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A Rural Urban Comparison of the Proposed 2020 Wage Index

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BACKGROUND

The Medicare hospital Inpatient Prospective Payment System (IPPS) is designed to pay hospitals for services provided to Medicare beneficiaries based on a national standardized amount adjusted for the patient's condition and related treatment. Further, Social Security Act Section 1886(d)(3)(E) requires that the standardized amount be adjusted for differences in hospital wage levels, which the Centers for Medicare & Medicaid Services (CMS) implemented through the wage index system. CMS also uses the hospital wage index for the Outpatient Prospective Payment System (OPPS), skilled nursing facilities, inpatient rehabilitation facilities and other providers, but not Critical Access Hospitals (CAHs), which are exempt because they are not paid under the IPPS. In computing the wage index, CMS calculates an average hourly wage for each urban and rural area (total wage costs divided by total hours for all hospitals in the geographic area) and a national average hourly wage (total wage costs divided by total hours for all hospitals in the nation). A labor market area's wage index value is the ratio of the area's average hourly wage to the national average hourly wage.

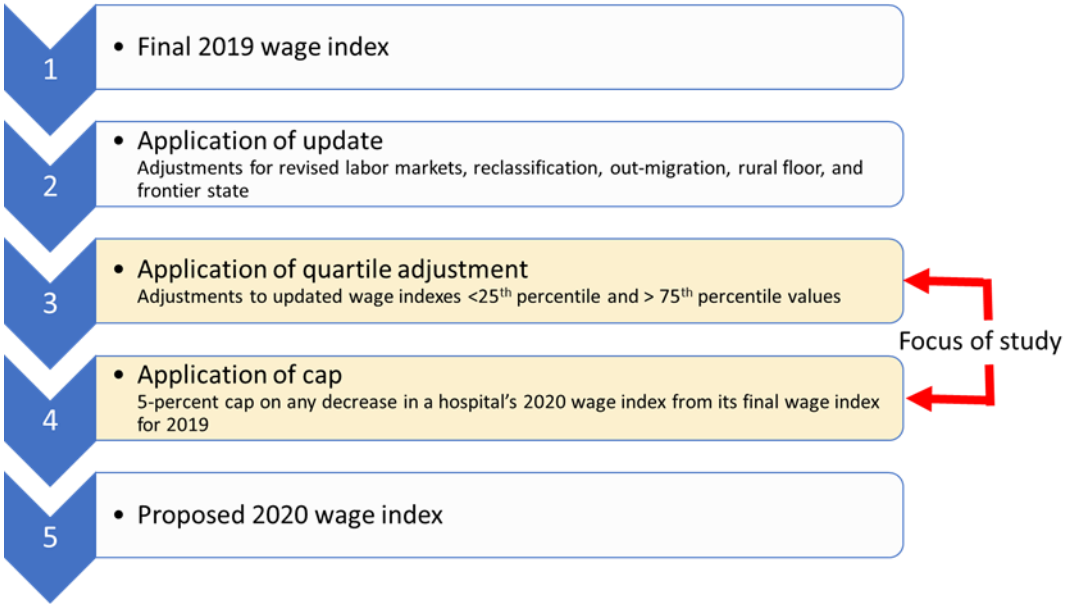
In a companion findings brief, we describe the long-standing problems with the wage index and rural hospitals.[1] On April 23, 2019, CMS released its annual proposed update for the hospital Inpatient Prospective Payment System for fiscal year 2020 that starts in October 2019.[2] In the proposed update, CMS recognizes that the current wage index system perpetuates and exacerbates the disparities between high and low wage index hospitals. To address these disparities, CMS is proposing the changes depicted in Figure 1.

KEY FINDINGS

In the FY 2020 Inpatient Prospective Payment System Proposed Rule, the Centers for Medicare & Medicaid Services proposes a method (consisting of a proposed quartile adjustment and cap) to reduce the disparities between high and low wage index hospitals. This study finds that:

- The proposed application of the quartile adjustment and cap decreases the wage index for 69 rural and 636 urban hospitals, leaves unchanged 385 rural and 1,205 urban hospitals, and increases the wage index for 476 rural and 421 urban hospitals.
- The states with the greatest number of rural hospitals with a positive wage index adjustment are in the South Census region: Texas (53), Alabama (43), Mississippi (38), Kentucky (32), Georgia (31) and Tennessee (30). The States with the greatest number of urban hospitals with a positive wage index adjustment are in Louisiana (57), Massachusetts (53), Texas (41), Alabama (40), and Arizona (34).
- The greatest increases are for hospitals with the lowest 2020 wage indexes.
- Among rural hospitals, the percentage with an increase in wage index is largest for hospitals with less than $25 million in net patient revenue and smallest for those with greater than $100 million in net patient revenue.
- The states with the highest percentage of hospitals with an increase in wage index (Alabama, Kansas, West Virginia, Mississippi, and Louisiana) also have higher percentages of rural hospitals with negative operating margins.
- The proposed quartile adjustment would increase the wage index for many: rural and urban hospitals with relatively low 2019 wage indexes; rural hospitals in states in the South Census region; and small rural hospitals with relatively low levels of net patient revenue.

