

# Personalization over Protocolization

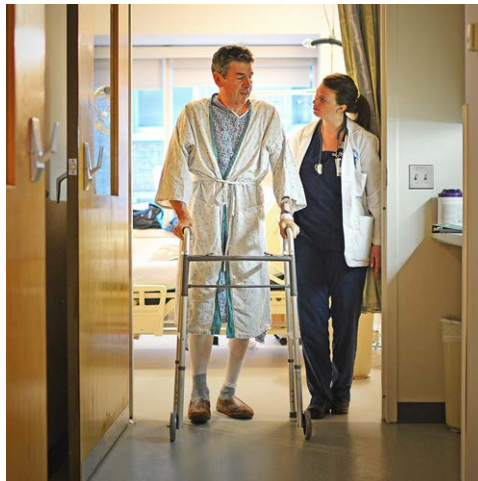
## Embracing Diversity of Pain Trajectories after Surgery

Kristin L. Schreiber, M.D., Ph.D., Jochen D. Muehlschlegel, M.D., M.M.Sc.

An estimated 240 million surgeries are performed worldwide each year.<sup>1</sup> The International Association for the Study of Pain named 2017 the “Year of Pain after Surgery,” highlighting the problem of acute and chronic postsurgical pain. Despite this increased recognition, as well as a longstanding history of excellent study of the mechanistic underpinnings of postsurgical pain in the preclinical literature<sup>2</sup> and all the enhanced recovery after surgery protocols that have been thrown at this problem, acute postsurgical pain remains a problem for a substantial number of patients. Previous larger studies (22,000 patients) suggest that 28% of patients still experience moderate-to-severe acute pain after surgery,<sup>3</sup> and higher pain trajectories have been associated with more frequent returns to the emergency department and readmission.<sup>4</sup>

In this issue of *ANESTHESIOLOGY*, Vasilopoulos *et al.*<sup>5</sup> report their empiric discrimination of the postoperative pain trajectories of patients in the 7 days after undergoing major elective noncardiac surgery. The importance of looking at pain trajectory *versus* a single point in time or an average of pain scores over time (area under the curve) is that it represents a patient’s pain experience over the duration of their care, graphically visualizing the time course of pain, including a sense of its stability and resolution, and allowing a more complete overall picture of analgesic benefit. As practicing anesthesiologists, we intuitively know that there is diversity in how people recover from surgery and that it is not bimodal (doing well, doing poorly).

The prospective and iterative approach taken by Vasilopoulos *et al.*<sup>5</sup> aimed to cluster patients with similar



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to go to improve postoperative pain management, and this is despite 78% of patients receiving some sort of regional block.

One of the most important improvements of this study over previous studies describing postoperative pain trajectory is the inclusion of more careful phenotypic measurement of patient traits to allow a more meaningful indexing of patients falling into a given trajectory. Although previous articles have described various trajectories, often no meaningful prediction could be attempted, because little other than demographic information was known about the patients within any given trajectory. In the article by Vasilopoulos *et al.*,<sup>5</sup> more numerous identifying markers were attached to the probability of falling into one of these trajectories. Consistent with prior studies assessing postoperative pain risk, being young, female, and scoring

patterns and identified five unique postoperative trajectories, which is distinct from most previous descriptions, which typically have discerned only two or three trajectories. Their concise, clinically relevant descriptions of each of these groups revealed that, similar to previous trajectory work, most of the groups were primarily defined by the pain intensity/severity (high, moderate-to-high, moderate-to-low, and low), with the exception of a single group with a vastly different temporal pattern (descending pain group). It is in fact somewhat surprising that, despite allowing for a variety of trajectory shapes, only one group was distinguished by its slope, whereas all others were distinguished primarily by severity. Furthermore, it is also notable that 63% of patients were in the moderate-to-high or high pain group. This suggests that we still have a long way

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high on anxiety is associated with a worse pain trajectory after surgery. However, the presence of urological procedures (which typically involve less actual tissue disruption) in older men in the sample may have falsely amplified the female–male divide. Interestingly, preoperative opioid use was not significantly associated with higher severity pain trajectories.

