# **RESPONSE TO LETTER** Response to the letter to the editor "Nasal high-flow versus non-invasive ventilation in patients with chronic hypercapnic COPD" [Response to letter]

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## **Dear editor**

We thank both authors for their thoughtful remarks to our study. We would like to point out that the trial was not formally designed as a non-inferiority study, but "to provide an estimate of the difference between the devices regarding pCO<sub>2</sub> change". This choice followed lengthy discussions with the statistics experts of this institution acknowledging the arbitrary choice of a margin (for pCO<sub>2</sub> reduction) of non-inferiority or equivalence. Defining these margins prior to the study would have had to be an estimate and we had aimed at a margin of 5mmHg for pCO<sub>2</sub> derived from prior NIV studies. Instead of choosing arbitrary margins, we generated data to compare non-invasive ventilation (NIV) and nasal high flow (NHF) in stable hypercapnic COPD patients and concur with Elshof and Duiverman that this is an important topic due to lack of sufficient studies to date.

At the level of hospital or general policy, the authors are correct in their remark that non-inferiority in effectiveness does not suggest the need to make any changes unless other benefits are demonstrated. Our study suggests approximate equivalence of NIV and NHF in relevant outcomes, albeit not formally. Hence, at the level of choice for individual patients, such results are highly relevant since a larger variety of therapy options allows for better consideration of personal preferences. The observation that the proportion "of drop-outs is comparable between groups" merely indicates that there is no strong preference in the study population as a whole for a particular device, but does not preclude strong individual predilections.

In this study, an important feature was the fact, that blood gas measurements were taken hours after the termination of ventilation support treatment. Thus, the differences in pCO<sub>2</sub> were somewhat smaller for both types of device compared to an in-hospital situation where blood gases are measured shortly after termination of ventilatory support.<sup>1</sup> An additional graphical illustration of the pCO<sub>2</sub> before and following each device arm is shown in Figure 1. However, the pCO<sub>2</sub> decrease in our study was comparable to most cited studies by other authors despite slightly different pressure support values and reduced usage times.

Elshof and Duiverman are right to note that 201/min is not what would have been chosen if one were to start a study today. However, at the time the study was conceived, machines delivering more than 201/min were not available and thus we had to stick to the protocol and provide all patients with the same NHF device. The newer models of

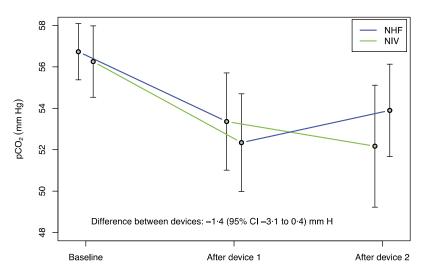


Figure I Partial pressure of carbon dioxide in capillary blood (pCO2) is shown for each device and time point. Whiskers depict 95% confidence intervals.

NHF deliver higher flows and as cited by Elshof and Duiverman also have the potential to lower  $pCO_2$  more efficiently. This point indicates, as stated in our discussion, that the effect demonstrated here is most likely a conservative view comparing an early NHF device to standard NIV.

## Disclosure

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### Reference

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