Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Study Population, Practice Attribution, and Practice Characteristics

Study population and practice attribution

Our sample included episodes of care between 2010 and 2017 for patients with one of four cancer types: melanoma, kidney cancer, lung cancer and head/neck cancer. Episodes were assigned a cancer type based on the Oncology Care Model (OCM) methodology. We excluded episodes beginning in January 2010 because these episodes included patients on long term chemotherapy that began before our study period.

Each episode was attributed to an oncology practice based on the plurality of outpatient medical oncology visits during the episode. Practices were defined using tax identification numbers. We identified medical oncology visits using evaluation and management (E&M) claims for outpatient visits with a specialty code of medical oncology, hematology/oncology, hematology, or gynecologic oncology. We attributed episodes to practices using the plurality of other visits if no medical oncology visits were present. If there was a tie in the number of visits, we identified the practice with the most recent visit.

Practice characteristics

Practices were classified as urban or rural based on 2010 Rural-Urban Commuting Area (RUCA) codes from the U.S. Department of Agriculture (USDA) for each practice's ZIP-code. Urban ZIP-codes were located in metropolitan areas (RUCA codes 1-3) and non-metropolitan areas that had significant commuting flows to urbanized areas (RUCA codes 4.1, 5.1, 7.1, 8.1, 10.1), while rural ZIP-codes were located in non-metropolitan areas without significant commuting flows to urbanized areas (all remaining RUCA codes). For multi-site practices, we categorized practices as rural if all practice locations were rural throughout the study period.

We also categorized practices as independent, part of a non-academic system or part of an academic system. Systems were defined as a set of jointly owned or managed providers with at least one general

acute care hospital, ten primary care physicians and fifty total physicians, all within the same market; we also included systems with only cancer hospitals (i.e., no general acute care hospital) and without primary care physicians.[1] We identified practices in academic systems using a list of academic practices developed by Welch and Bindman,[2] supplemented to include oncology practices whose oncologists included medical school faculty members.[3]

Immunotherapy use

We used two definitions of immunotherapy adoption in the main and supplemental analyses. In the main analyses, practice-level adoption corresponded to the start of the first attributed episode with immunotherapy treatment, coded as 1 for practices with any immunotherapy use in current or past periods and 0 otherwise. In a supplemental analysis, we re-defined adoption as the first time period in which immunotherapy was used for 10% of cumulative chemotherapy episodes since FDA approval, following work on bevacizumab adoption by Keating et al.[3] We did not include pre-approval episodes in the cumulative count because many of the J-codes for immunotherapy were not yet available. In Keating et al., bevacizumab had a permanent J-code available for the entirety of the study period, and the authors did not draw a distinction between pre- and post- approval cumulative patients.

eTable 1. Approved Immunotherapy Treatments Through 2016 and CPT Codes

Immunotherapy (approval date)	CPT Codes
Ipilimumab (March 2011)	C9284 (2011)
	J9999/J8999 (2011)
	J9228 (2012-2017)
Pembrolizumab (September 2014)	C9027 (2015)
	J9999/J8999 (2015)
	J9271 (2016-2017)
Nivolumab (December 2014)	C9453 (2015)
	J9999/J8999 (2015)
	J9299 (2016-2017)
Atezolizumab (May 2016)	C9483 (2016-2017)
	J9999/J8999 (2016-2017)
	Note: specific J-code (J9022) not available until 2018

C codes are temporary codes used in hospital outpatient departments (HOPD); we used nonspecific J codes to capture immunotherapy outside of HOPDs before permanent J codes were available.

eTable 2. Approved Immunotherapy Treatments by Cancer Type and Year

	Melanoma	Lung	Kidney	Head and Neck
2011	Ipilimumab (March)			
2014	Pembrolizumab (September)			
	Nivolumab (December)			
2015	Nivo+Ipil (October)	Nivolumab (March)	Nivolumab (November)	
	Ipilimumab (October)	Pembrolizumab (October)		
	Pembrolizumab (December)	Nivolumab (October)		
2016		Pembrolizumab (October)	Atezolizumab (May)	Pembrolizumab (August)
		Atezolizumab (October)		Nivolumab (November)

Immunotherapy was approved for treating Hodgkin lymphoma in 2016, but we did not include this cancer type in our study sample due to the very small number of Hodgkin lymphoma cases among older adults.

eTable 3. Full Model Results for the Association Between Practice Characteristics and Immunotherapy Adoption After FDA Approval

