

the estimated treatment effect can be biased. This is known as confounding by indication and can be adjusted for in the statistical analysis. However, adjustments can be made only for prognostic factors that were measured in the study. Prognostic factors that were not measured may introduce hidden bias, for which adjustment is not possible. Any statistical method that aims to adjust for confounding by indication suffers from this problem, which is by no means restricted to propensity score methods! Propensity score methods may even have particular advantages over other correction methods. Therefore, the chosen title of the Editorial View was in our view very unfortunate.¹

Prognostic factors can influence the treatment effect only if the factors are related both to the patient outcome and to the assignment of treatment. This implies that two different analytical strategies are possible. Conventionally, the measured prognostic factors are directly included in a regression model together with the assigned treatment and with the patient outcome as a dependent variable (treatment model). The propensity scores method contains two steps. First, the focus is on the association between the assigned treatment (dependent variable) and the prognostic factors, to develop a so-called propensity score. The propensity score predicts the probability of having received the index treatment based on the prognostic factors. Second, the focus is on the association between the patient outcome and the prognostic factors included as one combined variable (*i.e.*, the propensity score) together with the assigned treatment. The propensity score is here used to adjust the treatment effect for all prognostic factors.²

Nuttall *et al.* seem to suggest that both analytical methods are equally insufficient. We like to stress that propensity score methods have particular advantages when the outcome event is rare, the treatment is common, and many prognostic factors are collected.³ The low number of outcome events in fact limits the number of prognostic factors that can be included in the conventional treatment model. A low ratio of "number of events over number of included factors" jeopardizes proper estimation of the treatment effect in the regression analysis. In contrast, the numbers of patients in the two treatment groups are generally high. This allows for adequate modeling of the association between the treatment assignment and many prognostic factors—a high ratio of "number of patients with the treatment over number of included factors." Subsequently, the treatment model includes only the assigned treatment and the propensity score, allowing for a proper and adjusted estimation of the treatment effect, despite the low number of outcome events. The efficiency of propensity

scores in relation to the number of outcome events has been shown in a previous study, where propensity scores were found to produce less biased, more robust, and more precise estimates when fewer than seven events were available for each prognostic factor.⁴

Like any other correction method in observational therapeutic studies, propensity scores cannot control for hidden bias. However, sensitivity analysis has been proposed to indicate the magnitude of hidden bias that should be present to alter the conclusion of the study.⁵ Furthermore, propensity scores cannot fix other potential methodologic bias, as discussed by Nuttall *et al.*, which again applies also to the conventional approach. Propensity scores do not pretend to solve these problems. Hence, propensity scores can not be considered as "liars."

In conclusion, Nuttall *et al.* discussed confounding by indication as an important weakness of observational therapeutic studies. However, when for ethical, economical, or practical reasons randomized trials can not be conducted, observational studies are the only appropriate alternative.⁶ Imbalance in prognostic factors can be adjusted for in the analysis. Particularly when the number of outcome events is small, propensity score methods can more efficiently adjust for the imbalance than can conventional methods. Sensitivity analysis may complete the statistical analysis to study possible effects of hidden bias.

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In Reply:—I would like to thank the journal *ANESTHESIOLOGY* for the opportunity to respond to these letters to the editor. In general, the purpose of our editorial¹ was to educate the anesthesiologist community on the strengths and weaknesses of propensity analysis. It was not meant to advocate or demean this type of analysis. I will respond to each letter sequentially.

Dr. Engoren is correct that observational studies should be encouraged as a complement to prospective randomized studies. He is also correct that there are limitations and biases to prospective randomized control trials, which he enumerates. Despite these limitations, they are still considered the gold standard.

Drs. Vincent and Sakr are correct that one of the strengths of their study is the very large size of the Sepsis Occurrence in Acutely Ill Patients database.² It also is a weakness in that they are using data from another study that was designed for another purpose. They are correct that their statistical analysis is well performed. The comment in our editorial about the statistical process being opaque, simulating a "black box," was intended as a general comment about propensity analysis, not specifically their propensity analysis.

Drs. Boylan and Kavanagh are correct that our editorial was long on methods and short on biology. This was intentional because we had a limited word count and the goal of our editorial was to educate the

anesthesiologist community on the strengths and weaknesses of propensity analysis. In searching through the literature, I found very few articles describing propensity analysis in the anesthesia literature. The authors do a very nice job describing the biology.

Dr. Vergouwe *et al.* are correct that propensity scores do not necessarily lie, but to nonstatisticians they are mysterious. The authors are correct that the title was a play on the quote by the English Prime Minister Benjamin Disraeli (1804-1880). Though the title was provocative, we tried to write a balanced editorial on the strengths and weaknesses of propensity analysis. I trust that the anesthesiologist community is smart enough not to be biased by a title in a single editorial.

