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In Reply In their Letter, Dr Shen and colleagues incorrectly conclude that the primary finding of our FIRST-ABC trial[1] was that HFNC was associated with a similar time to liberation from respiratory support as CPAP. In our study, the median time to liberation was 50.5 hours for HFNC and 42.9 hours for CPAP, with an adjusted hazard ratio of 0.83 (95% CI, 0.70-0.99). Although our primary hypothesis was based on the noninferiority of HFNC, these results indicate that HFNC is in fact inferior to CPAP.

Shen and colleagues also highlight that the proportion of children aged 28 days or younger was higher in the HFNC group compared with the CPAP group. Based on previous trials, they suggest that the effect of HFNC may differ in this age group and propose that a subgroup analysis focusing on infants aged 28 days or younger is warranted. They also point out the higher mortality at day 60 in the HFNC group (which was statistically significant in multivariate analysis including age younger than 12 months vs 12 months or older) and suggest that an interaction analysis between HFNC and age should be performed.

Shen and colleagues cite 2 clinical trials to support their premise that the effect of HFNC differs across pediatric age groups. However, both trials were performed in preterm newborns (Uchiyama et al[2]: <34 weeks' gestational age; Roberts et al[3]: mean gestational age, 32 [SD, 2] weeks). Moreover, only the trial by Uchiyama et al[2] took place following extubation. The study by Roberts et al[3] included newborns or children with acute respiratory distress. In addition, these trials[2,3] used treatment failure as the primary outcome, which differed from our primary outcome of time to liberation from respiratory support. Moreover, our study[1] was a pragmatic trial of extubated children aged 0 to 16 years, and premature newborns (those <37 weeks' gestational age) were excluded. As such, we believe that it is not possible to directly compare the findings of these trials with ours.

In the FIRST-ABC trial,[1] we tested for an interaction between age (dichotomized at 12 months) and treatment allocation, which was nonsignificant (P = .16). Based on the request by Shen and colleagues, we have repeated this analysis with age categorized as 28 days or younger, 29 to 365 days, and older than 365 days. The interaction test remains insignificant (P = .20), although the point estimates (which had wide confidence intervals) were consistent with the hypothesis that time to liberation is longer in the HFNC group for children aged 365 days or younger, and this difference increased in infants aged 28 days or younger (adjusted hazard ratio, 0.67; 95% CI, 0.46-1.07). FIRST-ABC was powered to detect an overall difference across the pediatric critical care population ranging from 0 to 16 years. To draw firm conclusions regarding the effect of HFNC in each of the age groups, trials powered to detect differences in each age group would need to be performed. We agree with Shen and colleagues that future trials should focus on clarifying the differential effect of HFNC in clinically relevant age groups.

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Pricing of Drugs With Evidence Development

To the Editor A recent Viewpoint[1] by Dr Robinson that discussed the Alzheimer drug aducanumab (Aduhelm) argued that the US should adopt "pricing with evidence development." However, this approach appears to adopt some overly simplified assumptions about the nature of evidence and the definition of *value*.

In the case of aducanumab, is "value" the clinical benefit of slowing the onset of disease, maintaining capacity for continuing employment, reducing the need for long-term care and hospitalization, or a composite score of these and other possible indicators? Is it sufficient to rely on a surrogate measure, as was done by the US Food and Drug Administration when it approved aducanumab?[2] How much agreement among scientists is required to determine if an outcome is clinically meaningful? Are existing arrangements that rely on the pharmaceutical industry to finance and design clinical studies appropriate to ensure "evidence-based" studies? Might there be other approaches in collaboration with government or not-for-profit organizations?[3]

The answers to these questions will shape the evidence that is sought and analyzed. What counts as the "right" evidence, and the ways in which those who perform the studies are held accountable to the public, are politically and ethically embedded decisions. The challenge of applying the "principles of value-based drug pricing" pales in comparison to determining how to address these fundamental issues. While the proposals presented in the Viewpoint[1] might make the drug approval process more transparent, they would be strongly opposed by the lobbying power of those who currently benefit from minimal price controls, including Big Pharma and medical device manufacturers. The approach proposed by Robinson[1] reflects a strictly economic solution to a pressing policy issue. When invoking the German experience with price negotiations based on available evidence, the author ignored the societal factors and institutions that make implementation of these ideas so difficult.[4] Abstract models and tools based solely on economic models without recognition of the role of politics, culture, and societal values conjures up proposed ideal solutions that turn out to be neat, plausible, but simplistic given the current financing and organization of the US health system.

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In Reply In response to my recent Viewpoint,[1] the comments from Dr Gusmano and colleagues appear to abide by the principle that for every complex and challenging problem, there is a response that makes the problem even more complex and more challenging. Here, the challenge is that the extent of evidence of the clinical benefit of a drug often is limited at the time of initial launch and then increases and improves over time. My Viewpoint proposal was to begin with a low price of the drug at the time of market launch and then raise (or lower) the price commensurate with the evolution of the evidence. In contrast, Gusmano and colleagues suggest that before this can be done, there needs to be agreement on how to define and measure value (suggestions include clinical indicators, effects on productivity, reductions in other forms of care, composites, indexes, and surrogates); agreement on how much agreement counts; agreement on decisions about who gets to decide, who gets to finance clinical research, how studies can be held "accountable to the public"; and, last but not least, agreement on how to take into account "societal factors and institutions." This proposed list of required agreements is well intentioned but would ensure stasis and protect the dysfunctional status quo of pharmaceutical pricing.

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Review of the Diagnosis and Management of Lumbar Spinal Stenosis

To the Editor In a recent Review of the diagnosis and management of lumbar spinal stenosis,[1] the authors concluded that "[s]elected patients with continued pain and activity limitation may be candidates for decompression surgery." However, the assumption that surgery is beneficial is based on their statement, "These trials of decompression have important limitations including the substantial crossover in SPORT [the Spine Patient Outcomes Trial]." The conclusions of the SPORT trial[2] favoring surgery over nonoperative care were based on the as-treated analyses, in which 40% of participants from the nonoperative group crossed over to the surgical group; the intention-to-treat analyses, however, were not clinically or statistically significant. A 2015 study[3] that randomized 169 patients to decompressive surgery or nonoperative care found no between-group differences in physical function improvement or pain in the intention-to-treat or complier average causal effect analyses, concluding that "without a control group it is not possible to judge success attributable to either intervention." The most recent Cochrane review comparing surgery with nonoperative care for lumbar spinal stenosis was published in 2016 and included 5 randomized clinical trials with a total of 643 participants.[4] This Cochrane review concluded that existing evidence demonstrated no clear benefit of surgery compared with nonoperative treatment and that the quality of evidence was generally considered low.[4]

The lack of evidence supporting surgery for lumbar spinal stenosis extends to a lack of evidence about specific characteristics that identify patients who are more likely to benefit from surgery. Therefore, the statement that "[s]elected patients with continued pain and activity limitation may be candidates for decompression surgery" is unsupported.