Table 2. Bivariable and multivariable risk factors of the timing of return to work after ARDS

Variable	Bivariable Hazard Ratio (95% CI)[a]	*P* value	Multivariable Hazard Ratio (95% CI)[a]	*P* value
Baseline patient data				
Female	0.76 (0.59, 0.98)	0.033	0.81 (0.62, 1.07)	0.136
White	1.46 (1.03, 2.06)	0.033		
Age, per 10 years[b]	0.86 (0.79, 0.94)	0.001		
White			0.91 (0.81, 1.02)	0.114
Non-white			**0.68 (0.54, 0.84)**	**0.001**
BMI, per 10	0.87 (0.74, 1.01)	0.074	0.97 (0.82, 1.16)	0.773
Cardiovascular disease	0.75 (0.58, 0.97)	0.027	1.16 (0.85, 1.60)	0.351
Diabetes	0.63 (0.44, 0.91)	0.013	0.79 (0.54, 1.15)	0.212
Chronic pulmonary disease	1.00 (0.60, 1.66)	0.996		
Alcohol misuse	1.11 (0.81, 1.54)	0.514		
Baseline intensive care data				
Admission to medical ICU	1.01 (0.79, 1.28)	0.964		
APACHE III, per 20	0.91 (0.83, 1.00)	0.059	1.01 (0.91, 1.13)	0.841
Sepsis as ARDS risk factor	0.91 (0.70, 1.18)	0.456		
Daily intensive care data				
Maximum organ failure score	0.87 (0.76, 1.00)	0.051	0.94 (0.80, 1.09)	0.411
PaO_2/FiO_2, per 10	0.99 (0.97, 1.01)	0.238		
Other intensive care data				
Ventilation duration, per week	0.79 (0.70, 0.89)	<0.001		
ICU length of stay, per week	0.79 (0.72, 0.88)	<0.001		
Hospital length of stay, per week	0.80 (0.74, 0.87)	<0.001	**0.81 (0.74, 0.88)**	**<0.001**
Discharge to home with unassisted breathing	3.60 (1.21, 10.72)	0.021	1.65 (0.49, 5.55)	0.418

Abbreviations: CI (confidence interval), BMI (body mass index), ICU (intensive care unit), APACHE III (Acute Physiology and Chronic Health Evaluation III), ARDS (acute respiratory distress syndrome), PaO2/FiO2 (ratio between partial pressure of oxygen in arterial blood and fraction of inspired oxygen).

[a] Calculated using Fine and Gray regression models, with hazard ratios (HR) <1 indicating a longer time to return to work. Variables with bivariable p <0.20 were included in the multivariable model. Ventilator duration and ICU length of stay were collinear with hospital length of stay and were excluded from the final multivariable model. All significant associations (p <0.05) in multivariable models are highlighted in bold. The overall model Wald test was p<0.001. In this model, 344 of 386 (89%) previously employed survivors were included; 29 (8%) had missing timing of return to work data and 13 (3%) had missing data among included covariates. There were no important differences in baseline or intensive care variables when comparing individuals included versus not included in the multivariable model.

[b] Assessed using an interaction term for age and race (white versus non-white) in the multivariable model.

Table 3. Earnings and lost earnings following ARDS (N = 386)[a]

	First six months after ARDS (0 to 6 months)			Second six months after ARDS (6 to 12 months)		
Employment Status	**n (%)**	**Earnings[c] Mean ± SD $**	**Lost Earnings[c] Mean ± SD $**	**n (%)**	**Earnings[c] Mean ± SD $**	**Lost Earnings[c] Mean ± SD $**
Working greater or equal hours per week than before ARDS	110 (28%)	21,963±7,875	—	106 (27%)	22,738±8,055	—
Working fewer hours per week than before ARDS	80 (21%)	16,083±9,651	9,497±6,985	85 (22%)	19,020±9,621	8,298±7,407
Unemployed[b]	103 (27%)	2,561±7,211	18,602±12,228	72 (19%)	6,598±11,228	15,529±13,150
Receiving disability[b]	56 (15%)	910±4,338	23,124±11,468	76 (20%)	129±1,121	20,920±11,132
Paid sick leave	16 (4%)	22,441±3,601	—	3 (1%)	33,076±14,274	—
Retired[b]	14 (4%)	2,350±8,791	—	15 (4%)	3,396±8,982	—
Unknown employment status[b]	7 (2%)	—	—	22 (6%)	—	—
Died during period	N/A[d]	—	—	7 (2%)	—	—
Total among non-retired survivors who accrued lost earnings[e]	**233 (60%)**	**$6,271±9,773**	**$17,042±11,647**	**222 (59%)**	**$8,432±11,385**	**$15,375±11,685**
Total among all survivors in cohort[c]	**386 (100%)**	**$11,423±11,832**	**$10,287±12,305**	**379 (100%)**	**$12,301±12,596**	**$9,006±11,719**
Cumulative, non-retired who accrued lost earnings				**274 (71%)**	**$18,034±21,840**	**$26,949±22,447**
Cumulative, all subjects				**386 (100%)**	**$23,501±22,633**	**$19,130±22,522**

