Metastatic colorectal cancer (mCRC) is diagnosed in approximately 22% of newly diagnosed colorectal cancers (CRCs).1 Outcomes for mCRC are poor, with an estimated 5-year survival of approximately 15%, in part due to limitations of traditional treatment modalities.2 The advent of precision oncology, highlighting the molecular heterogeneity of CRC, has brought about an expansion of biomarker assessments for targeted treatment options. Genetic variants, including KRAS, microsatellite instability (MSI), BRAF, and ERBB2 (formerly HER2), represent actionable therapeutic targets for patients with mCRC.3,4 Accordingly, the National Comprehensive Cancer Network guidelines recommend universal biomarker testing in all patients with mCRC because these results can have substantial implications for therapeutic choices and treatment response.5 Nonetheless, uptake of biomarker testing remains suboptimal, with disparate variations in use among patients with mCRC.6

Sabbagh et al7 explored testing of 2 genetic biomarkers, MSI and KRAS, in patients with mCRC, investigating the association of sociodemographic factors (age, race and ethnicity, educational level in area of residence, median household income, insurance type, area of residence, facility type, and facility location) with completion of biomarker testing and overall survival (OS). The authors used the National Cancer Database to identify 41,061 patients diagnosed with mCRC over a 7-year period (2010-2017). Only 28.8% and 43.7% of these patients underwent MSI and KRAS testing, respectively. Sociodemographic factors associated with a lower likelihood of MSI and KRAS testing included advanced age (70-79 years), rural residence, lower educational level in area of residence, and treatment at a community (vs academic) cancer center. Geographic location (US Census division) was also a factor, with treatment at East South Central facilities associated with lower testing. Biomarker testing increased throughout the study duration and was associated with a modest OS improvement (hazard ratio, 0.93; 95% CI, 0.91-0.96) over a follow-up period of 13.96 months.

Based on these findings, the authors emphasized the substantial underuse of biomarker testing nationally and highlighted the sociodemographic disparities in biomarker testing. In this study,7 older age (70-79 years) was associated with lower biomarker testing. While it is plausible that older patients may want to avoid testing and treatment, this assumption may not fully explain the observed age disparity. It is unclear from this study how older age overlaps with comorbidity and in patients with an unknown CRC grade, limiting our understanding of why the older population may potentially avoid testing due to health status or disease severity. There is a need to carefully examine and eliminate the barriers encountered by older adults while accessing mCRC care.

Rural-urban disparities have long plagued the health care system and have been previously described for mCRC. Rural-dwelling individuals continue to experience inferior outcomes for mCRC compared with their urban-dwelling counterparts.8 A prior study of barriers to biomarker testing, as described by 99 rural and urban practicing oncologists in the US, found lack of insurance coverage, prolonged result turnaround time, and insufficient tissue samples for external laboratories to be the most cited barriers to biomarker testing in rural areas.6 This study also found that less than half of rural oncologists had access to reflex biomarker testing.6 Sabbagh et al7 found that rural residence was associated with a lower likelihood of MSI testing only but not KRAS testing. The authors did find a lower likelihood of testing for both MSI and KRAS testing in East South Central states (compared with the New England region), which have some of the highest rates of rural populations in the US. This

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study brought forth questions as to why there are differences in obtaining some biomarker tests but not others and whether there are opportunities to operationalize biomarker testing to decrease variability by treatment location.

To that end, the study by Sabbagh et al7 expanded on known outcome differences between academic and community cancer centers. With over 50% of patients with mCRC being treated within community settings,9 community health care facilities have an integral and indispensable role in the US health care infrastructure. If not bridged, the gaps in biomarker testing, as highlighted in this study, will likely be a factor in worsening outcome disparities, especially as effective biomarker-driven therapies become increasingly available.3 Future work should include identifying the facilitators of and barriers to accessing pathology services.

Medicaid coverage compared with private insurance was associated with lower KRAS testing only, supporting the integral role that insurance coverage likely plays in completing biomarker testing. Although it is reassuring that biomarker testing increased through the duration of the study, it remains unclear whether this pattern is indicative of increasing insurance coverage for testing or other undetermined factors that could not be explored in this analysis. Additionally, the study did not find an association between race and ethnicity and biomarker testing. Yet, the mitigation of confounding variables, specifically the interplay between race and ethnicity and insurance, was only briefly described.

We applaud Sabbagh et al7 for focusing on individual sociodemographic factors associated with biomarker testing. Their study elevated the need to assess and mitigate system-level barriers to accessing and completing biomarker testing for underserved populations. System-level interventions will be required to successfully facilitate community care in predominately rural areas with limited access to tertiary care testing and treatment. Considerations for future work may include identifying best practices to linkages to care in these areas, exploring opportunities for reflex testing for all biomarkers that could affect treatment options for mCRC, and creating infrastructure to apply best practices to all populations. Such work will need to occur in conjunction with developing and disseminating educational materials that are inclusive of all educational levels to highlight the importance of biomarker testing for personalized treatment options.

Moving forward, as giant strides are made toward the implementation of personalized medicine in mCRC care, sociodemographic-based disparities must continue to undergo a nuanced investigation, with increased focus on system-level barriers to ensure equitable access to testing and treatment. Work remains to be done to further disentangle the factors in these disparities. We must move beyond describing disparities and toward implementing strategies that mitigate disparities and decrease the divide in mCRC care.

ARTICLE INFORMATION
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