	Adjusted Percentage Point Difference (95% CI)	
	Main analysis	Adoption by Time Period
Rural vs. Urban	-11 (-16 to -6)	-19 (-28 to -10)
Independent vs. Academic System	-6 (-9 to -3)	-15 (-24 to -7)
Non-Academic System vs. Academic System	-9 (-11 to -6)	-20 (-26 to -13)
Small vs. Large	-27 (-32 to -22)	-44 (-53 to -34)
Time Since Approval (6-month increments)		
Time 0		[Reference]
Time 1		6 (3 to 10)
Time 2		12 (8 to 17)
Time 3		14 (10 to 19)
Time 4		16 (12 to 21)
Rural*(Time Since Approval)		
Time 0		[Reference]
Time 1		4 (-5 to 13)
Time 2		10 (1 to 19)
Time 3		13 (4 to 22)
Time 4		13 (4 to 22)
Independent*(Time Since Approval)		
Time 0		[Reference]
Time 1		13 (6 to 20)
Time 2		13 (5 to 21)
Time 3		15 (6 to 23)
Time 4		14 (6 to 23)
Non-Academic System*(Time Since Approval)		
Time 0		[Reference]
Time 1		13 (8 to 19)
Time 2		15 (9 to 21)
Time 3		17 (11 to 24)
Time 4		17 (10 to 23)
Small Practice*(Time Since Approval)		
Time 0		[Reference]
Time 1		14 (5 to 24)
Time 2		24 (14 to 34)
Time 3		28 (18 to 38)
Time 4		33 (23 to 43)
continued on next page		

eTable 3 (*continued*). Full Model Results for the Association Between Practice Characteristics and Immunotherapy Adoption After FDA Approval

	Adjusted Percentage Point Difference (95% CI)	
	Main analysis	Adoption by Time Period
Race and Ethnicity*		
Hispanic	-5 (-17 to 7)	-5 (-16 to 7)
Non-Hispanic Black	-9 (-19 to 1)	-7 (-16 to 3)
Non-Hispanic White	1 (-7 to 8)	3 (-4 to 10)
Other	[Reference]	[Reference]
Sex*		
Male	[Reference]	[Reference]
Female	-1 (-5 to 3)	-2 (-6 to 1)
Age*		
65-74	[Reference]	[Reference]
75-84	1 (-4 to 5)	0 (-4 to 4)
85+	1 (-6 to 9)	0 (-7 to 7)
Charlson comorbidity*		
0	[Reference]	[Reference]
1	-3 (-9 to 3)	-5 (-10 to 1)
2	-4 (-11 to 2)	-6 (-13 to 0)
3+	0 (-6 to 6)	-4 (-9 to 2)
Median household income (ZIP-code)*		
Under $40,000	[Reference]	[Reference]
$40,000-$69,999	4 (-1 to 9)	4 (-1 to 9)
$70,000	3 (-3 to 8)	3 (-2 to 8)
Cancer Type*		
Melanoma	[Reference]	[Reference]
Kidney Cancer	16 (5 to 26)	37 (26 to 48)
Lung Cancer	9 (0 to 17)	15 (8 to 23)
Head and Neck Cancer	-11 (-23 to 0)	44 (30 to 57)

Each column contains estimates from a separate regression model. Column 1 shows full results from our main model. The coefficients on practice type (e.g., rural versus urban) estimate the average difference in adoption rates in the post-approval period. Column 2 shows results from a model of adoption over time. Time is measured in 6-month increments, as in Figure 2. The coefficients on practice type (e.g., rural versus urban) estimate the difference in adoption rates immediately following approval (Time 0), while the interaction terms (e.g., Rural*(Time Since Approval)) measure the differential growth in adoption across practice type over time. Likewise, coefficients on cancer type show the association between having more patients with a certain cancer type in the post-approval period overall (Column 1) and in Time 0 (Column 2). Small practices include those with five or fewer physicians. "Other" Race and Ethnicity category includes Asian/Pacific Islander, American Indian/Alaska Native, and other or unknown race.
*Variables coded at the practice level.

eTable 4. Sensitivity Checks for Association Between Practice Characteristics and Immunotherapy Adoption