Figure 1. Proposed 2020 Wage Index



Step 1 is the final 2019 wage index. In step 2, the annual *update* consisting of adjustments for revised labor markets, reclassification, out-migration, rural floor, and frontier state[3] is applied. Next, in step 3 a *quartile adjustment* is applied: hospitals with a wage index value below the 25th percentile value (0.8482 for FY 2020) of the updated wage indexes receive an increase that is "half the difference between the otherwise applicable wage index value for that hospital and the 25th percentile wage index value across all hospitals". To ensure budget neutrality of this change, the wage index for hospitals above the 75th percentile value (1.0351 for FY 2020) is then decreased so "Medicare spending does not increase as a result of this proposal."[4] To mitigate payment decreases due to these proposals, in step 4, CMS applies a 5-percent *cap* on any decrease in a hospital's wage index from its final wage index for fiscal year 2019.[5] After the cap is applied, the result is the proposed 2020 wage index (step 5).

The purpose of this study is to describe and compare the effect of the proposed *quartile adjustment* and *cap* on the *updated* 2020 wage indexes for urban and rural hospitals.

METHOD

In figure 1, step 2 is the 2019 wage index after application of the wage index update: this can be considered the updated 2020 wage index BEFORE the proposed quartile adjustment and cap. Step 5 is the proposed updated 2020 wage index AFTER the proposed quartile adjustment and cap. The difference between these two wage indexes is the effect of the proposed quartile adjustment and cap on the 2020 updated wage indexes and is the focus of this study.

The following notation is used:

2019 Wage Index (WI)	=	final 2019 wage index
2020 WI update only	=	updated 2020 wage index update only (step 2)
2020 WI update + quartile + cap	=	updated 2020 wage + proposed quartile adjustment + cap (Step 5)
WI Increase	=	(WI update + quartile + cap) minus (WI update only) > 0
WI no change	=	(WI update + quartile + cap) minus (WI update only) = 0
WI decrease	=	(WI update + quartile + cap) minus (WI update only) < 0

Wage index values for facilities with acute care beds were obtained from the Impact Analysis from CMS Inpatient Prospective Payment System fiscal year 2020 Proposed Rule[6,7] and 2019 Final Rule (Correction Notice)[8]. Critical Access Hospitals are excluded because they are not paid under the IPPS. Maryland hospitals were analyzed separately because they are paid under an all-payer model. Indian Health Service (IHS) hospitals were analyzed separately – they all have a 2020 wage index of 1.4272 (in Arizona, Minnesota, Mississippi, Montana, New Mexico, North Carolina, North Dakota, Oklahoma, and South Dakota) or a 2020 wage index of 1.8956 in Alaska. Hospitals in Puerto Rico were analyzed separately because of data limitations. Financial data for the most recent year (generally 2017) was obtained from the Healthcare Cost Report Information System (HCRIS) (March 31, 2019). Facilities were classified as rural using the definition of the Federal Office of Rural Health Policy (FORHP).[9] The reader should note that rurality is defined here based on the geographic location of the hospital, NOT on any reclassification.

Comparison of 2019 Wage Index to 2020 Wage Index BEFORE and AFTER the Proposed Quartile Adjustment and Cap

Table 1 shows the median 2019 final wage index and 2020 wage indexes BEFORE and AFTER the proposed quartile adjustment and cap. The 473 rural hospitals with an updated 2020 wage index less than 0.8482 (25th percentile value stated by CMS) have a median 2019 wage index of 0.7879, a median 2020 wage index BEFORE the proposed quartile adjustment and cap of 0.7866, and a median 2020 wage index AFTER the proposed quartile adjustment and cap of 0.8197.

Table 1. Median 2019 Final and 2020 Wage Indexes BEFORE and AFTER Proposed Quartile Adjustment and Cap

			2019	2020 BEFORE	2020 AFTER
2020 Update Only Wage Index		Number of Hospitals	Median 2019 Wage Index	Median 2020 Wage Index Update Only	Median 2020 Wage Index Update + Quartile + Cap
< 0.8482	Rural	473	0.7894	0.7866	0.8197
	Urban	316	0.8117	0.8118	0.8302
0.8482 to 1.0351	Rural	383	0.9107	0.9134	0.9134
	Urban	1,239	0.9417	0.9392	0.9397
>1.0351	Rural	74	1.2500	1.2446	1.2557
	Urban	707	1.2747	1.2665	1.2714
	Maryland	47	0.9463	0.9519	0.9519
	IHS	29	1.4448	1.4448	1.4272
	Puerto Rico	50	0.4141	0.4106	0.6294
	Total	3,318			

What are the effects of the typical "update" process?

