Disparities in Adjuvant Endocrine Therapy

Elizabeth J. Cathcart-Rake, MD, and Kathryn J. Ruddy, MD, MPH

Multiple competing factors (economic, environmental, social, and personal) influence health outcomes. For many patients, the lack of adequate insurance coverage is an obstacle to timely and appropriate medical care. Cancer survivors may be particularly vulnerable to the ill effects of insufficient insurance benefits. In one recent study comparing cancer survivors with their unaffected siblings, cancer survivors were more likely to lack employer-sponsored coverage, have been denied coverage, have Medicaid, and have high out-of-pocket costs. They were also more likely than their siblings to borrow money for medical expenses, worry that they would not receive a medical procedure, and not fill a prescription.¹ Uninsured survivors suffered even greater disparities when compared with insured survivors, and were less likely to have a primary care provider or fill a prescription, and more likely to postpone preventive care.¹

Medicaid-Associated Disparities

Insufficient Medicaid benefits have frequently been implicated in the cancer-related medical disparities that are attributed to inadequate insurance. Although states are mandated to pay for certain aspects of care, such as inpatient hospital services, coverage for other needs (eg, prescription medications and colorectal cancer screening) varies by state.² Consequently, patients who are uninsured or covered under Medicaid are more likely to be diagnosed with breast and colon cancer at later stages (stage III and IV),³ and those with melanoma who have Medicaid are also more likely to experience surgical delays.⁴ In addition, in one study of patients with breast, colorectal, lung, and prostate cancers and non-Hodgkin's lymphoma, those who were uninsured and those insured by Medicaid had a significantly higher risk for death within 5 years of diagnosis than privately insured patients after adjusting for sex, age, race/ethnicity, marital status, socioeconomic status, and disease stage.⁵ Similarly, another large retrospective study of 976,178 women diagnosed with breast cancer showed that payer status was a statistically significant predictor of survival after adjusting for tumor stage, age, race, comorbidities, education, distance traveled for treatment, cancer program, diagnosing/treating facility, and treatment delay.⁶

Medicare-Associated Disparities

Although Medicare, as opposed to Medicaid, does require states to cover more comprehensive adult cancer screening, Part D prescription drug coverage still varies from state to state.² Inadequate Medicare Part D coverage may cause patients to stop taking life-saving therapies. In one large study of prescription fill rates among 10,302 women diagnosed with early-stage breast cancer and who were prescribed hormonal therapy, 24% were “nonadherent,” meaning that they possessed <80% of the number of pills that would be required for continuous therapy between their first and last prescription (termed the “medication possession ratio”), and patients with Medicare were less likely to be adherent than those with commercial insurance (odds ratio, 0.58; 95% CI, 0.46–0.72).⁷

Results and Interpretation of the Newly Published Study

The article titled, “Geographic Variation of Adjuvant Breast Cancer Therapy Initiation in the United States: Lessons From Medicare Part D,” in this issue of *JNCCN* (page 1509) adds to the current literature on cancer care disparities in that it reveals how state-level variability in Medicare Part D benefits influence adjuvant therapy prescriptions. Specifi-

Elizabeth J. Cathcart-Rake, MD

Dr. Cathcart-Rake is a Fellow in hematology-medical oncology at Mayo Clinic, Rochester, Minnesota. Her research interests include management of toxicities from cancer-directed therapy and cancer survivorship issues facing young women.

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Cathcart-Rake and Ruddy

Kathryn J. Ruddy, MD, MPH

Dr. Ruddy is an Associate Professor of Oncology and the Director of Cancer Survivorship at Mayo Clinic, Rochester, Minnesota. Dr. Ruddy is a panel member on the NCCN Guidelines for Survivorship, and she received a 2016 NCCN Young Investigator Award. She is also a Co-Chair of the Patient-Reported Outcomes Interest Group for the Translational Breast Cancer Research Consortium (TBCRC), and she serves as a Vice Chair of the Symptom Intervention Committee of the Alliance for Clinical Trials in Oncology. She primarily focuses her professional efforts on the care of patients with breast cancer and her research is focused on cancer survivorship.

cally, Charlson et al assessed the rates of initiation of aromatase inhibitors (AIs) versus tamoxifen in the treatment of postmenopausal women with breast cancer between 2006 and 2007. During this study period, AI therapy was recommended as part of treatment for postmenopausal breast cancer, but a switching strategy (ie, starting with tamoxifen and then switching to AI) was another standard treatment option. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer still permit switching from tamoxifen to AI, but allow providers to use clinical judgment when choosing among a variety of options for adjuvant endocrine therapy for postmenopausal women, including the following: AI for 5 to 10 years; AI for 2 to 3 years followed by tamoxifen to complete 5 years; tamoxifen for 2 to 3 years followed by an AI for 2 to 7 years (to either complete 5 or 10 years of total endocrine therapy); tamoxifen for 4.5 to 6 years followed by an AI for 5 years; or, for women who cannot or prefer not to take AIs, tamoxifen for 5 to 10 years.⁸ Unlike today, when both tamoxifen and generic AIs are of relatively low cost, in 2006 and 2007, AIs were substantially more expensive than tamoxifen. For this reason, the data from this study provide insights into the impact of prescription drug coverage plans on use of costly therapies.

Charlson et al found large differences between states in use of AIs as initial endocrine therapy, with percentages ranging from 57.3% in Wyoming to 92.6% in the District of Columbia. Because AIs are slightly more effective than tamoxifen at reducing risk of recurrence,⁹ these prescribing patterns are important because they may have led to lower rates of recurrence in the states where AI use was more common (although this was not evaluated in the article by Charlson et al). Consistent with prior data pertaining to disparities in other aspects of cancer care, the investigators found that several other variables were also associated with AI use, including higher income, receipt of chemotherapy (a surrogate for higher-risk disease), and living in a county with a greater density of physician specialists (measured by number of radiation oncologists). Rural women and those living in a community with a greater density of elderly women were more likely to receive tamoxifen. Interestingly, after controlling for these relevant covariates, the authors reported that variations in Part D plans explained 30% of the variability in practice patterns from state to state.

This study, coupled with prior work by Hershman et al,⁷ showing that insurance status is correlated with lower patient adherence to hormonal therapy, suggests that inadequate prescription coverage influences the therapies received by patients with cancer, potentially exacerbating disparities in outcomes. Compounding this concerning disparity is the increasing number of expensive oral oncologic therapies (many much more costly than AIs, even at their peak price). The relatively rapid approval of these pricey new medications has skyrocketed costs: many new oral cancer therapies cost more than \$100,000 USD.¹⁰

The finding that 70% of practice pattern variability was unrelated to Part D variability also deserves attention. The decision to prescribe a particular medication is subject to physician preference, which can be influenced by comfort with the medication and side effects. Charlson et al explain that both drug marketing efforts and the availability of treatments for a drug's side effects (eg, bisphosphonates for AI-induced osteoporosis) may have played a role in the state-to-state variations they found.

Conclusions

In 2006 and 2007, when AIs were much more expensive than tamoxifen, adjuvant endocrine therapy prescribing patterns were partly driven by Medicare Part D coverage. As the insurance market, healthcare policies, and cancer treatment recommendations rapidly change, additional studies that investigate contemporary cancer care patterns will be needed (particularly regarding newer oral targeted therapies that cost multiple thousands of dollars per month). As more oral antineoplastic therapies are introduced, oncologists will need to advocate for affordable drug prices, help patients identify and access financial assistance programs, and keep up-to-date on guideline-recommended care to facilitate informed treatment decisions.

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