LETTERS TO THE EDITOR

Comparative Effectiveness in Personalized Medicine—Clearly Defining the Intended Use Population

To the Editor—Najafzadeh et al. [1] recently published in Value in Health a cost-effectiveness analysis of a molecular diagnostic test to improve preoperative diagnosis of thyroid cancer. The target population for this analysis was patients with an initial indeterminate cytological diagnosis based on fine-needle aspiration biopsy (FNAB). The path to surgical excision of suspected thyroid cancer consists of a number of decisions, such as referral to an endocrinologist, obtaining tissue for initial diagnosis via a FNAB, referral to a surgical specialist, and ultimately surgical resection. Wang et al. [2] recently assessed in a large, multicenter cohort study (21 clinical sites, 753 prospectively collected FNABs) the proportion of patients who underwent surgical resection. Among the 61 patients with indeterminate pathology by FNAB, just 38 (62%) eventually underwent surgical resection, similar to the rate (58%) found in their companion “meta-review” of the literature. These rates are lower than expected based on guidelines from the American Thoracic Association [3], with Wang et al. speculating that the low rates may be related to 1) loss to follow-up, 2) resection at a different institution than where the FNAB was performed, and 3) comorbidities or preferences that preclude the patient undergoing surgery. After adjusting for these factors, they estimate that approximately 25% of the patients with indeterminate pathology on FNAB do not undergo surgical resection.

The sensitivity and specificity used in Najafzadeh et al.’s cost-effectiveness analysis presumably are based on studies of patients who have undergone surgical resection [4]. The test’s accuracy therefore is known for the population of patients with indeterminate pathology by FNAB who have undergone surgical resection, but is not directly known for the population of patients who do not undergo resection; hence, it may seem reasonable to assume that the rate of thyroid cancer and the test characteristics are similar in these two populations. But it is important that clinicians and policymakers appreciate that this remains an assumption.

Further research is needed to understand the appropriate use and cost-effectiveness of the test at the referral decision point. Long-term follow-up on the rate of thyroid cancer among the patients who were not referred is needed. It would also be useful to have direct evidence on the test’s accuracy in the population of patients who traditionally are not destined to undergo surgical resection. Enrolling such patients for the purpose of obtaining tissues for a “gold-standard” pathological diagnosis carries ethical considerations, and may require sponsorship and oversight by a nonpartial government research agency or nonprofit foundation. This commentary highlights the relevance of modeling the full sequence of decisions, who is making the decision, and how knowledge of a novel test’s results alters decisions.

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REFERENCES