Table 2 shows descriptive statistics for the median change between the 2019 final wage index and the 2020 wage indexes BEFORE the proposed quartile adjustment and cap; that is, this is the change resulting from the "typical" updating process. Among hospitals with the lowest wage indexes (an updated 2020 wage index less than 0.8482), 473 rural hospitals have a median change of +0.0002, and 316 urban hospitals have a median change of -0.0013. Among hospitals with the highest wage indexes (an updated 2020 wage index greater than 1.0351), 74 rural hospitals have a median change of +0.0081, and 707 urban hospitals have a median change of +0.0062. Note that the median change for all groups is relatively small.

Table 2. Median Change between 2019 Final Wage Index and 2020 Wage Index Update Only (BEFORE Applying the Proposed Quartile and Cap)

Wage Index		Number of Hospitals	Change between 2019 Wage Index (WI) and 2020 Wage Index *Update Only*				Number of Hospitals		
			Minimum	Median	Mean	Maximum	WI Decrease	WI No Change	WI Increase
< 0.8482	Rural	473	-0.3815	0.0002	-0.0011	0.1177	188	48	237
	Urban	316	-0.0816	-0.0013	-0.0038	0.0638	171	10	135
0.8482 to 1.0351	Rural	383	-0.1385	0.0023	0.0030	0.1411	150	24	209
	Urban	1,239	-0.1357	-0.0012	-0.0008	0.1832	664	23	552
>1.0351	Rural	74	-0.1488	0.0081	0.0022	0.1466	25	0	49
	Urban	707	-0.1685	0.0062	-0.0011	0.2820	231	0	476
	Maryland	47	-0.0022	0.0056	0.0079	0.0711	7	0	40
	IHS	29	0.0000	0.0000	0.0000	0.0000	0	29	0
	Puerto Rico	50	-0.0107	-0.0035	-0.0021	0.0579	47	0	3
	Total	3,318					1,385	47	1,886

What are the total changes hospitals would see from 2019 to 2020?

Table 3 shows descriptive statistics for the median change between the 2019 wage index and the 2020 wage index update AFTER applying proposed quartile adjustment and cap; that is, this is the change that hospitals will see. Among hospitals with the lowest wage indexes (an updated 2020 wage index less than 0.8482), 473 rural hospitals have a median change of +0.0318, and 316 urban hospitals have a median change of +0.0188. Among hospitals with the highest wage indexes (an updated 2020 wage index greater than 1.0351), 74 rural hospitals have a median change of -0.0067, and 707 urban hospitals have a median change of -0.0100. Note that in contrast to the results of Table 2, the median change is more consequential for the hospitals with low wage indexes.

Table 3. Median Change between 2019 Final Wage Index & 2020 Wage Index AFTER Applying Proposed Quartile and Cap

