

APPENDIX

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Table S1. Oral Opioids Included in the Analysis

Opioid Name
buprenorphine
codeine
dihydrocodeine
fentanyl
hydrocodone
hydromorphone
levorphanol
meperidine
methadone
morphine
oxycodone
oxymorphone
propoxyphene
sufentanil
tapentadol
tramadol

All forms and combinations of the named medications were identified with claims data.

Table S2. Diagnosis Codes for Cancers and History of Cancers

Cancers	ICD-10
Malignant neoplasms	C00.0, C00.1, C00.2, C00.3, C00.4, C00.5, C00.6, C00.8, C00.9, C01, C02.0, C02.1, C02.2, C02.3, C02.4, C02.8, C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.8.8C049, C05.0, C05.1, C05.2, C05.8, C05.9, C06.0, C06.1, C06.2, C06.80, C06.89, C06.9, C07, C07.8, C07.80, C08.0, C08.0.0, C08.1, C08.9, C09.0, C09.1, C09.8, C09.9 C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C11.0, C11.1, C11.2, C11.3, C11.8, C11.9, C12, C13.0, C13.1, C13.2, C13.8, C13.9, C14.0, C14.2, C15.3, C15.4, C15.5, C15.8, C15.9, C16.0, C16.1, C16.2, C16.3, C16.4, C16.5, C16.6, C16.8, C16.9, C17.0, C17.1, C17.2, C17.8, C17.9, C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19, C20, C21.0, C21.1, C21.2, C21.8, C22.8, C22.9, C23, C23.1, C24.0, C24.1, C24.8, C24.9, C25.0, C25.1, C25.2, C25.3, C25.4, C25.7, C25.8, C25.9, C26.0, C26.1, C26.9, C27.0, C27.1, C27.2, C27.3, C27.8, C27.9, C28.0, C28.1, C28.2, C28.3, C28.4, C28.5, C28.6, C28.7, C28.8, C28.9, C29.0, C29.1, C29.2 C41.0, C41.1, C41.2, C41.3, C41.4, C41.9, C44.00, C44.09, C44.100, C44.101, C44.102, C44.109, C44.191, C44.192, C44.199, C44.201, C44.202, C44.209, C44.291, C44.292, C44.299, C44.300, C44.301, C44.309, C44.390, C44.391, C44.399, C44.40, C44.49, C44.500, C44.501, C44.509, C44.590, C44.591, C44.599, C44.601, C44.602, C44.609, C44.691, C44.692, C44.699, C44.701, C44.702, C44.709, C44.791, C44.792, C44.799, C44.80, C44.89, C44.90, C44.99, C47.0, C47.20, C47.21, C47.22, C47.3, C47.4, C47.5, C47.6, C47.9, C48.0, C48.1, C48.2, C48.8, C49.3, C49.4, C49.5, C49.6, C49.8, C49.9 