Abbreviations: ARDS (acute respiratory distress syndrome); N/A (not applicable); SD (standard deviation); mo (Months)

[a] All estimated earnings adjusted to 2016 US dollars using the consumer price index. Includes only study participants with full- or part-time work before ARDS. Estimates based on hours of reported work and age- and gender-based hourly wages from the Bureau of Labor statistics. Based on this earnings estimation, patients reporting full-time (n = 312 of 386, 81%) and part-time (n = 74 of 386, 19%) work had $15,801,932 (mean±SD, $50,647±17,583) and $1,484,554 ($20,062±9,643), respectively, of estimated annual earnings immediately before ARDS (for entire group (N=386): $44,784±20,315).

[b] Survivors who worked but were subsequently unemployed, disabled, or retired at the time of follow-up were assumed to accrue earnings during that period. Among 6- and 12-month survivors who were unemployed (n = 103 and 72, respectively), disabled (n = 56 and 76), and retired (n = 14 and 15), 18 (17%) and 27 (38%), 3 (5%) and 1 (1%), and 1 (7%) and 2 (13%) accrued earnings over the prior 6 months. Survivors who had retired, had unknown employment status, or died at each time point were assumed to have zero potential earnings and therefore zero lost earnings.

[c] Calculated for 6-month period.

[d] Death during 0 to 6 month follow-up period is not applicable since survival until 6 months was required for inclusion in the study cohort

[e] Includes only survivors who accrued lost earnings. At 6- and 12-month follow-up, 6 (5 unemployed and 1 disabled) and 11 (all unemployed) survivors, respectively, reported work during the preceding 6-month period that was the same or greater than hours worked prior to ARDS, and were therefore assumed to accrue $0 lost earnings.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

