sessing the 2 determinants of successful extubation. During spontaneous breathing without an artificial airway (normal breathing), an open airway is a prerequisite for breathing. This fact is violated in clinical practice. When we evaluate a patient for extubation (a transition to breathing without an artificial airway), we frequently evaluate the breathing pattern first and then decide if the patient can keep the airway open. We believe that this practice is the result of 2 beliefs: the belief that one extra day on the ventilator is more harmful than failed extubation (confirmed by the fact that most physicians in the study were aggressive in extubating patients) and the belief that the available predictors of keeping the airway open are weak (supported by the fact that 21% of the physicians in the study were influenced by mental status and secretions).[1] These beliefs might result in the extubation of patients who ultimately required re-intubation because they cannot "protect the airway." If we perform weaning trials only on patients able to keep the airway open, we will reduce re-intubation from airway related reasons.

Before we replace our current practice with computer aided weaning and extubation algorithms, we should better understand the physiology of the upper airway after extubation and determine the strongest predictors of keeping it open. Then we should determine when to incorporate these predictors, before and after breathing trials. At that point we can use the new knowledge to create comprehensive computer aided algorithms. And even then, gut feeling might remain superior to computers, particularly in complex situations.[4]

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The authors respond:

We agree with Kallet that better tools may help physicians identify extubation candidates more accurately. However, while prediction models constructed along the lines described by Tulaimat and Mokhlesi might prove useful,[1] we do not know whether better modeling, in and of itself, would improve decision making. Prediction tools are indispensible when clinicians need to make complex, high risk decisions, but such tools rarely succeed in isolation: they are deeply intertwined with and dependent upon clinical judgment.

An intriguing but unanswered question raised by Tulaimat and Mokhlesi's study[1] is why some physicians, but not others, made accurate predictions. As we noted previously,[2] the cases studied were difficult, but some physicians clearly got the decision right. All the physicians who participated in Tulaimat and Mokhlesi's study were attendings or fellows in 3 respected teaching institutions[1] and presumably familiar with the factors associated with extubation failure. So why did so many choose extubation despite these factors? Did they discount their significance? Did other, unidentified factors persuade them to believe extubation would succeed despite data to the contrary? Did some unnamed bias or heuristic push physicians to make decisions that seem irrational in retrospect? Perhaps identifying the factors associated with accurate decision making would prove illuminating.

A well-constructed algorithm, as Kallet proposes, might improve physicians' ability to predict extubation success. However, the quest to develop such algorithms remains elusive. Despite years of study and countless expert reviews and clinical guidelines,[3-6] the pulmonary and critical care community still struggles to find better ways to identify extubation candidates. For example, a recent study by Girault et al showed that a substantial portion (63%) of patients could be successfully extubated despite "failing" a spontaneous breathing trial.[7] Clearly, more work is needed to optimize our approach to extubation. Both reliable data—and the optimal use of data available—are vital to the ongoing effort to extubate more of the right patients at the right time.

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Critical Illness Related Pneumonia Rather Than Ventilator-Associated Pneumonia (VAP)

We read with interest the review article entitled "New endotracheal tubes designed to prevent ventilator-associated pneumonia: do they make a difference?" by Deem and Treggiari.[1] In line with European experts,[2]

the American researchers state that "the high VAP rate in ventilated patients is probably due to factors associated with translaryngeal intubation rather than simply an effect of patient susceptibility from severity of illness." We disagree with this expert opinion and we would argue that the severity of underlying disease is the major determinant of developing pneumonia in patients requiring treatment on the intensive care unit (ICU).[3] Our statement that "the sicker the patients, the higher the pneumonia rate" is supported by the following quantitative data. The incidence of hospital-acquired pneumonia is approximately 5-10 per 1,000 admissions.[3,4] The pneumonia rate is 7% in patients requiring treatment on ICU without endotracheal intubation, and increases to 12% in ICU patients requiring endotracheal intubation.[3,4] The pneumonia rate is lower with noninvasive ventilation (1.58 per 1,000 ventilator days), compared with invasive ventilation (5.44 per 1,000 ventilator days).[5] Remarkably, the patients receiving noninvasive ventilation were less ill than the ones who were endotracheally intubated. Finally, a recent epidemiological study on the prevalence and outcomes of infection in ICUs showed that the infection rate was related to disease severity assessed by the Simplified Acute Physiology Score II.[6]

Apart from illness severity, the abnormal oropharyngeal carrier state is a higher risk factor than the endotracheal tube. It is generally acknowledged that underlying disease promotes the abnormal oropharyngeal carrier state.[7] Less known is that the presence of the nasogastric tube is another factor that promotes abnormal oropharyngeal carriage.[8]

Deem and Treggiari acknowledge that selective decontamination of the digestive tract (SDD) is an effective VAP prevention technique, referring to one of the first Italian meta-analyses in 1998.[9] They fail to mention the most recent Cochrane meta-analysis of randomized controlled trials of SDD from 2009, demonstrating that SDD reduces VAP by 72% (odds ratio 0.28, 95% CI 0.20-0.38).[10] As 2 of the originators of SDD, we would suggest that the efficacy of SDD is due to the control of gut overgrowth associated with critical illness.[11] Gut overgrowth harms the critically ill in 4 main ways. Overgrowth of "abnormal" aerobic Gram-negative bacilli and/or endotoxin has been shown to cause inflammation, immunosuppression, infection, and antimicrobial resistance. SDD is a prophylactic measure using selected antimicrobials to control gut overgrowth, thereby reducing the 4 harmful side effects, including restoration of suppressed systemic immunity and reduction of severe infections of lower airways.