C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.212, C50.219, C50.221, C50.222, C50.229, C50.312, C50.319, C50.321, C50.322, C50.329, C50.412, C50.419, C50.421, C50.422, C50.429, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929, C51.0, C51.1, C51.2, C51.8, C51.9, C52, C53.0, C53.1, C53.8, C53.9, C54.0, C54.1, C54.2, C54.3, C54.8, C54.9, C55, C56.1, C56.2, C56.9, C57.00, C57.01, C57.02, C57.10, C57.11, C57.12, C57.20, C57.21, C57.22, C57.30, C57.31, C57.32, C57.40, C57.41, C57.42, C57.50, C57.51, C57.52, C57.60, C57.61, C57.62, C57.80, C57.81, C57.82, C57.90, C57.91, C57.92, C61, C62.00, C62.01, C62.02, C62.10, C62.11, C62.12, C62.90, C62.92, C63.00, C63.01, C63.02, C63.10, C63.11, C63.12, C63.20, C63.7, C63.8, C63.9, C64.1, C64.2, C64.9, C65.1, C65.2, C65.9, C66.1, C66.2, C66.9, C67.0, C67.1, C67.2, C67.3, C67.4, C67.5, C67.6, C67.7, C67.8, C67.9, C68.0, C68.1, C68.8, C68.9, C69.00, C69.01, C69.02, C69.10, C69.11, C69.12, C69.20, C69.21, C69.22, C69.30, C69.31, C69.32, C69.40, C69.41, C69.42, C69.50, C69.51, C69.52, C69.60, C69.61, C69.62, C69.80, C69.81, C69.82, C69.90, C69.91, C69.92, C7B, C70.0, C70.1, C70.9, C71.0, C71.1, C71.2, C71.3, C71.4, C71.5, C71.6, C71.7, C71.8, C71.9, C72.0, C72.1, C72.20, C72.21, C72.22, C72.30, C72.31, C72.32, C72.40, C72.41, C72.42, C72.50, C72.59, C72.9, C73, C74.00, C74.01, C74.02, C74.10, C74.11, C74.12, C74.90, C74.91, C74.92, C75.0, C75.1, C75.2, C75.3, C75.4, C75.5, C75.8, C75.9, C76.0, C76.1, C76.2, C76.3, C76.40, C76.41, C76.42, C76.50, C76.51, C76.52, C76.8, C77.0, C77.1, C77.2, C77.3, C77.4, C77.5, C77.8, C77.9, C78.00, C78.01, C78.02, C78.1, C78.2, C78.30, C78.39, C78.4, C78.5, C78.6, C78.7, C78.80, C78.89, C79.00, C79.01, C79.02, C79.10, C79.11, C79.19, C79.2, C79.31, C79.32, C79.40, C79.49, C79.51, C79.52, C79.60, C79.61, C79.62, C79.70, C79.71, C79.72, C79.81, C79.82, C79.89, C79.9, C80.0, C80.1, C80.2, C96.20, C96.29, Z85.00, Z85.01, Z85.028, Z85.038, Z85.05, Z85.068, Z85.07, Z85.09, Z85.118, Z85.12, Z85.20, Z85.21, Z85.238, Z85.3, Z85.41, Z85.42, Z85.43, Z85.44, Z85.46, Z85.47, Z85.48, Z85.49, Z85.51, Z85.528, Z85.53, Z85.54, Z85.59, Z85.810, Z85.828, Z85.830, Z85.831, Z85.840, Z85.841, Z85.848, Z85.850, Z85.858, Z85.89, Z85.9, Z86.000, Z86.001, Z86.008, Z86.003
Melanomas	C43.0, C43.10, C43.11, C43.12, C43.20, C43.21, C43.22, C43.30, C43.31, C43.39, C43.4, C43.51, C43.52, C43.59, C43.60, C43.61, C43.62, C43.70, C43.71, C43.72, C43.8, C43.9, D03.0, D03.10, D03.11, D03.12, D03.20, D03.21, D03.22, D03.30, D03.39, D03.4, D03.51, D03.52, D03.59, D03.60, D03.61, D03.62, D03.70, D03.71, D03.72, D03.8, D03.9, Z85.820