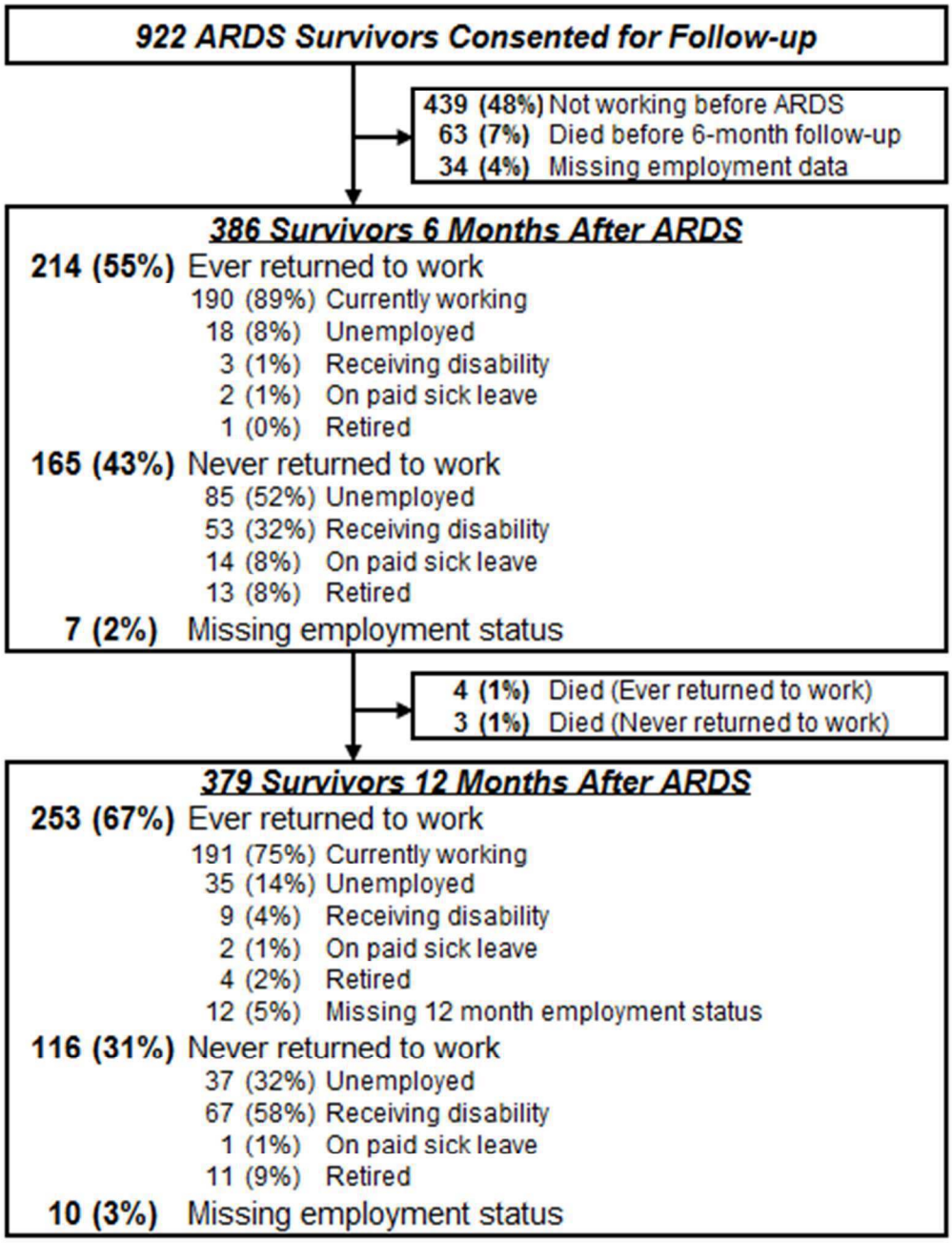

Figure 1. Patient flow chart. Some percentages do not add up to 100% due to rounding.

