

# Molecular Tumor Board Review and Improved Overall Survival in Non–Small-Cell Lung Cancer

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**PURPOSE** With the introduction of precision medicine, treatment options for non–small-cell lung cancer have improved dramatically; however, underutilization, especially in disadvantaged patients, like those living in rural Appalachian regions, is associated with poorer survival. Molecular tumor boards (MTBs) represent a strategy to increase precision medicine use. UK HealthCare at the University of Kentucky (UK) implemented a statewide MTB in January 2017. We wanted to test the impact of UK MTB review on overall survival in Appalachian and other regions in Kentucky.

**METHODS** We performed a case-control study of Kentucky patients newly diagnosed with non–small-cell lung cancer between 2017 and 2019. Cases were reviewed by the UK MTB and were compared with controls without UK MTB review. Controls were identified from the Kentucky Cancer Registry and propensity-matched to cases. The primary end point was the association between MTB review and overall patient survival.

**RESULTS** Overall, 956 patients were included, with 343 (39%) residing in an Appalachian region. Seventy-seven (8.1%) were reviewed by the MTB and classified as cases. Cox regression analysis showed that poorer survival outcome was associated with lack of MTB review (hazard ratio [HR] = 8.61; 95% CI, 3.83 to 19.31;  $P < .0001$ ) and living in an Appalachian region (hazard ratio = 1.43; 95% CI, 1.17 to 1.75;  $P = .004$ ). Among individuals with MTB review, survival outcomes were similar regardless of whether they lived in Appalachia or other parts of Kentucky.

**CONCLUSION** MTB review is an independent positive predictor of overall survival regardless of residence location. MTBs may help overcome some health disparities for disadvantaged populations.

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## BACKGROUND

The American Cancer Society estimates that 235,760 new cases of lung cancer will be diagnosed in the United States in 2021 and 131,880 patients will die of their disease. Lung cancer remains the leading cause of cancer mortality.<sup>1</sup> Kentucky leads the nation in both the rate of new cases and deaths because of lung cancer, with the Appalachian region carrying the highest cancer burden.<sup>2,3</sup> Non–small-cell lung cancer (NSCLC) is the major histologic subtype, comprising 76% of all lung cancer diagnoses. Despite these dire statistics, both incidence and mortality attributed to NSCLC are declining in the United States. Nationwide, incidence declined 3.1% among men and 1.5% among women annually between 2008 and 2016. It is even more encouraging that, during the same period, the incidence-based mortality decreased by 6.3% and 5.9%, among men and women, respectively. Improvements in survival exceed decreases in incidence, suggesting that treatment advances contribute substantially beyond efforts to

reduce incidence.<sup>4</sup> Unfortunately, Kentucky is not achieving these survival gains.<sup>2</sup>

Improvements in treatment for NSCLC therapies have come not only in the development of novel therapeutic modalities but also in the introduction of precision medicine.<sup>5</sup> Precision medicine requires testing tumor or blood for cancer-causing mutations with next-generation sequencing (NGS). Individuals with a particular mutation or biomarker can receive a targeted therapy specific to their mutation, and these targeted therapies consistently improve clinical outcomes and quality of life while reducing adverse effects, when compared with conventional chemotherapy not guided by NGS.<sup>6,7</sup> Given the benefits of targeted therapies and the many mutations identifiable by NGS, precision medicine is now guideline-concordant, evidence-based care for all patients with stage II-IV NSCLC.<sup>8</sup>

Despite these benefits, precision medicine remains underutilized,<sup>9-11</sup> especially in rural and medically

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## CONTEXT

### Key Objective

What is the impact of a state-wide, virtual, molecular tumor board (MTB) on overall survival (OS) in patients with non–small-cell lung cancer?

### Knowledge Generated

Patients with non–small-cell lung cancer reviewed by an MTB had improved OS when compared with propensity-matched controls without an MTB review. Benefit of the MTB was consistent for patients treated in both academic and community medical oncology practices and living in urban and rural areas.