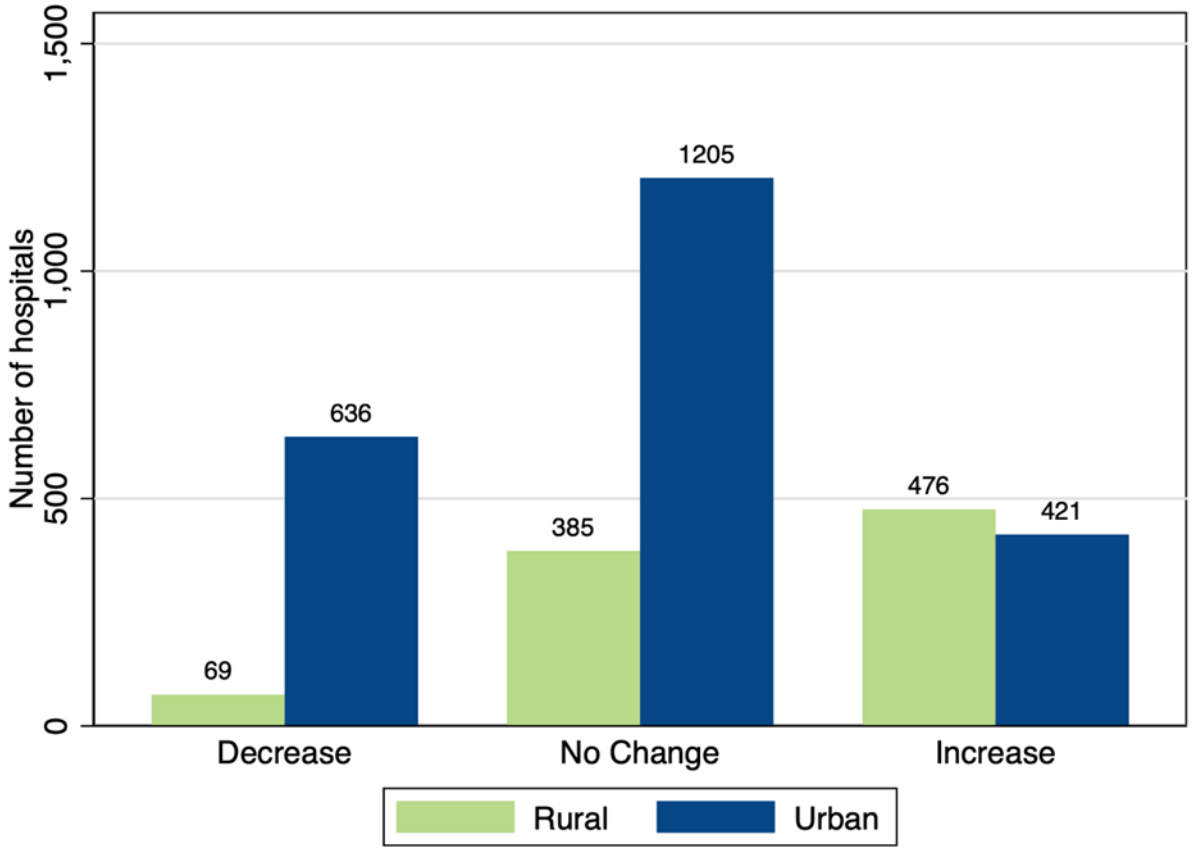
Wage Index		Number of Hospitals	Change between 2019 WI and 2020 WI *Update + Quartile + Cap*				Number of Hospitals		
			Minimum	Median	Mean	Maximum	WI Decrease	WI No Change	WI Increase
< 0.8482	Rural	473	0.0000	0.0318	0.0347	0.3228	-	9	464
	Urban	316	0.0000	0.0188	0.0217	0.0910	-	10	306
0.8482 to 1.0351	Rural	383	0.0000	0.0000	0.0006	0.0847	-	376	7
	Urban	1,239	0.0000	0.0000	0.0008	0.0853	-	1,195	44
>1.0351	Rural	74	-0.0356	-0.0067	-0.0028	0.0859	69	-	5
	Urban	707	-0.0356	-0.0100	-0.0048	0.1056	636	-	71
	Maryland	47	-0.0043	0.0000	-0.0001	0.0000	1	46	-
	IHS	29	-0.0387	-0.0176	-0.0191	-0.0176	29	-	-
	Puerto Rico	50	0.2096	0.2188	0.2227	0.2388	-	-	50
	Total	3,318					735	1,636	947

What are the effects of the quartile adjustment and cap?

Comparison of 2020 Wage Index AFTER Proposed Quartile Adjustment and Cap

Figure 2 shows the total number of rural and urban hospitals that would have an increase, no change, or a decrease in their 2020 wage index AFTER applying the proposed quartile adjustment and cap; that is, this is the change resulting from the proposed policy (the quartiles and cap). The chart shows that 69 rural and 636 urban hospitals would have a decrease in wage index, 385 rural and 1,205 urban hospitals would have no change in wage index, and 476 rural and 421 urban hospitals would have an increase in wage index.

Figure 2. Total Number of Rural and Urban Hospitals with Increase, No Change, and Decrease in 2020 Wage Index after Applying the Proposed Quartile Adjustment and Cap



Hospital sample in Figure 2: Total hospitals (3,318) minus hospitals in Maryland (47), Indian Health Service hospitals (29), and Puerto Rico hospitals (50), which equals 3,192.

Changes in 2020 Wage Index AFTER Proposed Quartile Adjustment and Cap by State

Table 4 shows the total number of rural and urban hospitals with an increase, no change,[10] and a decrease in their 2020 wage index AFTER applying the proposed quartile adjustment and cap by state; that is, comparing the 2020 Update Only to the 2020 With Quartiles and Cap. The states with the greatest number of rural hospitals with a positive wage index adjustment are in the South Census region: Texas (53), Alabama (43), Mississippi (38), Kentucky (32), Georgia (31) and Tennessee (30). The states with the greatest number of urban hospitals with a positive wage index adjustment are in Louisiana (57), Massachusetts (53), Texas (41), Alabama (40), and Arizona (34). The reasons behind the increases vary by state; for example, the quartiles adjustment is the primary driver in Alabama, while the cap is the primary driver in Massachusetts (the 2019 Wage Index was higher than the 2020 Update Only Wage Index).