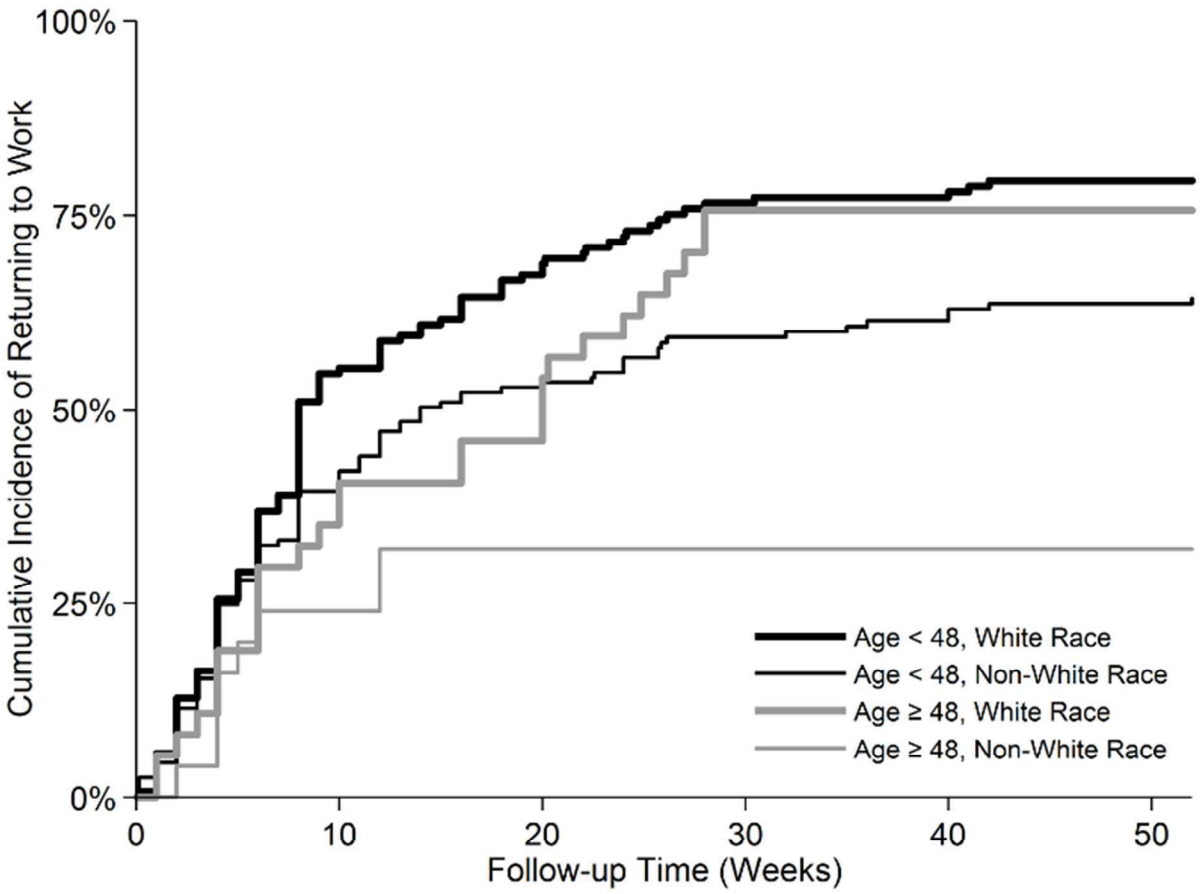

Figure 2. Cumulative incidence of returning to work over 12-month follow-up, stratified by age and race, with retirement and death treated as competing risks.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