### Relevance

MTBs improve OS and may be a strategy to overcome disparities in rural underserved populations.

disadvantaged areas, such as in Appalachian Kentucky.<sup>11-13</sup> There are both patient and physician barriers to NGS testing. Patients are not tested when they have rapidly progressive disease or inadequate tissue for testing, often because of being a poor surgical candidate. Physicians report a lack of awareness of NGS benefits, limited experience in interpreting and acting on NGS results, and lack of support and training needed to incorporate this testing into their routine practice.<sup>14-17</sup> Since NGS reports are often extensive and complex, it can be challenging for clinicians to use the information to determine the best therapy. Molecular tumor boards (MTBs) have been developed at multiple academic medical centers to address physician barriers to precision medicine, providing guidance on the use of NGS reports.<sup>18-22</sup> Importantly, availability of an MTB increases physician willingness to order and use NGS testing.<sup>23</sup>

MTBs are generally composed of a multidisciplinary team including medical oncologists, surgical oncologists, genetic counselors, pathologists, pharmacists, radiologists, and basic scientists,<sup>19,21</sup> working together to provide recommendations to clinicians for targeted therapy and clinical trials on the basis of each patient's diagnosis and NGS results. Inclusion of genetic counselors enables MTBs to also provide recommendations for genetic testing in cases where a potential germline mutation is identified, which can add further value to the family members of patients who may benefit from early cancer screening. A recent systematic review, including 14 studies and 3,328 patients with cancer who were assessed by an MTB, concluded that although the quality of data is limited, MTBs appear to improve clinical outcomes.<sup>24</sup> In addition, a large cohort from the University of California San Diego demonstrated improved progression-free survival and overall survival (OS) in patients where MTB recommendations were followed when compared with patients who received a physician's choice regimen.<sup>25</sup>

An MTB was implemented at the University of Kentucky (UK) Markey Cancer Center (MCC) in 2017. To assess the impact of the UK MCC-MTB on OS of patients diagnosed with NSCLC in Kentucky, we conducted a case-control

study to compare OS between patients reviewed by the UK MCC-MTB and patients without review.

## METHODS

### UK MCC-MTB

An MTB was implemented at the UK MCC on January 1, 2017, as a statewide resource, available at no charge to all Kentuckians, for review of genomic results and recommendations for treatment regardless of testing strategy. The UK MCC-MTB was publicized via the UK website and discussed with research and clinical affiliated hospitals throughout Kentucky and by personal communication. We anticipate that this was or is the only MTB available to treating physicians in Kentucky. There are no local MTBs at any Kentucky adult oncology practice, and although commercial testing companies provide interpretative support to treating physicians, this support is equally available to physicians accessing the UK MCC-MTB or not. A national registry with associated MTB is available, but there are no participating sites in Kentucky.<sup>26,27</sup>

The UK MCC-MTB is an interdisciplinary team with representation from medical oncology, surgical oncology, pathology, radiology, genetic counseling, and clinical pharmacology. The representatives from medical oncology and clinical pharmacology also have extensive early phase clinical trial experience. Meetings are held twice monthly for 1 hour; a teleconference option has been available since inception, allowing for remote participation, and Continuing Medical Education credit is provided for participants. Critically, the UK MCC-MTB focuses on guideline-concordant care and serves a crucial function in updating practicing physicians statewide on new treatment recommendations. In addition to reviewing NGS, the patient's treating physician or designee presents the clinical case, a radiologist reviews pertinent imaging, and a pathologist reviews the diagnostic slides. After the patient's case is discussed, treatment recommendations are made. The UK MCC-MTB can recommend, in order of priority: (1) standard-of-care therapy, (2) enrollment in a clinical trial, or (3) off-label therapy targeting a specific mutation (if no

standard therapies or clinical trials are available). A genetic counselor assesses whether germline testing is indicated, and the UK MCC-MTB may recommend additional testing if appropriate (eg, NGS test was performed on existing tissue from several years ago, which may no longer be relevant to the current cancer).