Table 4. Total Number of Rural and Urban Hospitals with Increase, No Change, and Decrease in 2020 Wage Index from "Update Only" to AFTER Applying the Proposed Quartile Adjustment and Cap by State

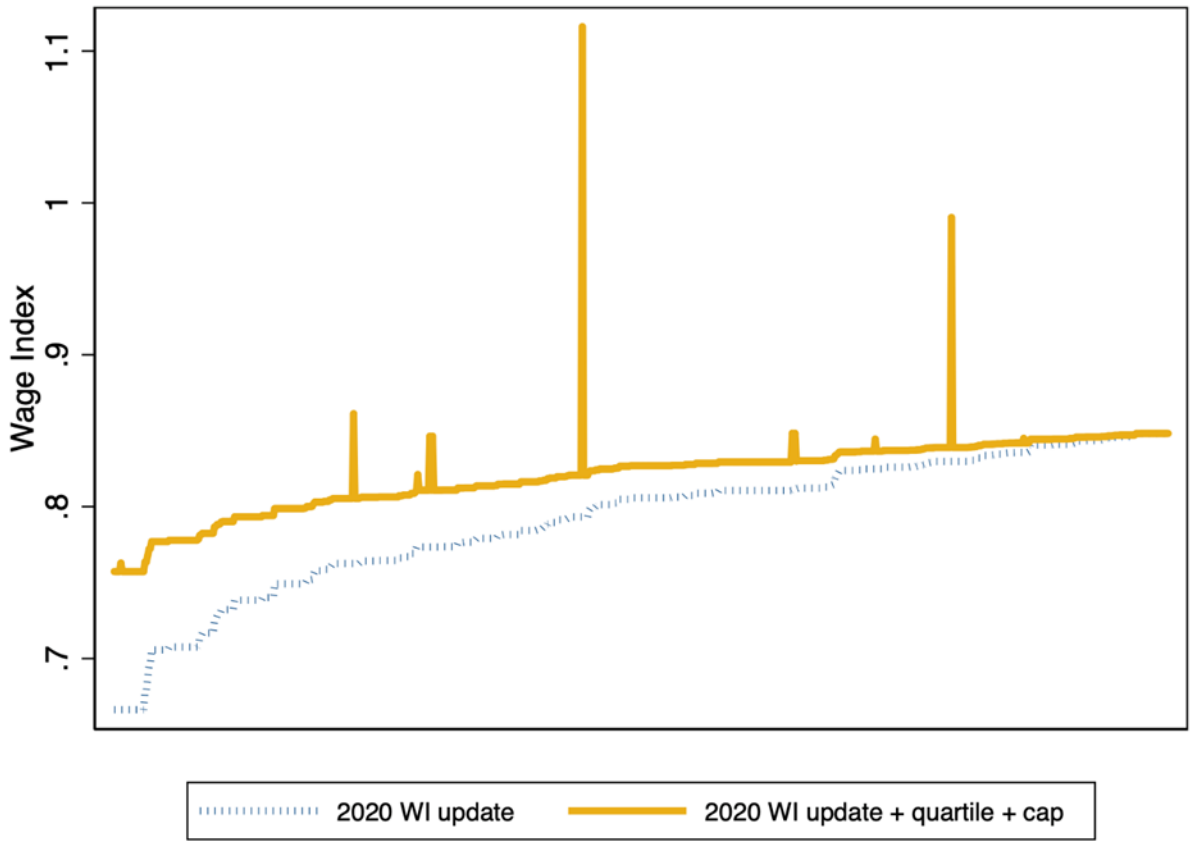
	Rural Hospitals				Urban Hospitals				Percent of Total Hospitals			
State	Decrease	No Change	Increase	Total	Decrease	No Change	Increase	Total	Decrease	No Change	Increase	Total
AK	3	0	0	3	3	0	0	3	100%	0%	0%	100%
AL	0	1	43	44	0	0	40	40	0%	1%	99%	100%
AR	0	1	20	21	0	3	22	25	0%	9%	91%	100%
AZ	0	4	2	6	2	12	34	48	4%	30%	67%	100%
CA	26	0	0	26	265	0	6	271	98%	0%	2%	100%
CO	0	11	0	11	0	38	0	38	0%	100%	0%	100%
CT	0	0	3	3	17	0	10	27	57%	0%	43%	100%
DC	0	0	0	0	0	7	0	7	0%	100%	0%	100%
DE	1	1	0	2	3	1	0	4	67%	33%	0%	100%
FL	0	6	6	12	0	139	17	156	0%	86%	14%	100%
GA	0	12	31	43	0	41	16	57	0%	53%	47%	100%
HI	4	0	0	4	8	0	0	8	100%	0%	0%	100%
IA	0	7	7	14	0	16	4	20	0%	68%	32%	100%
ID	0	1	2	3	2	10	1	13	13%	69%	19%	100%
IL	0	16	10	26	0	97	3	100	0%	90%	10%	100%
IN	0	17	3	20	0	64	1	65	0%	95%	5%	100%
KS	0	5	22	27	0	17	7	24	0%	43%	57%	100%
KY	0	13	32	45	0	16	3	19	0%	45%	55%	100%
LA	0	4	25	29	0	3	57	60	0%	8%	92%	100%
MA	0	0	2	2	0	0	53	53	0%	0%	100%	100%
ME	1	8	0	9	6	1	1	8	41%	53%	6%	100%
MI	1	30	0	31	8	51	4	63	10%	86%	4%	100%
MN	6	11	1	18	28	2	0	30	71%	27%	2%	100%
MO	0	10	20	30	0	34	8	42	0%	61%	39%	100%
MS	0	0	38	38	0	4	17	21	0%	7%	93%	100%
MT	0	7	0	7	0	6	0	6	0%	100%	0%	100%
NC	0	17	20	37	0	44	2	46	0%	73%	27%	100%
ND	0	1	0	1	0	5	0	5	0%	100%	0%	100%
NE	0	8	0	8	0	15	0	15	0%	100%	0%	100%
NH	4	0	0	4	9	0	0	9	100%	0%	0%	100%
NJ	1	0	0	1	62	0	1	63	98%	0%	2%	100%
NM	0	14	0	14	1	9	0	10	4%	96%	0%	100%
NV	0	1	0	1	19	2	0	21	86%	14%	0%	100%
NY	6	30	0	36	82	28	0	110	60%	40%	0%	100%
OH	0	22	18	40	0	81	8	89	0%	80%	20%	100%
OK	0	18	23	41	0	36	2	38	0%	68%	32%	100%
OR	8	0	0	8	26	0	0	26	100%	0%	0%	100%
PA	0	11	24	35	36	70	9	115	24%	54%	22%	100%
RI	0	0	0	0	11	0	0	11	100%	0%	0%	100%
SC	0	8	13	21	0	21	12	33	0%	54%	46%	100%
SD	0	8	0	8	0	8	0	8	0%	100%	0%	100%
TN	0	12	30	42	0	26	22	48	0%	42%	58%	100%
TX	0	26	53	79	0	183	41	224	0%	69%	31%	100%
UT	0	8	0	8	0	23	0	23	0%	100%	0%	100%
VA	0	8	14	22	0	44	6	50	0%	72%	28%	100%
VT	1	4	0	5	0	1	0	1	17%	83%	0%	100%
WA	3	3	0	6	38	5	0	43	84%	16%	0%	100%
WI	4	14	1	19	10	37	0	47	21%	77%	2%	100%
WV	0	0	13	13	0	2	14	16	0%	7%	93%	100%
WY	0	7	0	7	0	3	0	3	0%	100%	0%	100%
Total	69	385	476	930	636	1,205	421	2,262	22%	50%	28%	100%