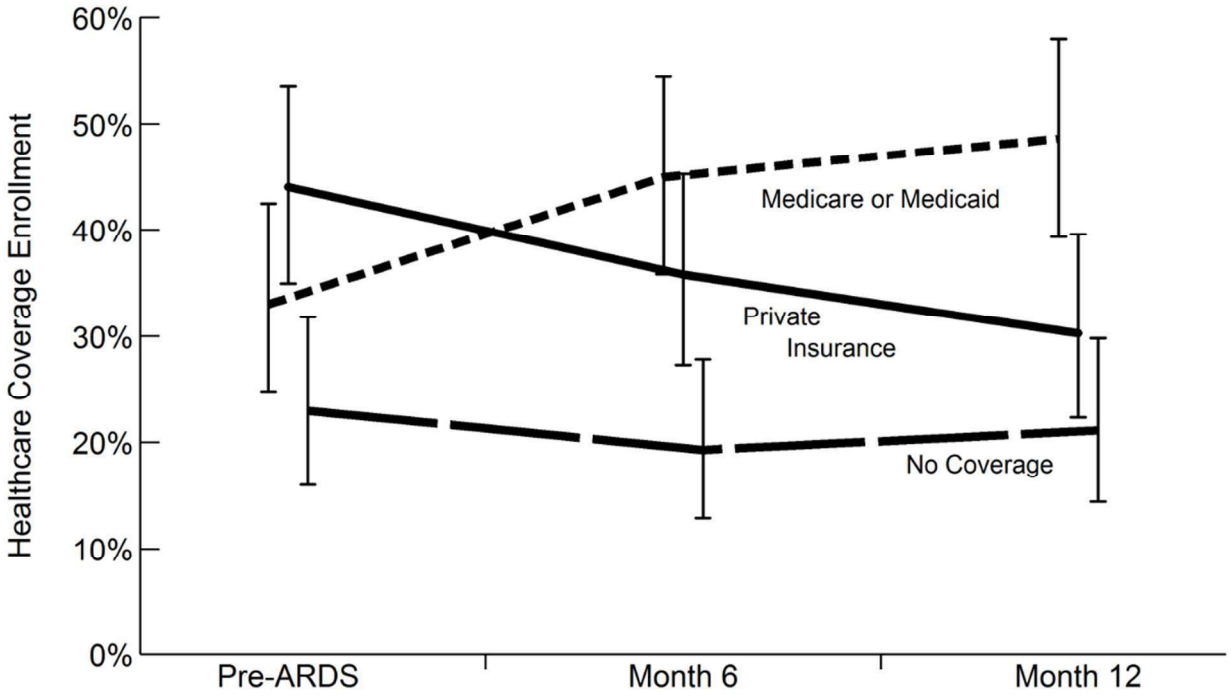

Figure 3. Primary healthcare coverage reported by ARDS survivors <65 years old who were unemployed or disabled at each post-ARDS time point. Plotted values are proportions (and 95% confidence intervals) of 12-month survivors enrolled in each healthcare coverage category at each of these 3 time points: pre-ARDS baseline, 6 months post-ARDS, and 12 months post-ARDS.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

Joblessness and Lost Earnings after ARDS in a 1-Year National Multicenter Study

Biren B. Kamdar, MD, MBA, MHS
Minxuan Huang, ScM
Victor D. Dinglas, MPH
Elizabeth Colantuoni, PhD
Till M. von Wachter, PhD
Ramona O. Hopkins, PhD
and Dale M. Needham, FCPA, MD, PhD
with the National Heart, Lung, and Blood Institute
Acute Respiratory Distress Syndrome Network

ONLINE DATA SUPPLEMENT

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

METHODS

Sensitivity Analyses

Timing of return to work: Three *post-hoc* sensitivity analyses were conducted. First, to account for possible age-related changes after the age of 65 (the traditional retirement age in the U.S.), the multivariable regression model was re-run excluding the 14 survivors (4% of cohort) who were ≥65 at hospital discharge. Second, the multivariable regression was re-run with only death, and not retirement, treated as a competing risk. Third, a multivariable regression model was created which included all covariates, rather than only those that had a bivariable association (at $p<0.20$) with the primary outcome.

Estimated lost earnings: Four *post-hoc* sensitivity analyses were performed for estimating lost earnings, using different methods to impute wages and hours worked, or involving different patient samples. In the first sensitivity analysis, survivors' sex and self-reported occupation was matched with weekly wages for 22 major occupational and sex categories (www.bls.gov/oes). Second, all retired survivors <65 years old were assumed to accrue lost earnings, with the rationale that these survivors may have been forced to retire early as a consequence of ARDS, and therefore, incur lost earnings. Third, lost earnings were estimated for only survivors <65 years old, under the assumption that these survivors ≥65 years old would be eligible retirement and/or social security payments after ARDS. Finally, rather than use of self-reported work hours per week, survivors reporting full- and part-time work were assigned the 40 and 20 work hours per week, representing the median values for all survivors, respectively.

RESULTS

Sensitivity Analyses

Timing of return to work: Three *post-hoc* sensitivity analyses were conducted: (1) restricting analysis to only survivors age <65 years old (Table E1), (2) having death, alone, as a competing risk in the statistical analysis (Table E2), and (3) including all available covariates in the statistical analysis (Table E3). Across all three sensitivity analyses, there were no important differences in results.

Estimated lost earnings: When imputing estimates wages using occupation and sex, the cumulative mean±SD lost earnings decreased minimally, from $26,949±22,447 to $23,954±20,362 (11% change). When lost earnings for retired survivors aged ≤65 were included in the lost earnings analysis, cumulative mean±SD lost earnings increased to $27,565±22,263 (2% increase). When lost earnings for survivors ≥65 years old were excluded, cumulative mean±SD lost earnings were $27,276±22,597 (1% increase). Finally, when lost earnings were computed using the cohort's median work hours (rather than individual survivor-reported hours), cumulative mean±SD lost earnings were $27,587±14,234 (2% increase).