Inclusion of validated and more detailed measures of pain (Brief Pain Inventory, a commonly used validated research measure of pain that includes an assessment averaging across 24h) ensured a higher fidelity assessment of the outcome. Similarly, use of validated brief measures of pain-relevant traits such as the Patient-Reported Outcomes Measurement Information System (PROMIS) short forms for anxiety, depression, and pain behaviors, as well as such measures as the Pain Catastrophizing Scale, ensured more sensitive measurement of predictors, a huge improvement over the typical dichotomous assessment of anxiety or depression diagnosis from the often-incomplete electronic medical record. The presence of these validated, sensitive measures likely allowed one of the key findings, which agrees with some other previous work, that the characteristics of the person having the surgery are more important than the surgery itself in determining how much postoperative pain one will experience. Notably, procedure type was not a key determinant of pain trajectory group assignment. This underscores the importance of including such measures in studies of acute pain, which has been recommended by an expert consensus group.<sup>6</sup>

Given this insight, we might ask ourselves why are all of our enhanced recovery after surgery protocols based on the surgical type? Perhaps moving forward toward more personalized perioperative medicine, distinct enhanced recovery after surgery protocols for the “person type” would prove more useful for treating pain. An example of this one-protocol-fits-all thought process, which the authors emphasize, is the application of regional anesthesia. Application of regional anesthesia has been based purely on the surgical type itself and how much pain a given surgery causes on average. The data of Vasilopoulos *et al.*<sup>5</sup> suggest that it may be more important to consider the individual and their particular pain phenotype in the decision to apply regional anesthesia. For example, if the individual’s risk factors suggest they will experience a more severe and prolonged pain trajectory after surgery, use of regional anesthesia should be more strongly considered, even for less extensive surgeries. Although there is some evidence that stratifying for high-risk characteristics (such as pain catastrophizing) may allow more sensitive assessment of postsurgical pain prevention by regional anesthesia,<sup>7</sup> future studies are needed to test this principle.

The authors included preoperative pain behavior as a predictor in the model, which was found to be an important predictor of trajectory group. The implication is that knowing how much pain a person has experienced in the

past will give insight into how they will react in the future. This is comparable to what the Pain Catastrophizing Scale does: it asks people to reflect on their own mental processes that occur when they have pain. Similarly, simply asking people how much pain they expect to have turns out to be a good predictor as well. Notably, despite a strong association between catastrophizing and postoperative pain intensity, the Pain Catastrophizing Scale score was not a predictor of group trajectory assignment, perhaps because both preoperative pain behavior and pain catastrophizing were included in the model.

As Vasilopoulos *et al.*<sup>5</sup> point out, modeling pain intensity rather than pain interference or other functional impacts of pain may not get as close to what is most relevant to the patient experience. Sorting patients by pain impact rather than pain intensity could arguably get us to a more clinically meaningful categorization. However, for now, the 0 to 10 pain scale still remains clinically ubiquitous and familiar and probably serves as a reasonable proxy for pain impact.

Last, although decreasing acute pain is laudable and important, a more important consideration is preventing chronic pain. We hope that by decreasing acute pain, we make chronic pain less likely. However, we should exercise caution in observing the strong association of acute and chronic pain. Although it is tempting to infer causality (acute pain is not well controlled, which leads to more chronic pain), it is likely that this strong association between acute and chronic postsurgical pain may simply reflect a higher tendency toward pain sensitivity within an individual, sampling at two different time points. Although as clinicians we would love to prevent chronic pain by simply improving acute pain management, this has yet to be definitively demonstrated. Future studies comparing predictors of acute *versus* longer-term trajectories might give insight into the most consistent modifiable targets for future interventions. In any case, the current work suggests that careful assessment of the traits of the individual patient may afford us better prediction of which patients may be at greater risk of uncontrolled pain, independent of and possibly more important than the surgery they are undergoing.

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## Correspondence

Address correspondence to Dr. Muehlschlegel: jmuehlschlegel@bwh.harvard.edu

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