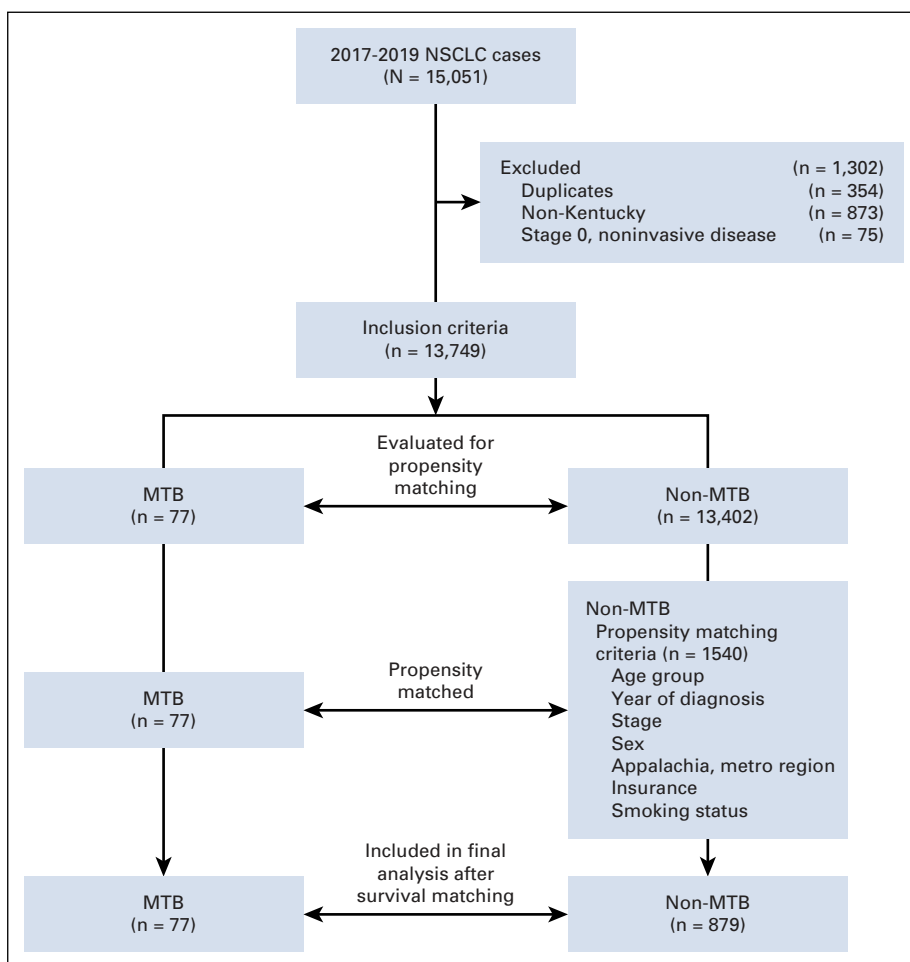
The UK MCC-MTB uses evidence grading for all recommendations. The highest level is category 1, which is either an US Food and Drug Administration (FDA)–approved indication or considered standard of care by national guidelines. Category 2 evidence is that the recommended drug is FDA-approved in another indication and at least one phase II trial has shown activity of the drug in the patient’s tumor type (eg, the UK MCC-MTB will recommend a poly [ADP-ribose] polymerase inhibitor for a patient with a BRCA1 mutation if the patient has no category 1 evidence options). Category 3 evidence is that the drug is FDA-approved in another indication and case reports demonstrate activity in the patient’s tumor type. These recommendations are provided in the form of a written letter and is uploaded into the patient’s electronic health record. All patients reviewed by the MTB are tracked using a REDCap database.<sup>28</sup>

**Data Source**

The Kentucky Cancer Registry (KCR) is a population-based central cancer registry for the Commonwealth of Kentucky. All health care facilities that diagnose or treat patients with cancer, including all acute care hospitals and associated outpatient facilities, freestanding treatment centers, private pathology laboratories, and physician offices, are required to report each case of cancer to the KCR. The KCR has been part of the Centers for Disease Control and Prevention’s National Program of Cancer Registries since 1994 and the National Cancer Institute’s SEER Program since 2000. KCR has received the highest level of certification from the North American Association of Central Cancer Registries, indicating its commitment to accuracy, completeness, and quality.<sup>29</sup>

Demographic variables extracted from the KCR data included age at diagnosis, sex, marital status, smoking status, metropolitan status, Appalachian residence status, insurance type, stage at diagnosis, and treatment setting. Metropolitan status was defined on the basis of the 2013 Rural-Urban County Continuum Codes with values 1-3 as Metro and 4-9 as Non-Metro.<sup>30</sup> Appalachian status was determined by the Appalachian Regional Commission.<sup>31</sup>