	Adjusted Percentage Point Difference (95% CI)				
	Main Analysis	Sensitivity Check 1: Permanent J-Code Only	Sensitivity Check 2: Practices with 20+ Episodes	Sensitivity Check 3: Episode-Level Regression	Sensitivity Check 4: Adoption at 10% of Episodes
Rural vs. Urban	-11 (-16 to -6)	-12 (-17 to -7)	-5 (-11 to 0)	-11 (-16 to -6)	-7 (-13 to -2)
Independent vs. Academic System	-6 (-9 to -3)	-4 (-8 to -1)	-5 (-8 to -3)	-6 (-9 to -3)	-11 (-16 to -5)
Non-Academic System vs. Academic System	-9 (-11 to -6)	-10 (-13 to -7)	-6 (-8 to -4)	-8 (-10 to -6)	-9 (-13 to -5)
Small vs. Large	-27 (-32 to -22)	-28 (-33 to -22)	-19 (-25 to -13)	-28 (-33 to -23)	-23 (-29 to -17)

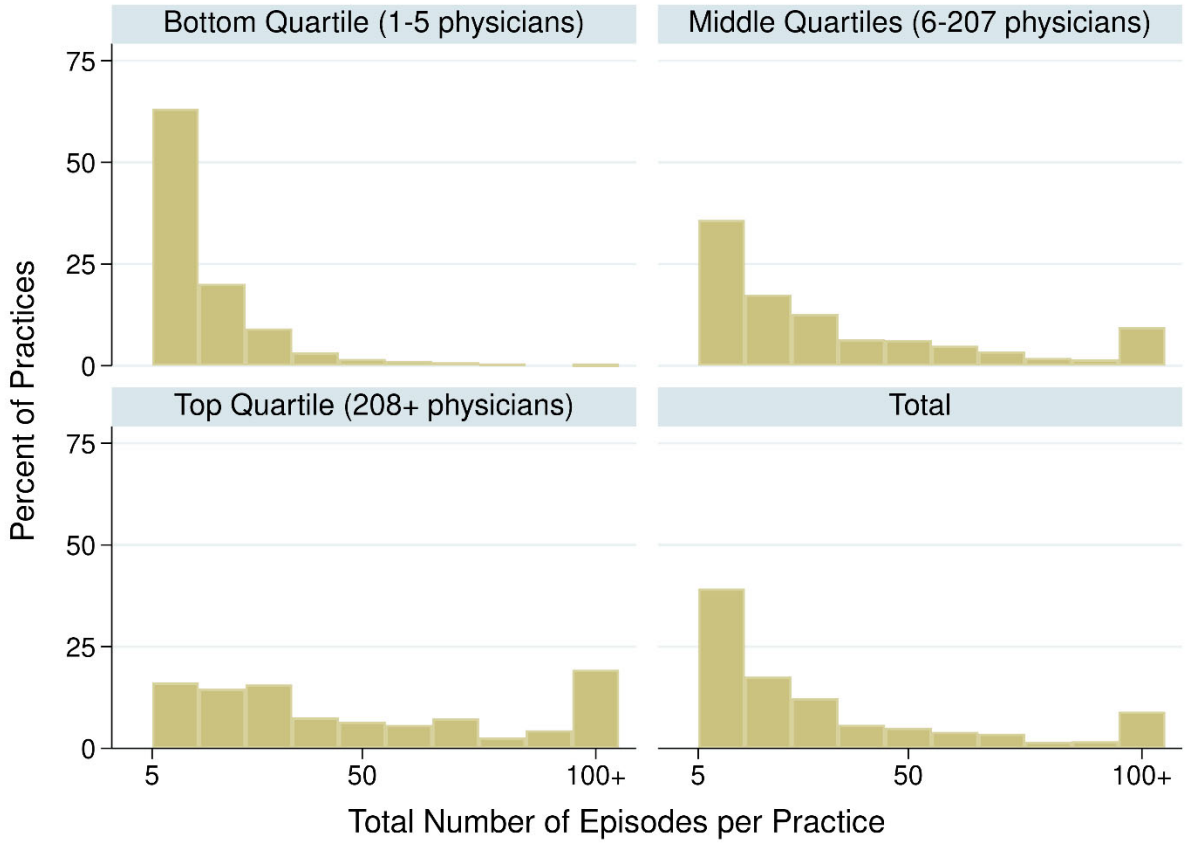
Each column contains estimates from a separate regression. The coefficients on practice type (e.g., rural versus urban) estimate the average difference in adoption rates in the post-approval period. All models adjust for the mix of patients at each practice (or individual patient characteristics in sensitivity check 3), including cancer type, age, sex, race and ethnicity, Charlson comorbidity score and median household income in the patient's zip code of residence. Small practices include those with five or fewer physicians.

eTable 5. Immunotherapy Adoption by Practice and Cancer Type After FDA Approval, Stratified by Cancer Type