Hospital sample in Table 4: Total hospitals (3,318) minus hospitals in Maryland (47), Indian Health Service hospitals (29), and Puerto Rico hospitals (50), which equals 3,192.

Magnitude of Proposed Quartile Adjustment and Cap for Rural and Urban Hospitals

Figure 3 shows the 2020 wage indexes BEFORE and AFTER applying the proposed quartile adjustment and cap for 789 hospitals with a 2020 updated wage index less than 0.8482. The data are sorted by 2020 wage index update only (i.e., before the proposed quartile adjustment and cap), from lowest to highest, and the gap between the two lines is the effect of the proposed quartile adjustment and cap. The figure shows that the greatest increases (the largest gaps) are for hospitals with the lowest 2020 wage indexes (at the left). Moving from left to right, the size of the gap decreases as the *2020 wage index update only* line approaches the 25th percentile value (0.8482). The few spikes are for hospitals receiving a large cap adjustment; their 2020 wage index post-quartile adjustment was less than 95 percent of their 2019 final wage index, and since the change was capped at 5 percent, their proposed 2020 wage index is increased to 95 percent of their 2019 wage index.[11]

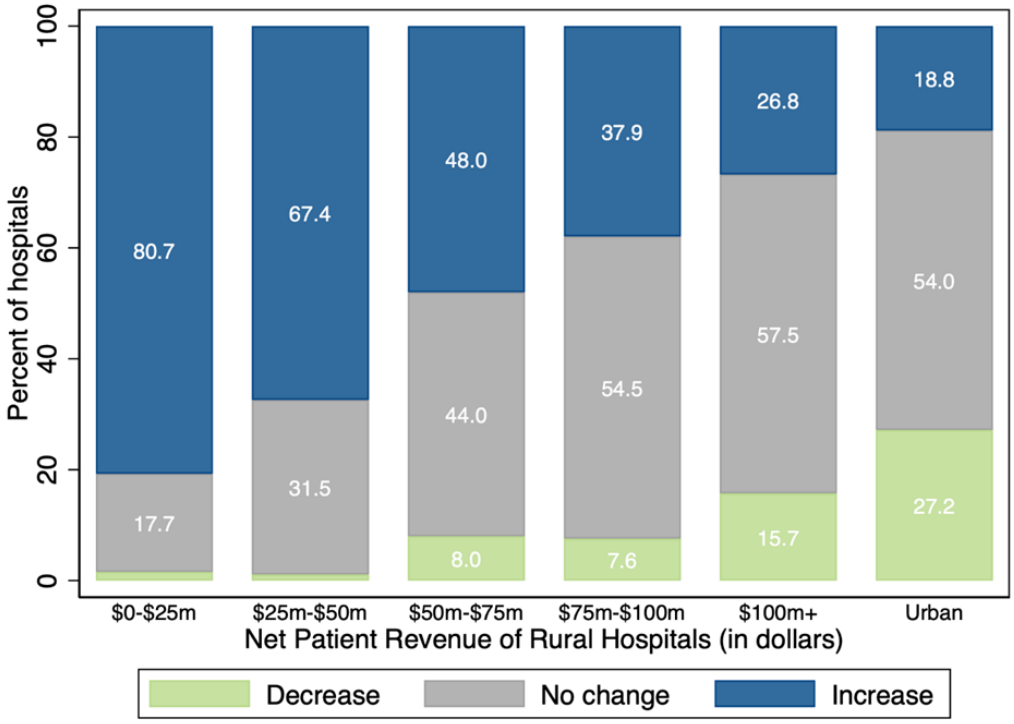
Figure 3. Proposed 2020 Wage Indexes BEFORE and AFTER Proposed Quartile Adjustment and Cap for 789 Hospitals with a 2020 Updated Wage Index Less than 0.8482 (25th percentile value)