**FIG 1.** CONSORT diagram. NSCLC, non–small-cell lung cancer; MTB, molecular tumor board.



**TABLE 1.** Demographics

Demographic Characteristic	Total No. (%)	Non-MTB No. (%)	MTB No. (%)	P
All patients	956 (100)	879 (91.9)	77 (8.1)	
Age, years				.1843
20-49	82	72 (8.2)	10 (13)	
50-64	530	483 (54.9)	47 (61)	
65-74	299	281 (32)	18 (23.4)	
≥ 75	45	43 (4.9)	2 (2.6)	
Sex				.1612
Male	458	427 (48.6)	31 (40.3)	
Female	498	452 (51.4)	46 (59.7)	
Married				.2653
No	415	386 (43.9)	29 (37.7)	
Yes	527	479 (54.5)	48 (62.3)	
Unknown	14	14 (1.6)	0 (0)	
Ever smoker				.2056
No	76	66 (7.5)	10 (13)	
Yes	872	806 (91.7)	66 (85.7)	
Unknown	8	7 (0.8)	1 (1.3)	
Lives in metropolitan area				.3537
No	586	535 (60.9)	51 (66.2)	
Yes	370	344 (39.1)	26 (33.8)	
Lives in Appalachian area				.0146
No	572	536 (61)	36 (46.8)	
Yes	384	343 (39)	41 (53.2)	
Insurance status				.5191
Not insured	9	7 (0.8)	2 (2.6)	
Not known	17	15 (1.7)	2 (2.6)	
Private insured	290	263 (29.9)	27 (35.1)	
Medicaid	212	196 (22.3)	16 (20.8)	
Medicare	406	378 (43)	28 (36.4)	
Veteran	22	20 (2.3)	2 (2.6)	
First primary cancer				.2338
First primary	814	752 (85.6)	62 (80.5)	
Second or more primary	142	127 (14.4)	15 (19.5)	
Tumor grade				.2454
Well-differentiated	36	36 (4.1)	0 (0)	
Moderately differentiated	190	175 (19.9)	15 (19.5)	
Poorly differentiated	209	195 (22.2)	14 (18.2)	
Undifferentiated	7	7 (0.8)	0 (0)	
Unknown	514	466 (53)	48 (62.3)	

(Continued in next column)

**TABLE 1.** Demographics (Continued)

Demographic Characteristic	Total No. (%)	Non-MTB No. (%)	MTB No. (%)	P
Stage <sup>a</sup>				.1101
I	171	153 (17.4)	18 (23.4)	
II	78	69 (7.8)	9 (11.7)	
III	120	110 (12.5)	10 (13)	
IV	564	528 (60.1)	36 (46.8)	
Unknown	23	19 (2.2)	4 (5.2)	
UK patient				
No	786	760 (86.5)	26 (33.8)	< .0001
Yes	170	119 (13.5)	51 (66.2)	

Abbreviations: MTB, molecular tumor board; UK, University of Kentucky.

<sup>a</sup>Stage of initial diagnosis is provided by KCR, however all patients had progressed or recurred to stage IIIb-IV at time of MTB review.

### Study Population and Matching

Invasive NSCLC cases diagnosed in 2017 through 2019 in Kentucky were extracted from the KCR database. Cases were defined as all patients with NSCLC reviewed by the UK MCC-MTB in the study period. To minimize bias, a propensity score matching method was used to select non-UK MCC-MTB patients with similar clinical characteristics associated with outcomes. To minimize the risk of survival bias in the UK MCC-MTB-reviewed patients, controls with shorter survival than matched cases were excluded. In other words, controls had to survive at least as long as the cases to be included in the analysis (Fig 1).

The SAS PS MATCH procedure was used to carry out this matching process (SAS 9.4, SAS Institute Inc, Cary, NC). UK MCC-MTB patients were matched by their year of diagnosis, age group (20-49, 50-64, 65-74, and ≥ 75 years), stage at diagnosis (I-IV and unknown), sex (male or female), Appalachian status (yes or no), metropolitan status (yes or no), insurance status (not insured, private insurance, Medicaid, Medicare, Veteran, and not specified), and smoking status (yes/no/unknown). An exact match was required for age group, stage, and sex to ensure matching of key variables between the two groups. Using the optimal variable ratio match method, one UK MCC-MTB patient could match up to 30 patients for the non-UK MCC-MTB group. A total of 1,540 controls (non-UK MCC-MTB) were matched to 77 cases (UK MCC-MTB) with a reasonable standardized mean difference. After excluding non-UK MCC-MTB controls whose survival was shorter than their matched cases, the final data analysis included 879 non-UK MCC-MTB and 77 UK MCC-MTB patients.

### Statistical Analysis

Descriptive analysis, including bivariate analysis, was conducted between nonreviewed and UK MCC-

MTB—reviewed patients overall and for those patients seen only at UK. Similar analysis was performed for patients reviewed by the UK MCC-MTB (again separating by site of care). Kaplan-Meier plots were used to present OS curves. Log-rank tests were used to compare the significance of survival curves. The Cox regression model was fitted to estimate the effect of UK MCC-MTB involvement on survival while adjusting for other variables. All statistical tests were two-sided. Statistical significance was defined as a *P* value of  $<.05$ , and analysis was conducted using SAS 9.4 (Cary, NC).

### Ethical Considerations

This study was approved by the University of Kentucky's Institutional Review Board (IRB #62105). Informed consent was waived as all data were deidentified before analysis. All data were treated as confidential and only accessible in password-protected files for authorized study staff.