	Percent of Practices with Immunotherapy Adoption			
	Melanoma	Lung Cancer	Kidney Cancer	Head/Neck Cancer
Practice Location				
Rural	54	75	66	90
Urban	62	91	82	98
Adjusted Difference	0 (-15 to 14)	-12 (-17 to -7)	-5 (-16 to 5)	-5 (-11 to 1)
Practice Affiliation				
Independent	57	88	81	95
Non-Academic System	54	89	74	97
Academic System	77	97	92	100
Adjusted Difference (Independent vs. Academic System)	-15 (-25 to -5)	-3 (-5 to -1)	-6 (-14 to 1)	-3 (-6 to 0)
Adjusted Difference (Non-Academic System vs. Academic System)	-22 (-33 to -10)	-7 (-10 to -5)	-18 (-25 to -11)	-2 (-4 to 0)
Practice Size				
1-5 physicians	47	63	58	87
6+ physicians	64	93	83	98
Adjusted Difference	-11 (-24 to 2)	-30 (-34 to -25)	-23 (-35 to -12)	-9 (-17 to -1)

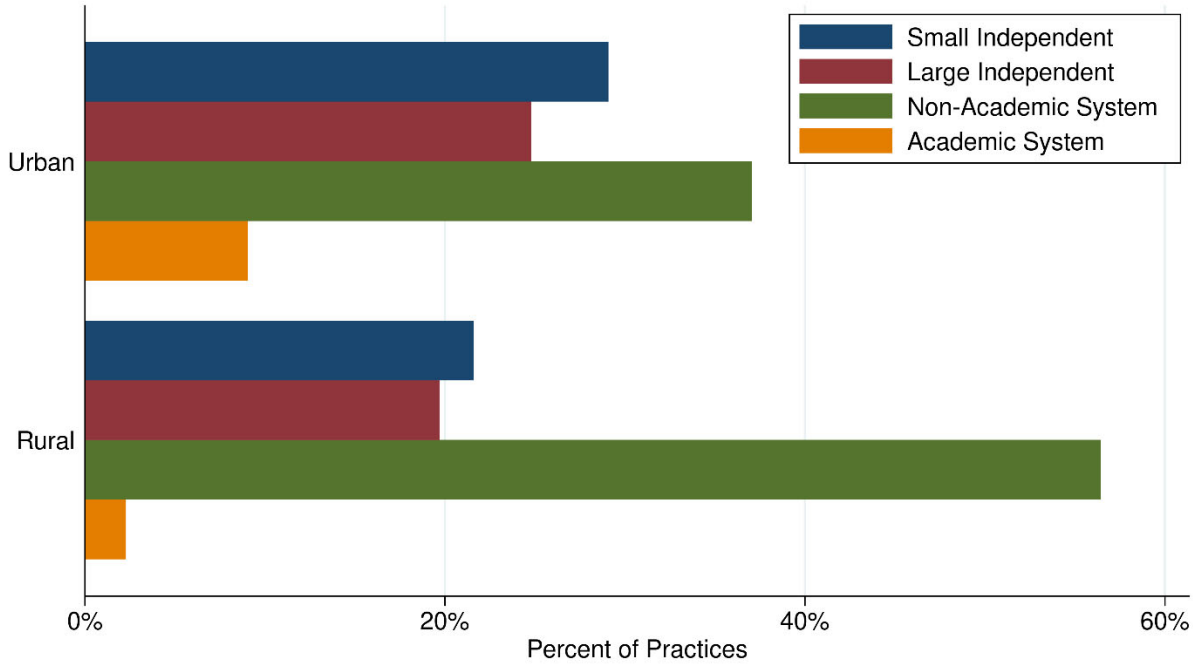
Each column contains estimates from a separate regression, where the sample is all practices treating patients with a given cancer type. The adjusted differences represent the average difference in adoption rates in the post-approval period. Kidney cancer and head and neck cancer episodes were observed for shorter time periods after FDA approval, given the later approval dates for immunotherapy use. All models adjust for the mix of patients at each practice, including age, sex, race and ethnicity, Charlson comorbidity score and median household income in the patient's zip code of residence. In each panel (e.g., Practice Location), the first two rows show the percent of practices with immunotherapy adoption. The subsequent row(s) show regression-adjusted differences in adoption rates across the practice type (e.g., rural versus urban) in percentage points.

eFigure 1. Distribution of Total Episode Volume Across Practices, by Practice Size Quartile



