Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Prone positioning might reduce the need for intubation in people with severe COVID-19

Authors' reply

We thank W Cameron McGuire and colleagues for their comments regarding our meta-trial on awake prone positioning in patients with COVID-19.[1] We would like to clarify some points.

First, concerning the fragility index, superiority randomised controlled trials are carefully designed to recruit the fewest patients necessary to detect a clinically meaningful and statistically significant difference. This is the objective of sample size calculations and interim analyses. This leads, by design, to low fragility index values. There is no specific cutoff value to classify a study as fragile or robust. Randomised trials that changed clinical practice, published in high-impact journals have a median fragility index of 5,[2] and the median fragility index in critical care randomised trials is 3.[3] Although fragility index is an increasingly popular metric to allegedly show the robustness of trial results, it has also been referred to as a p value in disguise and a potentially misleading metric.[4] In the hypothetical case regarding patients who withdrew consent, McGuire and colleagues could have calculated that 226 events in 567 patients in the awake prone positioning group and 257 events in 559 patients in the control group yields a p value of 0·041 with a Fisher's exact test. We must stress that the robustness of a study relies on its design, study implementation, analysis plan, effect sizes, CIs, generalisability, and limitations, and not on a single integer derived from an inappropriate secondary analysis of a hypothetical randomised trial that never occurred.[2]

Second, all patients in Mexico were recruited in a COVID-19-dedicated intensive care unit and two intermediate care units, which differed only by nurse-to-patient ratios (1:2 and 1:4, respectively). All patients were provided high-level care by experienced critical care physicians, and no intubations were delayed because of unavailability of ventilators or staff.

Third, McGuire and colleagues note a lower baseline SpO_2:FiO_2 ratio in the Mexican trial and worry that a lower threshold for intubation described in the Mexican protocol could have led to a lower intubation rate. These moderate variations in care and population between trials do not create any bias in the estimation of the intervention effect, as the randomisation was stratified on the trial. Indeed, it is clear from our appendix[1] that intubation rates were not different among the three large trials (158 [39%] of 402 patients in France, 77 [34%] of 222 patients in the USA, and 157 [36%] of 430 patients in Mexico). The decision to intubate is complex, comprising clinical judgement, and gestalt and tacit knowledge that have evolved even during the pandemic,[5] and cannot be decided by a single oxygenation parameter. Slight differences between protocols should not distract us from the pragmatic and robust finding of reduced intubation rates with awake prone positioning.

Taken together, the results of our meta-trial are at least as robust as most carefully designed randomised trials and are valid and practice changing.

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