### RESULTS

A total of 956 patients who were newly diagnosed with NSCLC in Kentucky between 2017 and 2019 were included in the analysis. Overall, patients were most commonly age 50-64 years, current or former smokers, and initially diagnosed with metastatic disease. Seventy-seven (8.1%) of the 956 patients were reviewed by the UK MCC-MTB (Table 1). Age, sex, marital status, smoking status, insurance coverage, grade, and stage of NSCLC were similar for patients reviewed by the UK MCC-MTB compared with patients not reviewed by the UK MCC-MTB. Since the UK MCC-MTB is based at UK MCC, which serves as a major referral center for the Appalachian region of Kentucky, patients presented to the UK MCC-MTB were more likely to receive care from UK MCC (51 of 77, 66.2%,  $P < .0001$ ) and to live in the Appalachian region (44 of 71, 53.2%,  $P = .0146$ ).

Cox regression survival analysis was performed to determine factors associated with likelihood of survival in patients with NSCLC (Table 2). When comparing individuals with and without UK MCC-MTB review, patients without UK MCC-MTB review had significantly poorer outcomes than those with a UK MCC-MTB review (hazard ratio [HR] = 8.61; 95% CI, 3.83 to 19.31;  $P < .0001$ ). Kaplan-Meier survival estimates (Fig 2A) indicate that OS was significantly improved in individuals reviewed by the UK MCC-MTB (HR = 8.15; 95% CI, 3.64 to 18.25;  $P < .001$ ). In addition, clinical characteristics associated with decreased survival included older age, ever smoking, and advanced cancer stage. Living in Appalachia was also associated with poorer survival compared with non-Appalachian residence (HR = 1.43; 95% CI, 1.17 to 1.75;  $P = .0004$ ).

We compared patients referred to the UK MCC-MTB by community sites with patients referred by UK MCC to assess the impact of the UK MCC-MTB across care settings.

**TABLE 2.** Cox Regression Analysis

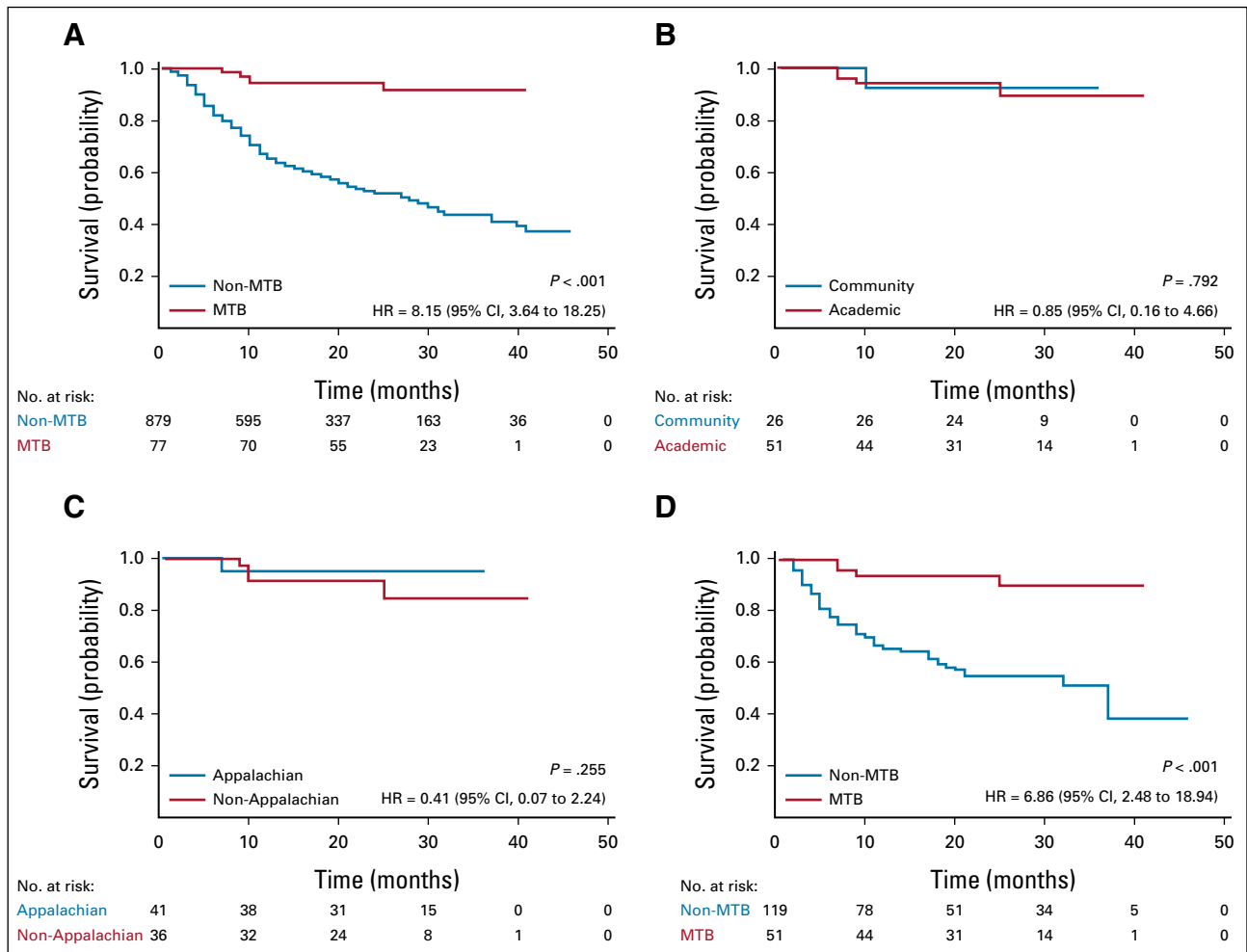
Demographic Characteristic	HR (95% CI)	<i>P</i>
UK MCC-MTB review		$< .0001$
Yes	Ref	
No	8.605 (3.833 to 19.318)	
Age, years		.0006
20-49	Ref	
50-64	0.762 (0.502 to 1.157)	
65-74	1.051 (0.68 to 1.625)	
$\geq 75$	2.25 (1.005 to 5.038)	
Sex		.2136
Female	Ref	
Male	1.137 (0.929 to 1.391)	
Current or former smoker		.0392
No	Ref	
Yes	1.876 (1.156 to 3.047)	
Stage <sup>a</sup>		$< .0001$
I	Ref	
II	2.904 (1.535 to 5.492)	
III	2.443 (1.377 to 4.337)	
IV	7.591 (4.67 to 12.338)	
Unknown	2.134 (0.878 to 5.186)	
Lives in Appalachian area		.0004
No	Ref	
Yes	1.432 (1.172 to 1.749)	