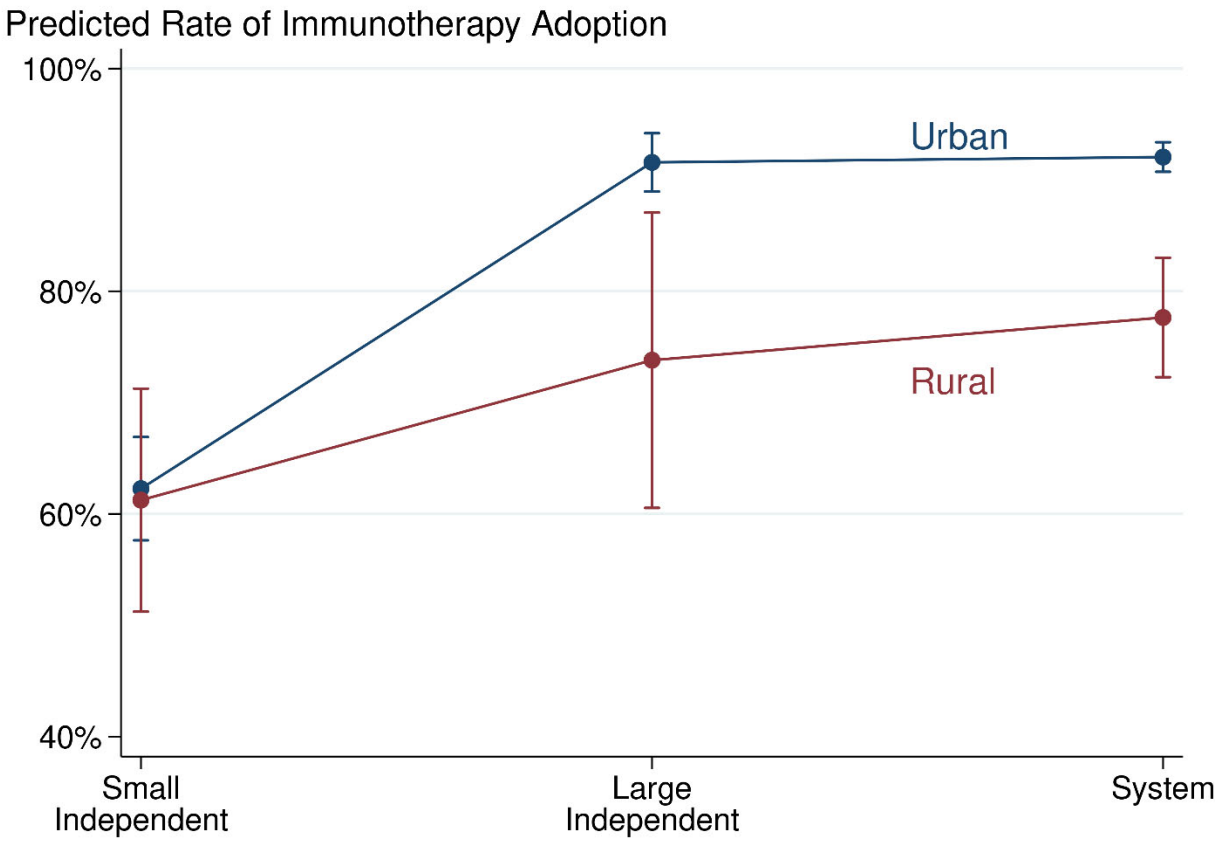
This figure plots histograms showing the total number of episodes attributed to each practice throughout the study period (2010-2017), according to the number of physicians working at that practice.

eFigure 2. Distribution of Practice Size and System Affiliation Type by Practice Location



Small practices include those with five or fewer physicians.

eFigure 3. Predicted Rate of Immunotherapy Adoption by Practice Type



The figure plots results from a single regression that include an interaction of rural practice location with practice type (small independent, large independent, system). The model also adjusts for the mix of patients at each practice, including cancer type, age, sex, race and ethnicity, Charlson comorbidity score and median household income in the patient's zip code of residence. Small practices include those with five or fewer physicians.

eReferences.

[1] National Bureau of Economic Research (2021). Methodology for Identifying and Classifying Health Systems. https://www.nber.org/sites/default/files/2021-03/HSPD%20Technical%20Documentation%20-%20January%202021.pdf
[2] Welch WP, Bindman AB. Town and Gown Differences Among the 100 Largest Medical Groups in the United States. *Acad Med*. 2016;91(7):1007-1014. doi:10.1097/ACM.0000000000001240
[3] Keating, Nancy L. Huskamp, Haiden A., Schrag, Deborah et al. Diffusion of Bevacizumab Across Oncology Practices, Medical Care: January 2018 - Volume 56 - Issue 1 - p 69-77 doi: 10.1097/MLR.0000000000000840