Changes in 2020 Wage Index AFTER Applying the Proposed Quartile Adjustment and Cap by Net Patient Revenue of Hospital

Figure 4 shows the percentage of hospitals with a decrease, no change, and an increase in their 2020 wage index AFTER applying the proposed quartile adjustment and cap to the 2020 Update Only. Hospitals are categorized by net patient revenue. The figure shows that: 1) among rural hospitals, the percentage with an increase in wage index is largest for hospitals with less than $25 million in net patient revenue (80.7 percent) and smallest for those with greater than $100 million in net patient revenue (26.8%), and 2) the percentage with an increase in wage index for all groups of rural hospitals is larger than for urban hospitals (18.8%).

Figure 4. Percentage of Rural and Urban Hospitals with Increase, No Change, and Decrease in 2020 Wage Index AFTER Applying the Proposed Quartile Adjustment and Cap by Net Patient Revenue (millions)

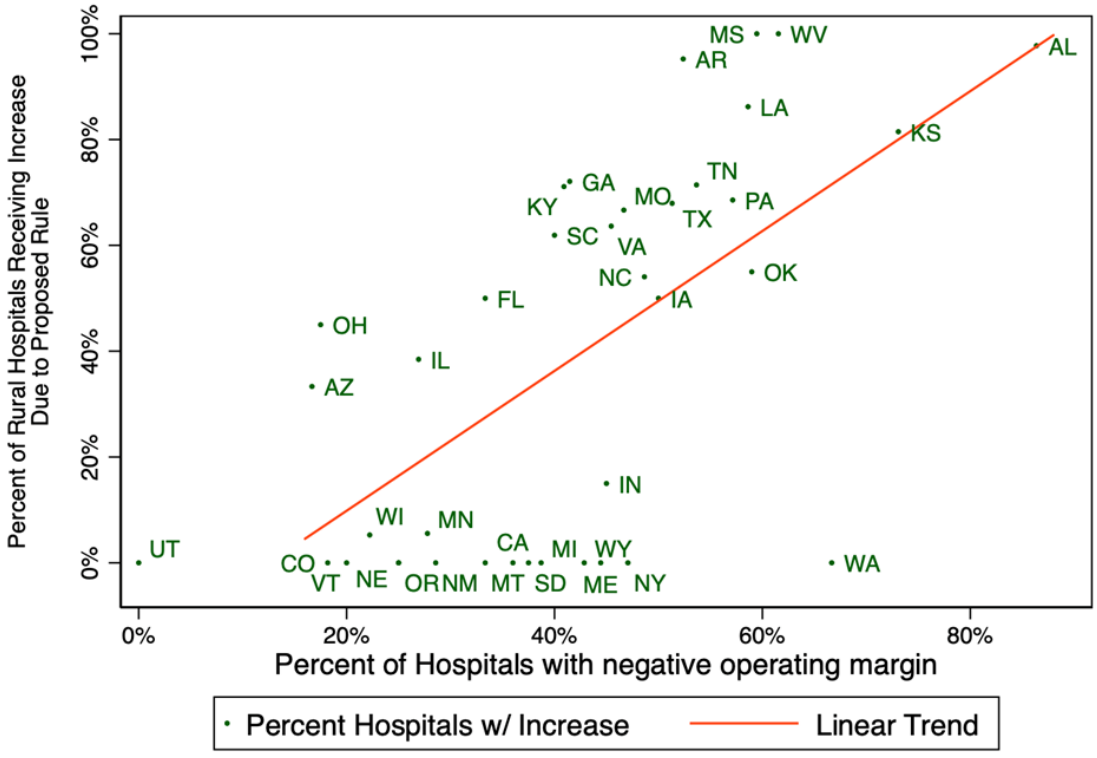


Hospital sample in Figure 4: Total hospitals (3,318) minus hospitals in Maryland (47), Indian Health Service hospitals (29), Puerto Rico hospitals (50), and 64 additional hospitals with negative, zero, or unavailable revenue which equals 3,128.