Abbreviations: HR, hazard ratio; MCC, Markey Cancer Center; MTB, molecular tumor board; ref, reference; UK, University of Kentucky.

<sup>a</sup>Stage of initial diagnosis is provided by KCR, however all patients had progressed or recurred to stage IIIb-IV at time of MTB review.

Of the 77 patients reviewed by the UK MCC-MTB, 26 were referred from community sites and 51 were UK MCC referrals. Patients were similar in terms of clinical characteristics, although UK MCC patients were less likely to be married, to have insurance, and to be diagnosed with later stage of disease (Table 3). Kaplan-Meier survival estimates (Fig 2B) indicate that OS was similar among individuals reviewed by the UK MCC-MTB regardless of where care was received ( $P = .792$ ). Similarly, we compared survival outcomes for patients reviewed by the UK MCC-MTB by county of residence, demonstrating no survival differences between those living in Appalachian and non-Appalachian counties (Fig 2C; HR = 0.41; 95% CI, 0.07 to 2.24;  $P = .255$ ).

To assess the impact of the UK MCC-MTB at a single site, we compared UK MCC patients who were reviewed by the UK MCC-MTB versus those who were not. Between 2017 and 2019, 170 patients with newly diagnosed with NSCLC were treated at MCC, of which 51 of 170 (30%) were referred to the UK MCC-MTB (Table 4). There were no significant differences between patients who were referred



**FIG 2.** Kaplan-Meier plots depicting overall survival in patients on the basis of (A) all patients in cohort comparing MTB review versus no MTB review; (B) all patients with an MTB review, comparing community setting with academic setting; (C) all patients with an MTB review, Appalachian county versus non-Appalachian county; and (D) patients treated at University of Kentucky Markey Cancer Center only comparing MTB review versus no MTB review. HR, hazard ratio; MTB, molecular tumor board.

and not referred to the UK MCC-MTB at UK MCC. Similar to what was observed when evaluating all individuals at UK MCC, lack of UK MCC-MTB review was significantly associated with poorer survival when compared with those with a UK MCC-MTB review (Fig 2D; HR = 6.86; 95% CI, 2.48 to 18.94;  $P = .001$ ).