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

Table E1. Multivariable risk factors of timing of return to work after ARDS: Survivors Age <65

Variable	Multivariable Hazard Ratio (95% CI)[a]	*P* Value
Baseline patient data		
Female	0.85 (0.65, 1.11)	0.239
Age, per 10 years[b]		
White	0.93 (0.82, 1.05)	0.245
Non-white	0.61 (0.37, 1.00)	0.051
BMI, per 10	0.97 (0.82, 1.15)	0.714
Cardiovascular disease	1.16 (0.84, 1.59)	0.361
Diabetes	0.75 (0.51, 1.11)	0.149
Chronic pulmonary disease		
Alcohol misuse		
Baseline intensive care data		
Admission to medical ICU		
APACHE III, per 20	0.98 (0.88, 1.10)	0.763
Sepsis as ARDS risk factor		
Daily intensive care data		
Maximum organ failure score	1.06 (0.84, 1.33)	0.623
PaO_2/FiO_2, per 10		
Other intensive care data		
Ventilation duration, per week		
ICU length of stay, per week		
Hospital length of stay, per week	**0.78 (0.72, 0.86)**	**<0.001**
Discharge to home with unassisted breathing	1.53 (0.46, 5.09)	0.490

Abbreviations: CI (confidence interval), BMI (body mass index), ICU (intensive care unit), APACHE III (Acute Physiology and Chronic Health Evaluation III), ARDS (acute respiratory distress syndrome), PaO2/FiO2 (ratio between partial pressure of oxygen in arterial blood and fraction of inspired oxygen).

[a] Calculated using a Fine and Gray proportional subdistribution hazards regression models, with a hazard ratio (HR) <1 indicating a longer time to return to work. Variables with bivariable p <0.20 were included in the multivariable model. Ventilator duration and ICU length of stay were collinear with hospital length of stay and were excluded from the final multivariable model. All significant associations (p <0.05) in multivariable models are highlighted in bold. The overall model Wald test was p<0.001. In the model, 330 of 386 (85%) previously employed survivors were included; 16 (4%) had missing timing of return to work data and 40 (10%) had missing data among included covariates. There were no important differences in baseline or intensive care variables when comparing individuals included versus not included in the multivariable model.

[b] Assessed using an interaction term for age and race (white versus non-white) in the multivariable model.

Table E2. Multivariable risk factors of timing of return to work after ARDS: Only death (and not retirement) treated as competing risk

Variable	Multivariable Hazard Ratio (95% CI)[a]	*P* Value
Baseline patient data		
Female	0.83 (0.64, 1.09)	0.181
Age, per 10 years[b]		
White	0.91 (0.81, 1.03)	0.137
Non-white	**0.56 (0.35, 0.90)**	**0.017**
BMI, per 10	0.97 (0.82, 1.16)	0.762
Cardiovascular disease	1.17 (0.85, 1.60)	0.336
Diabetes	0.79 (0.54, 1.15)	0.218
Chronic pulmonary disease		
Alcohol misuse		
Baseline intensive care data		
Admission to medical ICU		
APACHE III, per 20	0.97 (0.87, 1.09)	0.651
Sepsis as ARDS risk factor		
Daily intensive care data		
Maximum organ failure score	1.06 (0.85, 1.33)	0.599
PaO_2/FiO_2, per 10		
Other intensive care data		
Ventilation duration, per week		
ICU length of stay, per week		
Hospital length of stay, per week	**0.80 (0.74, 0.87)**	**<0.001**
Discharge to home with unassisted breathing	1.66 (0.50, 5.53)	0.409

Abbreviations: CI (confidence interval), BMI (body mass index), ICU (intensive care unit), APACHE III (Acute Physiology and Chronic Health Evaluation III), ARDS (acute respiratory distress syndrome), PaO2/FiO2 (ratio between partial pressure of oxygen in arterial blood and fraction of inspired oxygen).

[a] Calculated using a Fine and Gray proportional subdistribution hazards regression models, with a hazard ratio (HR) <1 indicating a longer time to return to work. Variables with bivariable p <0.20 were included in the multivariable model. Ventilator duration and ICU length of stay were collinear with hospital length of stay and were excluded from the final multivariable model. All significant associations (p <0.05) in multivariable models are highlighted in bold. The overall model Wald test was p<0.001. In the model, 344 of 386 (89%) previously employed survivors were included; 16 (4%) had missing timing of return to work data and 36 (9%) had missing data among included covariates. There were no important differences in baseline or intensive care variables when comparing individuals included versus not included in the multivariable model.

[b] Assessed using an interaction term for age and race (white versus non-white) in the multivariable model.

