We thank Dr. Rello for his comments on the results of the ‘Preventive Nebulization of Mucolytic Agents and Bronchodilating Drugs in Intubated and Ventilated Intensive Care Unit Patients (NEBULAE)’ study (1), a randomized clinical trial in invasively ventilated critically ill patients that compared routine with on-demand nebulization of acetylcysteine with salbutamol with respect to duration of ventilation (2).

Invasive ventilation increases the risk for sputum retention, since mucociliary clearance is impaired in the presence of the endotracheal tube and because relatively dry gases cause mucosa to produce more mucus. Routine airway care, consisting of repetitive endotracheal suctioning and humidification of inspired air, is thought to protect against mucus retention in the lower airways (3,4), though robust evidence for this is largely lacking. Routine nebulization of mucolytics was thought to have additive preventive effects against sputum retention in invasively ventilated patients. The NEBULAE study, however, taught us that routine nebulizations may not be so effective, as it does not translate in shorter time spend on a ventilator (2). We would like to echo the final line in Rello’s comment that ‘prevention is better than cure, but attempts at prevention must not entail other dangers’—this certainly applies for routine nebulization of mucolytics.

Ineffective coughing, resulting from depressed levels of consciousness, sedation and paralysis, together with weakness before and after extubation, is another reason why invasively ventilated patients are at increased risk for airway obstruction (5). Cough augmentation techniques, such as ‘lung volume recruitment’ or ‘assisted cough’, are suggested to prevent respiratory complications associated with chronic conditions like neuromuscular disease (6). With ‘lung volume recruitment’, also known as ‘air stacking’ or ‘breath stacking’, multiple successive insufflations result in a maximum long volume potentially improving the strength of a natural cough (7,8). With ‘assisted cough techniques’, like ‘mechanical in-exsufflation’ or ‘cough assist’ not only the tidal volume is increased, but also an inspiratory hold and a quick maximal release of air is performed, provoking an artificial cough. By creating expiratory flows higher than inspiratory flows, secretions may move cephalad (9,10).

By now, it is increasingly suggested that the above-described techniques may also benefit patients with acute respiratory failure who need invasive ventilation. Some even suggest that these techniques should be used routinely in these patients. One recently published meta-analysis focused on the question whether cough augmentation techniques have beneficial effects in invasively ventilated critically ill patients (11). An intensive search of the medical literature resulted in a meager number of three small investigations that studied these techniques. One trial reported a higher
extubation success rate in patients that received a strategy using mechanical in-exsufflation (12), and another trial a reduction in duration of mechanical ventilation duration with this intervention (13). There were, however, several severe adverse events including secretion encumbrance with severe hypoxaemia requiring reintubation. Other well imaginable risks like hypotension, due to the high intrathoracic pressures created with these techniques, and pneumothorax, caused by the large volumes of air in the lungs, were not reported, though maybe not collected sufficiently. These risks, for sure, are very likely to occur in critically ill patients, in whom they can also have severe consequences.

Indications for and contra-indications against cough augmentation techniques remain poorly defined. Lack of guidelines regarding indications and contra-indications, timing, machine settings, and technique to be used lead to varied use. Continuing research on this topic is eagerly awaited. Studies should not only investigate efficacy of these interventions, but also, or particularly feasibility and safety in this population of frail patients. While we think all these techniques have great potential in individual cases, we strongly argue against routine use as long as studies fail to provide robust evidence for efficacy, but certainly also for safety: ‘primum non nocere’.

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Footnote

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