## DISCUSSION

This case-control study clearly demonstrates that UK MCC-MTB review and input into care decisions are strongly and independently associated with a decreased risk of death for patients with NSCLC. Although several MTBs have published outcomes associated with their MTBs and generally report positive outcomes including clinical benefit, improved progression-free survival, or improved OS, these studies are usually small, retrospective, and observational and do not include a control group.<sup>24,25</sup> To our knowledge, this study is the first to demonstrate the benefit of MTB review in a large population-level case-control design focused on NSCLC.

Although we cannot conclusively determine why MTB review is associated with more positive outcomes, we purposefully designed this study to control for patient factors predicting use of NGS. First, we required controls to survive at least as long as cases to control for patient characteristics (rapidly progressive disease and inadequate tissue for NGS because of being a poor surgical candidate) that prevent the use of NGS testing. We also used propensity matching on clinical characteristics associated with survival outcomes to balance these between cases and controls. Finally, since targetable mutations are associated with clinical characteristics,<sup>32-34</sup> especially smoking, propensity matching was also used to reduce the risk of imbalances in targetable mutations between the cases and controls. We anticipate that imbalances in patient characteristics between cases and controls do not account for these findings. Therefore, since the UK MCC-MTB was specifically designed to overcome physician barriers to NGS testing, like lack of experience, we suggest that the UK MCC-MTB<sup>18</sup> drives improved

**TABLE 3.** Demographics of Patients Reviewed by the UK MCC-MTB

Demographic Characteristic	Total	Non-UK MCC-MTB No. (%)	UK MCC-MTB No. (%)	P
Total	77 (100)	26 (33.8)	51 (66.2)	
Age, years				.0522
20-49	10	3 (11.5)	7 (13.7)	
50-64	47	21 (80.8)	26 (51)	
65-74	18	2 (7.7)	16 (31.4)	
≥ 75	2	0 (0)	2 (3.9)	
Sex				.4709
Male	31	9 (34.6)	22 (43.1)	
Female	46	17 (65.4)	29 (56.9)	
Married				.004
No	29	4 (15.4)	25 (49)	
Yes	48	22 (84.6)	26 (51)	
Current or former smoker				.1394
No	10	6 (23.1)	4 (7.8)	
Yes	66	20 (76.9)	46 (90.2)	
Unknown	1	0 (0)	1 (2)	
Lives in metropolitan area				.6913
No	51	18 (69.2)	33 (64.7)	
Yes	26	8 (30.8)	18 (35.3)	
Lives in Appalachian area				.94
No	36	12 (46.2)	24 (47.1)	
Yes	41	14 (53.8)	27 (52.9)	
Insurance status				.001
Not insured	2	2 (7.7)	0 (0)	
Not specified	2	2 (7.7)	0 (0)	
Private insured	27	13 (50)	14 (27.5)	
Medicaid	16	3 (11.5)	13 (25.5)	
Medicare	28	4 (15.4)	24 (47.1)	
Veteran	2	2 (7.7)	0 (0)	
First primary cancer				.0622
First primary	62	24 (92.3)	38 (74.5)	
Second or more primary	15	2 (7.7)	13 (25.5)	
Tumor grade				.0937
Moderately different	15	8 (30.8)	7 (13.7)	
Poorly differentiate	14	6 (23.1)	8 (15.7)	
Unknown	48	12 (46.2)	36 (70.6)	
Stage <sup>a</sup>				.0005
I	18	9 (34.6)	9 (17.6)	
II	9	4 (15.4)	5 (9.8)	
III	10	5 (19.2)	5 (9.8)	
IV	36	4 (15.4)	32 (62.7)	
Unknown	4	4 (15.4)	0 (0)	

Abbreviations: MCC, Markey Cancer Center; MTB, molecular tumor board; UK, University of Kentucky.

<sup>a</sup>Stage of initial diagnosis is provided by KCR, however all patients had progressed or recurred to stage IIIb-IV at time of MTB review.