AJRCCM Articles in Press. Published on 27-April-2017 as 10.1164/rccm.201611-2327OC

Table E3. Multivariable risk factors of timing of return to work after ARDS: All covariates

Variable	Multivariable Hazard Ratio (95% CI)[a]	*P* Value
Baseline patient data		
Female	0.83 (0.62, 1.11)	0.209
Age, per 10 years[b]		
White	0.91 (0.80, 1.03)	0.126
Non-white	**0.53 (0.32, 0.87)**	**0.012**
BMI, per 10	0.98 (0.81, 1.17)	0.788
Cardiovascular disease	1.21 (0.86, 1.70)	0.280
Diabetes	0.87 (0.58, 1.30)	0.497
Chronic pulmonary disease	1.34 (0.72, 2.48)	0.355
Alcohol misuse	1.10 (0.78, 1.55)	0.570
Baseline intensive care data		
Admission to medical ICU	1.02 (0.77, 1.34)	0.909
APACHE III, per 20	0.99 (0.88, 1.12)	0.881
Sepsis as ARDS risk factor	1.11 (0.80, 1.56)	0.531
Daily intensive care data		
Maximum organ failure score	1.05 (0.82, 1.35)	0.693
PaO_2/FiO_2, per 10	0.98 (0.96, 1.00)	0.067
Other intensive care data		
Ventilation duration, per week		
ICU length of stay, per week		
Hospital length of stay, per week	**0.79 (0.72, 0.86)**	**<0.001**
Discharge to home with unassisted breathing	2.49 (0.67, 9.25)	0.174

Abbreviations: CI (confidence interval), BMI (body mass index), ICU (intensive care unit), APACHE III (Acute Physiology and Chronic Health Evaluation III), ARDS (acute respiratory distress syndrome), PaO2/FiO2 (ratio between partial pressure of oxygen in arterial blood and fraction of inspired oxygen).

[a] Multivariable model including all covariates. Calculated using a Fine and Gray regression model, with a hazard ratio (HR) <1 indicating a longer time to return to work. Ventilator duration and ICU length of stay were collinear with hospital length of stay and were excluded from the multivariable model. The overall model Wald test p-value was <0.001. In this model, 312 of 386 (81%) previously employed survivors were included; 29 (8%) had missing timing of return to work data and 45 (12%) had missing data among included covariates. There were no important differences in baseline or intensive care variables when comparing individuals included versus not included in the multivariable model.

[b] Assessed using an interaction term for age and race (white versus non-white) in the multivariable model.

Table E4. Return to Work and Mean (SD) Quality of Life Measures in Survivors of ARDS

	6 months after ARDS			12 months after ARDS		
Quality of Life Measure[a]	**Returned to Work (N=214)**[b]	**Did Not Return to Work (N=165)**[b]	***P* Value**[c]	**Returned to Work (N=253)**[b]	**Did Not Return to Work (N=116)**[b]	***P* Value**[c]
EQ-5D						
VAS score	78.8 (16.2)	63.2 (22.3)	< 0.001	79.6 (17.3)	62.3 (21.2)	< 0.001
Utility score	0.83 (0.17)	0.63 (0.23)	< 0.001	0.84 (0.16)	0.63 (0.21)	< 0.001
SF-36						
PCS score	46.7 (10.1)	34.0 (10.5)	< 0.001	47.8 (10.9)	34.2 (9.8)	< 0.001
MCS score	50.2 (11.5)	43.1 (15.0)	< 0.001	50.2 (12.5)	41.5 (15.0)	< 0.001

Abbreviations: ARDS (Acute Respiratory Distress Syndrome), SD (Standard deviation), EQ-5D, VAS (Visual Analogue Scale), SF-36 (Medical Outcomes Study 36-item Short Form), PCS (Physical Component Summary), MCS (Mental Component Summary)

[a] Higher scores indicate better quality of life for all measures. The EQ-5D VAS scale ranges from 0 to 100; EQ-5D utility score ranges from -0.11 to 1.00 (score <0.0 represents a state worse than death); SF-36 PCS and MCS are normalized scores (range: 0 to 100) with mean = 50 and SD = 10.

[b] N represents the cumulative number of 6 and 12-month survivors who had ever versus never returned to work by that post-ARDS follow-up time point. The number of missing values at 6 and 12 months, respectively: EQ-5D = 9 and 22; SF-36 = 8 and 29.

[c] Calculated using Student's *t* test