and all-cause readmissions. *Ann Am Thorac Soc* 2017;14: 1305–1311.
7. Broeders ME, Molema J, Hop WC, Vermue NA, Folgering HT. The course of inhalation profiles during an exacerbation of obstructive lung disease. *Respir Med* 2004;98:1173–1179.
8. Mahler DA, Waterman LA, Ward J, Gifford AH. Comparison of dry powder versus nebulized β-agonist in patients with COPD who have suboptimal peak inspiratory flow rate. *J Aerosol Med Pulm Drug Deliv* 2014;27:103–109.
9. Mahler DA, Ohar J, Barnes C, Moran E, Pendyala S, Crater G. Efficacy of revefenacin by nebulization and tiotropium by HandiHaler in subjects with COPD and suboptimal peak inspiratory flow rates (PIFR). *Chest* 2018;154(Suppl):732A–733A.

Reply to Mahler

From the Authors:

We appreciate Mahler's correspondence related to our research statement (1), the goal of which was to identify knowledge gaps that future research studies can address to efficiently translate biomarkers into clinical practice. To reach this goal, we chose to focus on example biomarkers for select lung diseases rather than create a comprehensive list of all biomarkers for all pulmonary diseases. As stated in the article, "the biomarkers discussed in this research statement are not intended to be comprehensive." Thus, we did not state or intend to imply that fibrinogen is the "sole" biomarker in chronic obstructive pulmonary disease (COPD). We agree with Mahler that the peak inspiratory flow rate is a promising COPD biomarker, and encourage studies of this and other promising biomarkers for COPD and other lung diseases. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Ann Chen Wu, M.D., M.P.H.*
Harvard Pilgrim Health Care Institute and Harvard Medical School
Boston, Massachusetts

Blanca E. Himes, Ph.D.
University of Pennsylvania
Philadelphia, Pennsylvania

*Corresponding author (e-mail: ann.wu@childrens.harvard.edu).

Reference

1. Wu AC, Kiley JP, Noel PJ, Amur S, Burchard EG, Clancy JP, *et al*. Current status and future opportunities in lung precision medicine research with a focus on biomarkers: an American Thoracic Society/National Heart, Lung, and Blood Institute Research Statement. *Am J Respir Crit Care Med* 2018;198:e116–e136.

Long-Term Outcomes after Prolonged Mechanical Ventilation: What of Those Cast Away?

To the Editor:

We read with interest Jubran and colleagues' article titled "Long-term outcome after prolonged mechanical ventilation: a long-term acute-care hospital study" (1). As critical-care survivorship increases, we will increasingly need to confront the issue of whether interventions made *in extremis* result in outcomes consistent with the long-term wishes of patients. Jubran and colleagues' findings that more than half of the patients in their study were detached from a ventilator by discharge from a long-term acute-care hospital, and that 85% of survivors of prolonged mechanical ventilation would choose to again undergo prolonged ventilation could potentially inform decision-making regarding prolonged mechanical ventilation. However, to apply the findings of Jubran and colleagues to patient care, it is necessary to understand the selection process by which patients were enrolled in the clinical trial on which the study was based (2).

Our interpretation of the original randomized trial's Consolidated Standards of Reporting Trials flow diagram is that 2,267 patients were screened and 316 were enrolled, and these 316 patients represent the cohort included in the current secondary observational analysis. Acknowledging the challenges of enrolling patients with prolonged mechanical ventilation in a randomized trial, we note that most patients were excluded from the trial owing to an inability or refusal to consent, and many others were excluded owing to profound neurologic deficits or a life expectancy of <3 months. We wonder if the exclusion of most long-term acute-care hospital patients—the 316 patients enrolled reflect less than 14% of the originally screened sample—introduced substantial selection bias into the estimates of ventilator liberation and patient satisfaction. We speculate that the excluded patients had disease characteristics (including an inability to participate in handgrip, maximum inspiratory pressure maneuvers, or quality-of-life and preference questionnaires) that would decrease the total proportion of patients detached from the ventilator, leading to different conclusions. Could the authors expand upon how their results should be interpreted in light of the narrow selection criteria that led patients to participate in the original trial?

Finally, we noted also that the authors invoked Daniel Kahneman's "experiencing self" and "remembering self" in the context of 85% of survivors being "willing to [again] undergo a further episode of prolonged ventilation." We wish to note that only survivors—and only those with an intact mental status, at that—are afforded the opportunity to convey a remembering self. It is impossible to ask either decedents or survivors without an intact

Originally Published in Press as DOI: 10.1164/rccm.201902-0432LE on March 20, 2019

Originally Published in Press as DOI: 10.1164/rccm.201901-0210LE on March 12, 2019

mental status whether they harbor any regrets. We are reminded of a quote from Diogenes the Cynic. In reference to a painting of shipwreck survivors, Diogenes was asked, "Look, you who think the gods have no care of human things, what do you say to so many persons preserved from death by [the gods'] especial favour?" He replied, "Why, I say that their pictures are not here who were cast away, who are by much the greater number" (3). ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Anica C. Law, M.D.*
Beth Israel Deaconess Medical Center
Boston, Massachusetts

Allan J. Walkey, M.D., M.S.
Boston University School of Medicine
Boston, Massachusetts
and
Boston University School of Public Health
Boston, Massachusetts

ORCID ID: 0000-0003-3616-0316 (A.C.L.).

