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Commentary: Picking the winners—Leaning into selection bias

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CENTRAL MESSAGE

In rare conditions requiring specialized care, treatment success is often driven by careful selection. One must be aware of this selection bias and strive to understand the critical selection factors.

To this day, mesothelioma remains a deadly disease with few treatment options. Although immunotherapy, new radiation techniques, and improving surgical safety and efficacy have revolutionized most of thoracic oncology, the principles of treatment for this rare and fatal malignancy have remained largely unchanged for a generation. Particularly for the aggressive histologic subsets of the disease, outcomes are driven by biology, and surgeons have been reluctant to offer aggressive surgery when the recurrence rates and survival have been so poor. Thus, before we take away any further conclusions from their article in this issue of the *Journal*, Lococo and colleagues¹ are to be commended for approaching a topic that most view with a great degree of nihilism.

Given the rarity of these diagnoses and the difficulty in recruiting patients for clinical trials, retrospective studies may provide the highest standard of evidence practicable. This presents many difficulties for the practicing surgeon—first and foremost is the challenge in interpretation of studies so clearly saddled by selection bias. How do practicing surgeons know which results are “real” and which are the result of mathematical chance or the limitations of statistical adjustment? The answer may lie in a better understanding of the context of the results, that is, the inclusion/exclusion criteria and practice patterns that produced the findings. Lococo and colleagues¹ attempt to demonstrate a comparison between patients receiving pleurectomy and

decortication (27.2%) and those treated without surgery, usually in the form of systemic chemotherapy (46.5%). They conclude that surgery is indicated for these patients because their survival in the study was “better.” Certainly, the influence of selection cannot be ignored, but, perhaps more significantly, Lococo and colleagues¹ only provide minimal information on the criteria for said selection: for example, the exclusion of patients undergoing extrapleural pneumonectomy, or the decision process by which a patient is deemed by these surgeons as having “resectable” disease, or how surgeons in this series decided to submit a patient to an “aggressive” pleurectomy versus what amounts to a debulking, with a complete resection achieved in only 40%. Of additional import is the fact that 26.3% were treated only with best supportive care, but it is not clear either how the decisions for no treatment were made. These crucial details could help others to understand what outcomes can be expected should they similarly select (and similarly treat) their patients. Furthermore, these details can help us to understand otherwise seemingly incongruent results, such as the fact that complete resection or TNM stage did not predict outcomes in this investigation. The surgical research community has focused largely on the advantage of addressing selection bias provided by a randomized trial, but such trials also have the advantage of internal validity; in other words, if you select a similar patient to those

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included, the outcomes described should likewise be achievable with the described treatment protocol. Whereas most investigators have approached the issue of selection bias with the mind-set that it should be eradicated at all costs, a “lean in” approach to selection might in fact produce results that are more meaningful and useful to the practicing surgeon when a retrospective look at patient outcomes is the only practical possibility. For example, these data are not likely to be useful in centers where surgeons are offering aggressive approaches, such as complete resection through extrapleural pneumonectomy, usually in combination with radiation and chemotherapy.² Given that Lococo and colleagues¹ do not fully elucidate their criteria for selecting patients who receive pleurectomy, debulking, or palliative care, however, it is difficult to know whether these new results apply. Surgeons have always “picked the winners”—that is part of the specialized expertise that requires such rigorous training to develop—but we need to describe this process better so that we can understand and compare results.

One other point that should be emphasized is that the study of Lococo and colleagues¹ is based at 4 centers

that specialize in mesothelioma. Whereas most regionalization schemes depend on a volume framework, mesothelioma may present an example of a situation in which a “disease-specific” regionalization tactic could be applied. Even among general thoracic surgeons, it is likely that the vast majority do not have the volume, interest, or complex care team required to ensure successfully that aggressive treatment can be provided appropriately and safely. Further policy experimentation, for example through statewide collaborative efforts, should focus on how to facilitate the creation and utilization of disease-specific regionalized networks for the provision of complex care to patients with these rare and difficult tumors.

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