effective method to integrate goals of care discussions more seamlessly into the preVAD process.[5]

5. Finally, while preparedness planning and PC are important components of preVAD care, we should incorporate these elements into the care of VAD patients not only before implant but also after implantation and throughout the entirety of the "VAD lifecycle." Patients with VADs typically experience improved survival and health-related quality of life (HRQOL),[6–8] but adverse events may affect one or both of these important outcomes.[9] Patients and caregivers may benefit from a comprehensive curriculum that incorporates intermittent, perhaps, semiannual discussions focused on quality of life, caregiver distress, and hopes for the future. The development and implementation of such a curriculum will require a multidisciplinary effort and has the potential to help patients live better with VADs.

We would like to thank the authors for sharing their experience with preVAD evaluation and allowing us to expand on some additional points. More research is clearly needed to determine the best way to integrate PC into VAD patient care.

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Response to "Hyoscine Butylbromide for the Management of Death Rattle: Sooner Rather Than Later"

We read with interest the article "Hyoscine Butylbromide for the Management of Death Rattle: Sooner Rather Than Later" by Mercadante et al.,[1] comparing pre-emptive hyoscine butylbromide for the management of noisy upper respiratory tract secretions (RTS) in patients in the last days of life with treatment of RTS when they occurred. Previous studies have administered anticholinergic drugs to treat already formed noisy RTS rather than preventing their formation, but anticholinergic drugs are unable to remove secretions already formed.[2,3]

This exploratory study presents promising effects; however, the data should be interpreted in the context of its methodological limitations. The natural history of RTS is poorly described, so attribution of outcomes is difficult in an unblinded trial. In addition, no power calculations were reported, making it difficult to evaluate the significance of the findings. Importantly,

harms were not reported, but it is vital to know about toxicity when proposing a prophylactic treatment (potentially for the benefit of family and staff rather than the patient)[4-6] where a significant number of people would never develop noisy RTS (40% in comparator arm of present study) but nevertheless have now been exposed to a drug with a significant harm profile (including dry mouth, constipation, and urinary retention).[2,3] In particular, anticholinergics are known to contribute to delirium—of concern in this high-risk population.[7] To make clinical judgments, we must be able to evaluate the net-benefit (harms-benefit balance) of exposing patients to a medication they might not need but might cause clinically important harms. Furthermore, we cannot identify and target patients at higher risk of developing RTS.[8]

These data are useful to inform a subsequently adequately powered double-blinded randomized placebo-controlled trial, but until high quality data are available (of both effectiveness and harms), a change in practice cannot be recommended.

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Author's Response

Dear Editor

Thanks again for the further comments. The debate continues and I'm happy that this paper has raised such interest, giving me the occasion to further clarify its meaning.

The colleagues emphasize that the natural history of respiratory tract secretions, presumably how death rattle has developed in time, is poorly described. Possibly it is right, but I did not have access to any information of this type in literature published on this topic. The reason probably relies on the individual differences that are unlikely to be reported in a trial.

The second point regards the power calculation. In methods, they partially have the answer: "for sample size for each arm of the research a 'small' Cohen effect size was used. The sample size estimation was affected by an expected drop out in group 1 because of the drug administration inclusion criteria, of 65%, so that we had to adjust for this unbalancing in our study arms." To complete this information, we compared the failure rates according to the study estimates using few lines of code on **R**: > pA=0.60, pB=0.06, kappa=1.6, > alpha=0.05, (Power=pnorm(z-qnorm(1-alpha/2))+ pnorm(-z-qnorm(1-alpha/2) [1] 0.800001. Thus, the power 1-b achieved is 80%. Original data are available.

They also stress that a proportion of patients who receive an early medication may not develop death rattle and consequently are exposed to unnecessary harms. From a clinical point of view, I have many doubts that patients may perceive the effects feared by authors, such as dry mouth, constipation, and urinary retention. I recognize that dying patients having a progressive decrease of the level of consciousness did not complained of these problems or, better, were able to do that. It is surprising to note that, according to authors' opinion, dying patients with a low level of consciousness may not feel death rattle, but they may feel such unpleasant adverse effects.