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From the authors:

I thank B.C. Creagh-Brown and C. Shee for their complimentary comments. Furthermore, I completely agree with the principles described in their letter regarding the use of noninvasive ventilation (NIV) in selected patients who have chosen to forego, or are not offered, endotracheal intubation and invasive mechanical ventilation. In fact, I had the privilege of co-authoring a recent statement published by the Society of Critical Care Medicine [1] regarding the use of noninvasive ventilation for patients with ''do not intubate'' orders that I think is entirely consistent with the comments by B.C. Creagh-Brown and C. Shee. In that statement, we argued that the use of NIV for patients with acute respiratory failure can be classified into three categories. 1) NIV as life support with no preset limitations on life-sustaining treatments. 2) NIV as life support when patients and families have decided to forego endotracheal intubation. 3) NIV as a ''purely palliative'' measure when patients and families have chosen to forego all life support and are receiving comfort measures only.

As pointed out by B.C. Creagh-Brown and C. Shee, there is compelling evidence that some patients in our ''second category'' (those for whom invasive ventilation is not desired or indicated but who do want life-sustaining treatments) will benefit from NIV, especially those patients with acute respiratory failure from chronic obstructive pulmonary disease or congestive heart failure.

As for those in the ''third category'' (patients for whom NIV is used purely for the palliation of symptoms), I also agree with B.C. Creagh-Brown and C. Shee that highly selected patients at the end-of-life may receive some palliative benefit from NIV, provided their clinicians are experienced with NIV. This is an important area in need of further research, but one in which some indirect evidence of benefit exists [1]. However, I suspect I may differ from B.C. Creagh-Brown and C. Shee with regard to my area of greatest concern regarding NIV in this purely palliative setting. In my clinical experience, I see many more patients at the end-of-life exposed to NIV that is unlikely to provide any benefit than for whom this potentially beneficial therapy is withheld.

Perhaps B.C. Creagh-Brown, C. Shee and I agree that both of these concerns about the misapplication of nonivasive ventilation are problematic and we should work to limit them both.

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STATEMENT OF INTEREST

None declared.

REFERENCES

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No effects of EPHX1 polymorphisms on the level or change of FEV1 in the general population

To the Editors:

CHAPPELL *et al.* [1] recently found that several single nucleotide polymorphisms (SNPs) in the glutamate cysteine ligase (catalytic subunit; GCLC) and epoxide hydrolase 1 (EPHX1) do not associate with the presence or severity of chronic obstructive pulmonary disease (COPD). We have previously shown in two independent population-based cohorts that the functional polymorphism rs17883901 and the trinucleotide GAG repeat in GCLC form unique genotype combinations that are associated with lower lung function in interaction with smoking [2]. CHAPPELL *et al.* [1] did not study the latter variation in GCLC, nor the interaction between SNPs and smoking in relation to COPD severity, which is of special interest given the *in vivo* role of GCLC. They additionally studied SNPs in EPHX1, including nonsynonymous SNPs (nsSNPs) Tyr113His and His139Arg that previously provided both positive and negative associations with COPD across studies and races [1, 3–7]. We aimed to extend these findings by showing the effects of EPHX1 SNPs on the level and change of forced expiratory volume in one second (FEV_1) in the general population, and additionally investigated whether EPHX1 SNPs smoking interactions are associated with both outcomes, as was the case with GCLC.

We genotyped five SNPs in EPHX1 (three SNPs tagging the 5 kb promoter region: rs3753658, rs10753410 and rs2854450; and two nsSNPs: rs1051740 (Tyr113His) and rs2234922