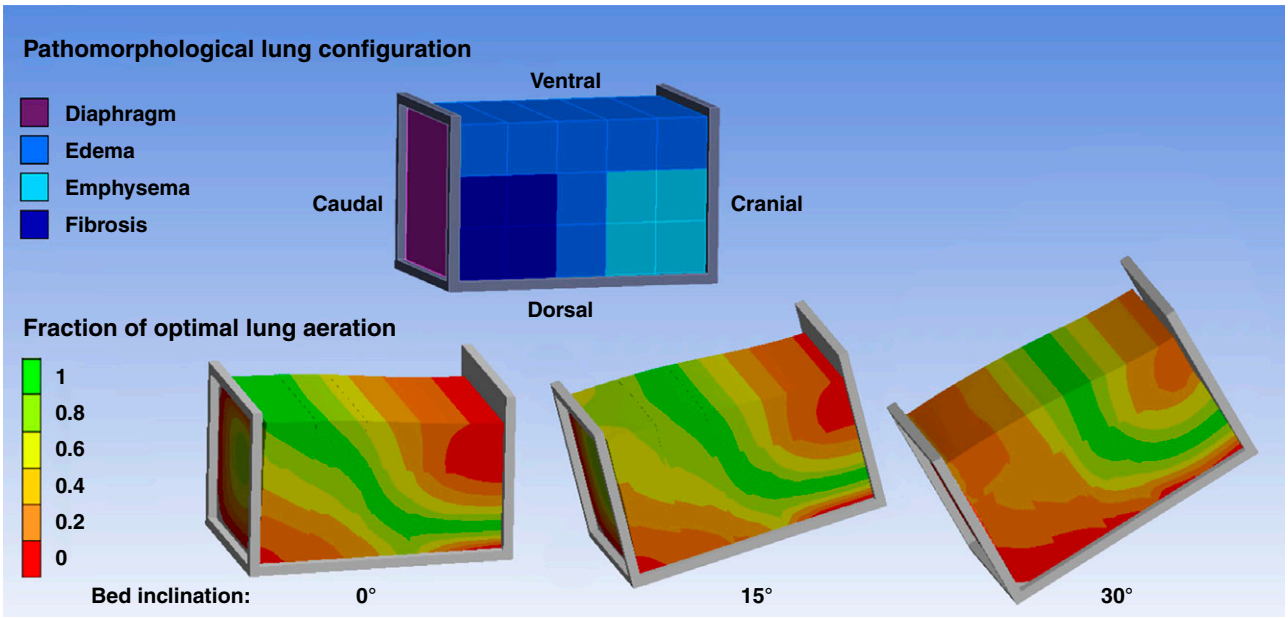

Figure 1. Example configuration of the finite element method lung model (upper part) and representation of the resulting lung aeration in 0°, 15°, and 30° bed inclination (lower part).

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Reply to Oppersma *et al.*

From the Authors:

We thank Dr. Oppersma and colleagues for their interest in our study, in which we described the effects of changes in trunk inclination on respiratory mechanics in mechanically ventilated patients with COVID-associated acute respiratory distress syndrome (ARDS) (1). Reducing trunk inclination from semi-recumbent (40° head-of-bed elevation) to supine-flat (0° head-of-bed elevation) increased markedly (and reversibly) the compliance of the respiratory system, both due to an increase in chest wall and lung compliance. We did not measure changes in lung aeration (end-expiratory lung volume [EELV]); however, we think that the most relevant underlying mechanisms is the decrease in EELV in supine-flat position, favoring a reduction of

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overdistension of some, most likely ventral non-dependent, lung regions. Of note, similar observations regarding changes in respiratory mechanics were made in patients with "classical" ARDS (2, 3). Moreover, a reduction in EELV caused by a change in trunk inclination from semi-recumbent to supine-flat position has been described in "classical" ARDS (2, 3), mechanically ventilated patients with normal lungs (4) and in spontaneously breathing subjects (5).

Dr. Oppersma and colleagues developed a mathematical model aimed at simulating the changes in lung aeration due to variations in trunk inclination. The model consisted of 15 blocks of homogenous material, with specific properties of either edematous, fibrotic or emphysematous lung tissue. In addition, the simulated pressure applied to the diaphragm (intra-abdominal pressure) changed according to body position, and the gravitational forces (likely proxies of pleural and abdominal pressure gradients) were adapted according to the applied angle. The authors simulated several combinations of mechanical properties of the 15 blocks, having as output variable lung aeration. They found that the combination of an edematous lung with apical emphysema and basal fibrosis predicted the largest increase in lung aeration changing position from supine-flat to semi-recumbent (in their experiment up to 30° head-of-bed elevation).

As stated above, the change in EELV associated with variations in trunk inclination is well-established (2–5). However, we agree with the authors that, in the specific context of ARDS, it might be of interest to understand the pathophysiologic mechanisms underlying the variable change in EELV induced by the variation of trunk inclination (2, 3). Heterogeneity of lung lesions/density is a key feature of ARDS and the distribution of lesions might play a role also in this context. In our study, patients were enrolled early, i.e., a median of 2.5 days after intubation. The timing of our observations makes it therefore difficult to ascertain the relative role of fibrosis and emphysema.

Another aspect worth discussing is that the authors focus on lung aeration, while they did not model (or present) information regarding V_T distribution. Besides changing lung aeration, i.e., the starting pulmonary volume, variations in trunk inclination most likely affect the pleural pressure and abdominal pressure gradients. As a result, it is conceivable that also the distribution of V_T changes with trunk inclination, ultimately affecting ventilation homogeneity.

In conclusion, we look forward to seeing a study in which their interesting computational model is integrated with patient data regarding lung aeration and V_T distribution (e.g., electric impedance tomography). We agree with the authors that this approach could improve our understanding regarding the effects of trunk inclination on respiratory mechanics in mechanically ventilated patients with ARDS. ■

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

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Erratum: Optimizing the Design of Latent Tuberculosis Treatment Trials: Insights from Mathematical Modeling

A funding statement is missing from the opening footnote section in the article by Stout and colleagues (1), published in the March 1, 2020, issue of the *Journal*. There should have been a footnote for Dr. Nicholas A. Turner that read:

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