*Corresponding author (e-mail: alaw1@bidmc.harvard.edu).

References

1. Jubran A, Grant BJ, Duffner LA, Collins EG, Lanuza DM, Hoffman LA, *et al*. Long-term outcome after prolonged mechanical ventilation: a long-term acute-care hospital study. *Am J Respir Crit Care Med* [online ahead of print] 9 Jan 2019; DOI: 10.1164/rccm.201806-1131OC. Published in final form as *Am J Respir Crit Care Med* 2019;199:1508–1516 (this issue).
2. Jubran A, Grant BJ, Duffner LA, Collins EG, Lanuza DM, Hoffman LA, *et al*. Effect of pressure support vs unassisted breathing through a tracheostomy collar on weaning duration in patients requiring prolonged mechanical ventilation: a randomized trial. *JAMA* 2013;309:671–677.
3. de Montaigne M. The complete works of Michel de Montaigne. East Sussex, UK: Delphi Classics; 2016.

Reply to Law and Walkey

From the Authors:

We thank Dr. Law and Dr. Walkey for their thoughtful comments about our study (1). The main reason why patients were excluded from the clinical trial is that we could not obtain informed consent (patient refusal or unavailability of an authorized surrogate); only 17% of screened patients were excluded because of medical reasons (hemodynamic instability, profound neurological deficits, bilateral phrenic nerve injury, or life expectancy of less than 3 mo). Accordingly, it is not likely that the excluded patients were sicker than the patients included in the study. Further evidence that selection bias did not influence our results is the fact that our ventilator-detachment rate (53.7%) is virtually identical to the ventilator-detachment rate (54.1%) reported in a multicenter, observational study conducted in 23 long-term acute care hospitals and involving 1,418 patients receiving prolonged ventilation (90% of 1,587 transferred patients were enrolled) (2).

Drs. Law and Walkey cite Michel de Montaigne for a quotation attributed to Diogenes the Cynic. The quotation is taken from Montaigne's essay "Of Prognostications." Some translators of Montaigne's essay attribute the quote to Diogenes the Cynic (of Sinope), whereas other translators attribute the quote to Diagoras the Atheist (of Melos) (3). All Montaigne translators note that the quote is taken from Cicero's "*De Natura Deorum*" ("On the Nature of the Gods"), Book III (4). Reading Cicero in the original Latin[1], we see that §89 refers to Diagoras, not Diogenes.

Leaving aside the error concerning the provenance of the quotation, Dr. Law and Dr. Walkey are correct in noting that the opinions of nonsurvivors are never included in accounts of a shipwreck. A small number of historians draw attention to the lack of first-hand evidence from the victims of cataclysmic events. Instead, the voices of victims are commonly filtered through comments of their oppressors (5).

Writing of his own experience, Primo Levi adjured that "we, the survivors, are not the true witnesses . . . we are those who by their prevarications or abilities or good luck did not touch bottom" (6). Levi admits that survivors speak only by proxy, attempting to bear witness for their now mute coevals. Survivors of prolonged ventilation are likewise the only available witnesses of a struggle endured. Their inability to capture the thoughts of nonsurvivors is not a reason to discount their own testimony.

We thank Dr. Law and Dr. Walkey for drawing attention to the striking finding in our study—that 85% of survivors were willing to undergo a further episode of prolonged ventilation—and providing us an opportunity to elaborate on the significance and limitations of survivor testimony. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Amal Jubran, M.D.*
Hines VA Hospital
Hines, Illinois
Loyola University of Chicago
Maywood, Illinois
and
RML Specialty Hospital
Hinsdale, Illinois

Brydon J. B. Grant, M.D.
University at Buffalo
Buffalo, New York

[1]*At Diagoras cum Samothracam venisset, Atheus ille qui dicitur, atque ei quidam amicus: 'Tu, qui deos putas humana neglegere, nonne animadvertis ex tot tabulis pictis quam multi votis vim tempestatis effugerint in portumque salvi pervenerint?', 'Ita fit', inquit, 'illi enim nusquam picti sunt, qui naufragia fecerunt in marique perierunt'*.

Originally Published in Press as DOI: 10.1164/rccm.201902-0368LE on March 12, 2019