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When Is a Single-injection Nerve Block Not Really a Single Injection?

To the Editor:—I read, with interest, the case report describing a brachial plexopathy after an ultrasound-guided interscalene block in a patient with multiple sclerosis¹ and the accompanying editorial² and would like to make an observation not mentioned in either.

Interscalene blocks have been performed using either mechanical paresthesia or electrical nerve stimulation, for decades, with success rates reported to be 94–99%.^{3–5} In both of these techniques, the entire dose of local anesthetic is injected upon eliciting the initial desired response. These true single-injection techniques occur at the first nerve root, and likely the most superficial one, encountered. Perlas *et al.* used real-time ultrasound to quantify the sensitivity of both paresthesia and motor nerve stimulation techniques. A 22-gauge insulated needle was in the axilla of 103 patients, and after visualizing direct needle-nerve contact, the patients were asked whether they felt any paresthesia. The nerve stimulator was then turned on, and a motor response was sought at 0.5 mA or less. The authors concluded that there are a significant number of false-negative responses (direct needle-nerve contact *not* resulting in paresthesia or motor response) with these traditional methods of localization.⁶ This study showed that direct ultrasound visualization does not prevent intimate needle-nerve contact. Although Koff *et al.*¹ note that their needle “was not seen to penetrate the epineurium by [their] ultrasound image” after the first injection at C5, one must wonder how that initial volume of injection altered the ability to discern the needle-nerve relation of the three subsequent injections/maneuvers used to complete the block.

One of the many questions that needs to be addressed, as we continue to promote the benefits of ultrasound for peripheral nerve blocks, is whether there are any advantages to repositioning a needle

multiple times to be able to visualize local anesthetic spread around each of the nerve roots, because our historic success rates imply that this occurs adequately, with the initial injection. That is, does this practice of diving for individual and deeper nerve roots actually increase the risk to patients? The enemy of very good may prove to be better.

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Ultrasound-guided Regional Anesthesia: Why Can't We All Just Stay Away from the Nerve?

To the Editor:—Hebl's response¹ to the case report by Koff *et al.*² highlights the quagmire that anesthesiologists have been stuck in since the invention of the nerve stimulator. This quagmire is “How close can I get to the nerve?” Because mechanical trauma and the risk of intraneural injection are two risk factors we have control over, shouldn't we be asking instead “How can I stay away from the nerve?”

Great regional anesthesiologists such as Winnie, Beck, and Dalens have published elegant block techniques using a detailed understanding of anatomy and fascial planes that do not require immediate proximity of the needle to the nerve.^{3–5} Today, we can use high-resolution ultrasound to visualize nerves, blood vessels, and fascial planes. Why not use this new technology to position the needle accurately in a fascial plane containing the nerve rather than as the “visual equivalent of a nerve stimulator”? Small wonder that those still trying to “position the tip of the needle next to the nerve and get a donut sign” have not demonstrated any outcome differences using ultrasound techniques.

At the University of Utah (Salt Lake City, Utah), we have adopted the philosophy correctly stated by Marhofer *et al.*⁶: “Nerves are not blocked by the needle but by the local anesthetic.” The results have been encouraging. All of our techniques for single and continuous nerve block placements are performed by injection into fascial planes containing the nerve and *not* by attempting to place the needle in close proximity to the nerve. We have performed more than 6,000 blocks using only ultrasound guidance, including more than 3,800 continuous catheters. A recent prospective study of 200 single and continuous

interscalene blocks performed here using only ultrasound guidance showed a success rate of 99%, with only 1% of patients having mild, transient sensory deficits.⁷ This is a considerable improvement over existing data for nerve stimulator techniques.^{8,9} Our published data for 620 outpatients with ultrasound-guided femoral, sciatic, and interscalene catheters also show high success and low complications in comparison with nerve stimulator techniques.¹⁰ As ultrasound gains more widespread application, additional outcome data will follow.

To say that ultrasound will not significantly improve patient safety is shortsighted. Many of the early techniques for ultrasound-guided blocks are still a variation on the nerve stimulator theme of “put the needle as close as possible to the nerve.” As we learn to use ultrasound to stay away from the nerve instead of getting close to it, we may be pleasantly surprised by the results. Dr. Hebl and others suggest that in ultrasound we have not found the “holy grail” of regional anesthesia.^{1,11} In our opinion, it could be the “holy grail”; we simply must know how to use it.

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