Changes in 2020 Wage Index after Applying the Proposed Quartile Adjustment and Cap by Hospital Profitability

Figure 5 shows that the states with the highest percentage of rural hospitals with an increase in wage index (Alabama, Kansas, West Virginia, Mississippi, and Louisiana) also have a higher percentage of rural hospitals with negative operating margins. Overall, states with lower profitability among rural hospitals were more likely to experience an increase in their wage index.

Figure 5. Percentage of Rural Hospitals with Increase in 2020 Wage Index AFTER Applying the Proposed Quartile Adjustment and Cap by Percent of Rural Hospitals with a Negative Operating Margin, by State



States with 5 or more rural hospitals only.

DISCUSSION

This study found substantial variation in the hospital wage index adjustment of rural and urban hospitals. The results show that the proposed quartile adjustment and cap would increase the wage index for:

- *Many rural and urban hospitals with relatively low 2019 wage indexes*. This is consistent with the stated CMS aim of reducing the disparities between high and low wage index hospitals;
- *Many rural hospitals in states in the South census region*. In a companion findings brief,[1] we identify the states with the lowest median wage indexes for rural hospitals as Alabama, Louisiana, Tennessee, Mississippi, and Virginia, and three of these states have the greatest number of rural hospitals with a positive wage index adjustment; and
- *Small rural hospitals with relatively low levels of net patient revenue*. In a 2017 article,[12] we found a higher risk of financial distress among rural hospitals with lower levels of net patient revenue. Given that a positive wage index adjustment could result in an increase in Medicare revenue, the proposed quartile adjustment may reduce the risk of financial distress for some rural hospitals.

However, it is important to note that: 1) differences between the 2019 and proposed 2020 wage indexes are due to the combined effects of all adjustments to the wage index (e.g., revised labor markets, reclassification, out-migration, adjustment, rural floor, and frontier state adjustment), and not the proposed quartile adjustment only; 2) the proposed 2020 wage indexes apply to hospitals paid under IPPS only and won't affect Critical Access Hospitals which are more than half of all rural hospitals; and 3) an ultimate test of the proposed 2020 wage indexes will be whether the resultant change in Medicare revenue has a material effect on profitability and long term financial viability of rural hospitals paid under IPPS.

REFERENCES AND NOTES

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3. Acute Inpatient PPS Wage Index. Centers for Medicare & Medicaid Services. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/wageindex.html.
4. CMS also proposes removing the urban to rural hospital reclassifications for calculating the rural floor wage index value starting in fiscal year 2020.
5. King R. CMS proposes $4.7 billion more for inpatient spending, changing wage index, *Modern Healthcare* April 23 2019. Available at: https://www.modernhealthcare.com/government/cms-proposes-47-billion-more-inpatient-spending-changing-wage-index.
6. The CMS Impact File includes all facilities with a wage index and paid using the IPPS. In addition to acute care hospitals, the list of facilities includes a small number of Long Term Care Hospitals, mental health centers, and other facilities that have small acute inpatient units. These facilities are included in the data because they: have a wage index and are paid using the IPPS for the acute care provided to Medicare patients.
7. FY 2020 Proposed Rule Tables 2, 3 and 4 (Wage Index Tables) [ZIP, 663KB]: Table 2- Proposed Case-Mix Index and Wage Index Table by CMS Certification Number (CCN); Table 3- Proposed Wage Index Table by CBSA; Table 4- Proposed List of Counties Eligible for the Out-Migration Adjustment under Section 1886(d)(13) of the Act (Updated Tables 2 and 3 on May 16, 2019). Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/FY2020-IPPS-Proposed-Rule-Home-Page-Items/FY2020-IPPS-Proposed-Rule-Tables.html?DLPage=1&DLEntries=10&DLSort=0&DLSortDir=ascending.
8. FY2019 Wage Index Public Use Files (Final Rule and Correction Notice). Centers for Medicare & Medicaid Services. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Downloads/FY2019-CMS-1694-FR-Wage-Index-PUF.zip.
9. The FORHP definition of rural area differs from the rural area definition and rural reclassification criteria used by CMS for payment purposes. Available at: https://www.hrsa.gov/rural-health/about-us/definition/index.html.
10. Some hospitals in frontier states like ND, WY, and MT have a wage index adjustment of 0 because they are in a frontier state and their wage indexes are fixed at 1.0.
11. The very high spike a hospital whose 2019 final wage index was 1.1747, and its 2020 update BEFORE the quartile adjustment and cap is 0.7932. The hospital was reclassified from CBSA to rural, and thus the 2020 update fell considerably, but the cap reduced the decrease to 1.1747*0.95 = 1.116.
12. Holmes GM, Kaufman BG, Pink GH. Predicting Financial Distress and Closure in Rural Hospitals, *Journal of Rural Health* 2017;33:239–249. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27500663.