how they align with patients' preferences and treatment limitations may be informative as we look ahead at strategies for palliative care in patients with COPD. It is certainly possible that as noninvasive ventilation becomes more broadly accepted by patients (perhaps through increased familiarity with positive airway pressure therapy for treatment of obstructive sleep apnea or home noninvasive ventilation), more patients who would not want or tolerate invasive mechanical ventilation will survive a hospitalization for AECOPD. Whether the observed reduced mortality after hospital discharge is accompanied by a reduced longer-term mortality, fewer hospital readmissions, or improved quality of life remains to be determined.

The overall reduction in mortality for patients admitted to the ICU with AECOPD, as reported in this largest study to date of trends in COPD mortality, is positive news for patients and physicians. The decrease in mortality from AECOPD over the past decade is encouraging as we look ahead. It is notable that the improvement in mortality is observed in patients who are sicker and are more likely to have comorbidities. The mortality for asthma, which was much lower to begin with, has remained unchanged over the past decade. The lack of improvement in asthma mortality may be due to the fact that with such a low rate to begin with, it is hard to observe additional improvement. However, the reduction in mortality in COPD may also suggest that clinicians in ICUs and health systems are getting better at caring for complex patients with multimorbidities. The reduction in AECOPD mortality suggests that we are improving with time, and that is good news for all. ■

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More Than Dollars and Cents: Putting a Price on Indwelling Pleural Catheter Drainage

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Malignant pleural effusions (MPEs) are common and seen in up to 15% of patients with cancer (1). They are estimated to affect over 150,000 people per year in the United States, and this is projected to increase as the global incidence of cancer rises and patients' life expectancy improves (2, 3).

MPEs are associated with poor survival, disabling dyspnea, and considerable distress. Approximately 75% of patients experience symptoms, and the mainstay for alleviating these symptoms is effective fluid control (4).

The traditional management paradigm of MPE has been slow and primarily delivered in the inpatient setting, with admission for talc pleurodesis via a chest drain being the mainstay of treatment (5). However, this approach is associated with high levels of healthcare use, with MPEs believed to account for more than 125,000 admissions annually, and more than $5 billion in inpatient-care costs per year in the United States alone (3).

Indwelling pleural catheters (IPCs) are now increasingly used as a first-line intervention for definitive control of fluid recurrence in MPEs. Two randomized controlled trials (RCTs) have demonstrated that they provide a level of dyspnea control equivalent to that obtained with conventional treatment, with lower associated inpatient stays and a reduction in subsequent reinterventions (6, 7). Despite the benefits of these catheters, however, the rates of spontaneous pleurodesis reported in retrospective studies, and more recently in prospective RCTs, have been variable and are typically lower than those achieved by talc pleurodesis via a standard chest drain (8).

In the last few years, three high-quality RCTs have explored optimal IPC drainage strategies and their effects on pleurodesis

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rates. In the North American ASAP (Impact of Aggressive versus Standard Drainage Regimen Using a Long-Term Indwelling Pleural Catheter) trial Wahidi and colleagues randomized patients to either aggressive (daily) drainage or standard (second daily) drainage, and demonstrated a significantly higher pleurodesis rate (47%) in the daily drainage group compared with the standard drainage group (24%) (9). This result was mirrored in the AMPLE-2 (Australasian Malignant Pleural Effusion 2) trial by Muruganandan and colleagues (10). They showed that there was no difference in breathlessness between an aggressive drainage strategy and more conservative, symptom-guided drainage, but the aggressive approach resulted in higher rates of spontaneous pleurodesis with a possible improvement in quality of life.

More recently, Bhatnagar and colleagues randomized 154 patients across 18 centers in the IPC PLUS (efficacy of indwelling pleural catheter placement versus placement PLUS talc sclerosant in patients with malignant pleural effusions managed exclusively as outpatients) trial (8). This demonstrated a pleurodesis rate of 43% in the intervention arm at Day 35 which was significantly higher than the 23% in the placebo group.

Although these various approaches have been shown to improve autopleurodesis rates, the associated health costs and service impacts of these strategies have not been evaluated. Establishing new strategies for the management of malignant pleural disease is a recognized priority, not only for patients but also for health services (3, 11).