**TABLE 4.** Demographics of Patients Receiving Care at UK MCC

Demographic Characteristic	Total	Non-UK MCC-MTB No. (%)	UK MCC-MTB No. (%)	P
Total	170	119 (70)	51 (30)	
Age, years				.4926
20-49	15	8 (6.7)	7 (13.7)	
50-64	96	70 (58.8)	26 (51)	
65-74	53	37 (31.1)	16 (31.4)	
≥ 75	6	4 (3.4)	2 (3.9)	
Sex				.973
Male	73	51 (42.9)	22 (43.1)	
Female	97	68 (57.1)	29 (56.9)	
Married				.2122
No	68	43 (36.1)	25 (49)	
Yes	100	74 (62.2)	26 (51)	
Unknown	2	2 (1.7)	0 (0)	
Ever smoker				.8205
No	14	10 (8.4)	4 (7.8)	
Yes	154	108 (90.8)	46 (90.2)	
Unknown	2	1 (0.8)	1 (2)	
Lives in metropolitan area				.3834
No	118	85 (71.4)	33 (64.7)	
Yes	52	34 (28.6)	18 (35.3)	
Lives in Appalachian area				.3076
No	70	46 (38.7)	24 (47.1)	
Yes	100	73 (61.3)	27 (52.9)	
Insurance status				.6126
Not specified	3	3 (2.5)	0 (0)	
Private insured	44	30 (25.2)	14 (27.5)	
Medicaid	42	29 (24.4)	13 (25.5)	
Medicare	78	54 (45.4)	24 (47.1)	
Veteran	3	3 (2.5)	0 (0)	
First primary cancer				.1896
First primary	137	99 (83.2)	38 (74.5)	
Second or more primary	33	20 (16.8)	13 (25.5)	
Tumor grade				.5151
Well-differentiated	5	5 (4.2)	0 (0)	
Moderately different	23	16 (13.4)	7 (13.7)	
Poorly differentiate	24	16 (13.4)	8 (15.7)	
Unknown	118	82 (68.9)	36 (70.6)	
Stage <sup>a</sup>				.3369
I	39	30 (25.2)	9 (17.6)	
II	19	14 (11.8)	5 (9.8)	
III	12	7 (5.9)	5 (9.8)	
IV	95	63 (52.9)	32 (62.7)	
Unknown	5	5 (4.2)	0 (0)	

Abbreviations: MCC, Markey Cancer Center; MTB, molecular tumor board; UK, University of Kentucky.

<sup>a</sup>Stage of initial diagnosis is provided by KCR, however all patients had progressed or recurred to stage IIIb-IV at time of MTB review.

survival through the advancement of guideline-concordant care, including promoting NGS, assisting with the interpretation of NGS findings, and providing guideline-concordant treatment recommendations.<sup>6,8,35</sup>

Since differences in cancer outcome are reported between academic and community medical centers,<sup>36-38</sup> we also compared outcomes between academic and community settings for all patients reviewed by the UK MCC-MTB, demonstrating no difference in survival. We also show that, when only considering an academic setting, those without UK MCC-MTB review have significantly decreased OS. Improved outcomes in academic settings are generally attributed to higher compliance with clinical practice guidelines,<sup>37</sup> use of best surgical practices, and high patient volumes.<sup>39</sup> However, in a comparison of clinical outcomes after NSCLC resection between small-volume and high-volume practices, von Itstein recently demonstrated that although OS was improved at high-volume centers, when controlling for best surgical practices, there was no difference between high-volume and low-volume practices.<sup>39</sup> Consistent with these findings, our study strongly suggests that survival outcome did not differ between patients treated at an academic medical center and those treated at a community oncology practice, when reviewed by the UK MCC-MTB.

As expected, residing in an Appalachian county was independently associated with poorer survival.<sup>40</sup> Therefore, we also compared outcomes between Appalachian and non-Appalachian counties among individuals who received a UK MCC-MTB review, demonstrating similar survival. Poor outcomes in Appalachian populations are generally attributed to disparities in income, education, and access to health care observed in the region.<sup>41</sup> Our study suggests,

since survival outcome did not differ between patients residing in Appalachian and non-Appalachian counties, when reviewed by the UK MCC-MTB, that MTBs are an effective strategy for improving access to health care for this rural and medically underserved population.

A significant strength of this study was the inclusion of all cases of NSCLC who received a UK MCC-MTB review and controls that were obtained from the Kentucky Cancer Registry, which represents a population-level sampling strategy. In addition, as part of the SEER network, the Kentucky Cancer Registry provides a comprehensive data set that allows for an evaluation of relevant clinical and demographic factors associated with outcomes. Propensity matching on clinical characteristics and survival was also a significant strength, enabling minimization of survival bias and balancing clinical characteristics associated with survival between cases and controls. Limitations of this study include the observational design and potential lack of generalizability since this study was conducted only in Kentucky. In addition, data related to treatments, NGS, and mutation profile are not available for controls, and although we hypothesize that the reason MTB review was associated with improved outcomes was improved adherence to guideline-concordant care, we cannot assess differences in care delivered to these populations.

In conclusion, this study demonstrates that UK MCC-MTB review is an independent predictor of survival regardless of the setting where care is received or the county of residence. Providing UK MCC-MTB access to community medical oncology practices, especially in rural and underserved regions like Appalachia, may overcome some health disparities for this disadvantaged population.

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## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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