In conclusion, severity of underlying disease promoting oropharyngeal overgrowth and subsequent lower airway infection following migration is the major determinant factor for developing pneumonia, rather than factors associated with translaryngeal intubation.

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The authors respond:

We appreciate the interest that Zandstra and colleagues have shown in our review of "New endotracheal tubes designed to prevent ventilator-associated pneumonia." We agree with Zandstra et al that severity of illness is an important risk factor for the development of ventilator-associated pneumonia (VAP). However, we stand by our original statement that VAP "is probably due to factors associated with translaryngeal intubation." This is borne out by the nearly 50% reduction in VAP associated with subglottic secretion drainage,[1] polyurethane-cuffed tracheal tubes,[2] and a variety of other interventions designed to either reduce microaspiration or the bacterial burden of aspirated oropharyngeal secretions.[3,4] The general decline in VAP rates over the past 5 years, as reported by the Center for Disease Control (CDC), and in association with widespread implementation of "VAP bundles" also supports the notion that VAP is a modifiable event. Zandstra and colleagues make this case very cogently in their argument for selective decontamination of

the digestive track as a VAP-preventive measure.

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Additional Experimental Evidence That Statins Protect Against Acute Lung Injury

Altintas and colleagues made a nice contribution on the field of acute lung injury (ALI), showing that pretreatment with simvastatin attenuates lung injury induced by oleic acid and endotoxin in mice.[1]

Although the authors cited a few papers to state that "the available studies on statins in ALI are limited,"[1] we believe that the evidence regarding the beneficial role of statins against ALI is growing. For example, our colleagues could mention another recent article that explored the impact of statin administration on the development of ALI induced by high-stretch mechanical ventilation.[2] Indeed, by implementing an isolated perfused mechanically ventilated rabbit lung model, our research team demonstrated that pretreatment with atorvastatin improves alveolar capillary permeability and hemodynamics, and thus attenuates ventilator-induced lung injury (VILI).[2] Our results were later confirmed by another contribution, which also noted that pretreatment with simvastatin protects against VILI in an in vivo murine model.[3] On the basis of the above 2 articles[2,3] it could be argued that administration of statins protects against VILI from the acute until the late phases of lung injury, through variable (not only anti-inflammatory/anti-oxidative) mechanisms.[4] Additional contributions revealing the protective role of statins against ALI induced by other stimuli, such as cotton smoke inhalation or irradiation, could also be retrieved and cited.[5]

On the other hand, the histological finding of Altintas and colleagues that animal lungs in the statin group without injurious stimulus showed vascular dilatation and stasis is interesting.[1] In our above-mentioned study we also found that the statin group without injurious stimulus had more (albeit statistically nonsignificant) intra-alveolar hemorrhage than the control (ie, no statin and non-injurious stimulus) group.[2] This finding did not correlate with any difference in pulmonary artery pressure between these 2 (ie, statin and non-injurious stimulus vs no statin and non-injurious stimulus) groups.[2] We agree with the authors that the clinical importance of this histological finding may need further investigation.

In conclusion, on the basis of the rapidly accumulating evidence, we share the concluding comment of our colleagues that clinical trials regarding the potential prophylactic value of statin administration in the prevention of ALI seem to be fully justified.

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The authors respond:

We have read with interest the encouraging constructive comments of Siempos and colleagues about our paper "Long-term simvastatin attenuates lung injury and oxidative stress in murine acute lung injury models induced by oleic acid and endotoxin," which was published in RESPIRATORY CARE.[1]

They especially focused on the finding of vascular dilatation and stasis in animal lungs in the statin pretreatment group without injurious stimulus. The clinical importance of this histological finding may need to be discussed. We have some "unpublished data" that supports the beneficial effects of simvastatin even on healthy animals (Fig. 1).

An interesting and very important finding was the higher mesenteric artery indices in mice that received only simvastatin (2 mg/kg/d in a volume of 10 mL/kg, for 15 d), compared to those that received only saline injections. This unknown vasodilatory action of simvastatin and also the observed vascular dilatation and stasis in lungs (in the manuscript) can be explained with some valuable previous works. It was demonstrated that statins up-regulate endothelial nitric oxide synthase (eNOS) activity and nitric oxide (NO) production by increasing eNOS expression (and eNOS mRNA stability) after hypoxic conditions and even under baseline conditions.[2,3] The ability of statins to exert this effect on eNOS expression was independent of cholesterol concentrations, which revealed one of the most significant pleiotropic effects of acute statin therapy.[4] This increase in physiological,