In this issue of *AnnalsATS*, Shafiq and colleagues (pp. 746–753) report the results of an innovative approach, using a decision-tree model–based analysis designed to evaluate the cost-effectiveness of the three most commonly used IPC drainage strategies (12). The authors developed the model using theoretical event probability data based on aggregate data from 390 patients recruited to the three key clinical trials in the area (ASAP, AMPLE-2, and IPC-PLUS). Costs were estimated based on 2019 U.S. Medicare reimbursement data. The primary outcome was the incremental cost-effectiveness ratio (ICER) for each drainage strategy compared with alternatives over an analytic horizon of 6 months, to reflect the average survival of patients with this condition. The standard threshold of $100,000 (U.S.) per quality-adjusted life year (QALY) was used, and health utility estimates for each state (having an IPC *in situ* or achieving pleurodesis) were converted to QALYs. Health utility was assigned based on a recent observational cohort study by Jiang and colleagues (13).

A Monte Carlo probabilistic sensitivity analysis was performed to estimate the uncertainty around the ICER, given the multiple variables involved. For those with nonexpandable lung (NEL), which affects up to 30% of patients with MPE, a separate decision-tree analysis was performed that excluded the IPC+talc treatment arm.

The study results suggest that both daily drainage and talc instilled via an IPC were more effective but also more costly than symptom-guided drainage. Daily drainage was more expensive and less effective than IPC+talc, and therefore this strategy was considered "dominated" for the cost-effectiveness analysis. In financial terms, compared with symptom-guided drainage, IPC+talc provided ~0.005 additional QALYs for an additional $315. This represented an ICER of just under $60,000/QALY. A sensitivity analysis suggested that the IPC+talc strategy was more cost-effective in 54% of the simulations, whereas symptom-guided drainage was cost-effective in the remaining 46%. Symptom-guided drainage was also more cost-effective if the life expectancy was under 4 months.

According to Shafiq and colleagues' model, instilling talc through an IPC appears to be a cost-effective way to control MPE, with symptom-guided drainage being the preferred option for patients with NEL. This result prompted the authors to propose a novel algorithm for managing the average patient in the U.S. healthcare system, which involves initial symptom-guided drainage with subsequent review for talc via the IPC for patients who show no evidence of NEL and have a life expectancy of >4 months.

To date, there are limited data regarding the impact of IPC use beyond the insertion and removal of the catheter. This study by Shafiq and colleagues is the first to explore the costs associated with different IPC strategies, and is an important contribution to an area that has been underrecognized and hitherto unexplored. However, as the authors concede, this analysis is based on theoretical data, with all of its limitations, and there are several persistent uncertainties with regard to both the model and its estimates. As the authors note, if the autopleurodesis rate is >20%, such as the 24% reported in the conservative drainage arm of the ASAP study and the 27% reported in the placebo arm of the IPC-PLUS trial, the sensitivity analysis would suggest that symptom-guided drainage is the most cost-effective strategy, regardless of prognosis.

Furthermore, the analysis draws on health utility data from a small group of ambulant patients with $EGFR^+$ lung cancer, from a single Canadian center (13). This not only limits the generalizability of this work, which is already U.S.-specific, but also highlights how little we know about the true burden of continued IPC use. Jiang and colleagues calculated health utility based on the presence or absence of pleural effusion or metastases, but did not attempt to quantify the challenges that patients who undergo long-term drainage through an IPC face, and the associated impact on health utility (13).

In our center, patients with IPCs describe a therapeutic journey that involves frequent healthcare intrusions into their personal space, increased hospital and clinic visits to troubleshoot IPC-related issues, and limitations on clothing choices and activity (14). As such, it is difficult to believe that the health utility of having an IPC *in situ* is equal to not having an effusion at all.

Despite its limitations, this novel comparison is an important first step in exploring the financial burden of the three major IPC drainage strategies. Given the increasing resource constraints of modern healthcare, this analysis may guide decision making at a health policy and system level. However, as the authors acknowledge, it is important to note as clinicians that this study offers an economic perspective and not a patient-centered one. The sad reality is that despite the increasing use of IPCs, we have a limited understanding of the health utility they provide, let alone the utility provided by different drainage strategies, or how they compare with the more traditional treatment of inpatient talc pleurodesis. Until we have that desperately needed data, our role as clinicians is to understand our patients' individual needs and circumstances before helping them choose the "right" option for them. ■

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