Sarcomas	C22.3, C22.4, C46.0, C46.1, C46.2, C46.3, C46.4, C46.50, C46.51, C46.52, C46.7, C46.9, C92.30, C92.31, C92.32, C96.22, C96.4, C96.A
Lymphomas	C84.Z, C85.9, C81.00, C81.02, C81.03, C81.06, C81.07, C81.08, C81.10, C81.12, C81.13, C81.16, C81.17, C81.18, C81.20, C81.22, C81.23, C81.26, C81.27, C81.28, C81.30, C81.32, C81.33, C81.36, C81.37, C81.38, C81.40, C81.41, C81.42, C81.43, C81.44, C81.46, C81.47, C81.48, C81.49, C81.70, C81.71, C81.72, C81.73, C81.74, C81.75, C81.76, C81.77, C81.78, C81.79, C81.90, C81.91, C81.92, C81.93, C81.94, C81.95, C81.96, C81.97, C81.98, C81.99, C82.00, C82.01, C82.02, C82.03, C82.04, C82.06, C82.07, C82.08, C82.09, C82.10, C82.11, C82.12, C82.13, C82.14, C82.16, C82.17, C82.18, C82.19, C82.20, C82.22, C82.23, C82.26, C82.27, C82.28, C82.30, C82.31, C82.32, C82.33, C82.34, C82.36, C82.37, C82.38, C82.39, C82.40, C82.41, C82.42, C82.43, C82.44, C82.46, C82.47, C82.48, C82.49, C82.50, C82.52, C82.53, C82.56, C82.57, C82.58, C82.60, C82.61, C82.62, C82.63, C82.64, C82.66, C82.67, C82.68, C82.69, C82.80, C82.82, C82.83, C82.86, C82.87, C82.88, C82.90, C82.91, C82.92, C82.93, C82.94, C82.95, C82.96, C82.97, C82.98, C82.99, C83.00, C83.01, C83.02, C83.03, C83.04, C83.06, C83.07, C83.08, C83.09, C83.10, C83.11, C83.12, C83.13, C83.14, C83.15, C83.16, C83.17, C83.18, C83.19, C83.30, C83.31, C83.32, C83.33, C83.36, C83.37, C83.38, C83.39, C83.50, C83.51, C83.52, C83.53, C83.54, C83.55, C83.56, C83.57, C83.58, C83.59, C83.70, C83.71, C83.72, C83.73, C83.74, C83.75, C83.76, C83.77, C83.78, C83.79, C83.80, C83.81, C83.82, C83.83, C83.84, C83.85, C83.86, C83.87, C83.88, C83.89, C83.90, C83.91, C83.92, C83.93, C83.94, C83.96, C83.97, C83.98, C83.99, C84.40, C84.42, C84.43, C84.46, C84.47, C84.48, C84.60, C84.62, C84.63, C84.66, C84.67, C84.68, C84.70, C84.72, C84.73, C84.76, C84.77, C84.78, C84.90, C84.92, C84.93, C84.96, C84.97, C84.98, C84.A0, C84.A1, C84.A2, C84.A3, C84.A4, C84.A6, C84.A7, C84.A8, C84.A9, C84.Z0, C84.Z2, C84.Z3, C84.Z6, C84.Z7, C84.Z8, C85.10, C85.11, C85.12, C85.13, C85.14, C85.15, C85.16, C85.17, C85.18, C85.19, C85.20, C85.22, C85.23, C85.26, C85.27, C85.28, C85.80, C85.82, C85.83, C85.86, C85.87, C85.88, C85.90, C85.91, C85.92, C85.93, C85.94, C85.95, C85.96, C85.97, C85.98, C85.99, C86.0, C86.1, C86.2, C86.3, C86.4, C86.5, C91.51, C91.52, Z8571, Z8572
Leukemias	C90.10, C90.11, C90.12, C91.00, C91.01, C91.02, C91.11, C91.12, C91.30, C91.31, C91.32, C91.40, C91.41, C91.42, C91.60, C91.61, C91.62, C91.90, C91.91, C91.92, C91.A0, C91.A1, C91.A2, C91.Z0, C91.Z1, C91.Z2, C92.00, C92.01, C92.02, C92.11, C92.12, C92.21, C92.22, C92.40, C92.41, C92.42, C92.50, C92.51, C92.52, C92.60, C92.61, C92.62, C92.90, C92.91, C92.92, C92.A1, C92.A2, C92.Z0, C92.Z1, C92.Z2, C93.00, C93.01, C93.02, C93.10, C93.11, C93.12, C93.30, C93.31, C93.32, C93.90, C93.91, C93.92, C93.Z0, C93.Z1, C93.Z2, C94.00, C94.01, C94.02, C94.20, C94.21, C94.22, C94.30, C94.31, C94.32, C94.80, C94.81, C94.82, C95.00, C95.01, C95.02, C95.10, C95.11, C95.12, C95.90, C95.91, C95.92, C96.2
Carcinoid tumors and Carcinomas	C44.01, C44.02, C44.111, C44.112, C44.119, C44.121, C44.122, C44.129, C44.202, C44.209, C44.211, C44.212, C44.219, C44.221, C44.222, C44.229, C44.310, C44.311, C44.319, C44.320, C44.321, C44.329, C44.41, C44.42, C44.49
Other	C94.40, C94.41, C94.42, C88, C96.0, C96.5, C96.6, C96.21, C17.3, C22.2, C84.00, C84.01, C84.02, C84.03, C84.04, C84.05, C84.06, C84.07, C84.08, C84.09, C84.10, C84.11, C84.12, C84.13, C84.14, C84.15, C84.16, C84.17, C84.18, C84.19

Table S3. Diagnosis Codes for Sickle-Cell Anemia

Sickle-Cell	ICD-10
Hb-SS disease with crisis, unspecified	D57.00
Hb-SS disease with acute chest syndrome	D57.01
Hb-SS disease with splenic sequestration	D57.02
Sickle-cell disease without crisis	D57.1
Sickle-cell/Hb-C disease without crisis	D57.20
Sickle-cell/Hb-C disease with acute chest syndrome	D57.211
Sickle-cell/Hb-C disease with splenic sequestration	D57.212
Sickle-cell/Hb-C disease with crisis, unspecified	D57.219
Sickle-cell trait	D57.3
Sickle-cell thalassemia without crisis	D57.40
Sickle-cell thalassemia with acute chest syndrome	D57.411
Sickle-cell thalassemia with splenic sequestration	D57.412
Sickle-cell thalassemia with crisis, unspecified	D57.419
Other sickle-cell disorders without crisis	D57.80
Other sickle-cell disorders with acute chest syndrome	D57.811
Other sickle-cell disorders with splenic sequestration	D57.812
Other sickle-cell disorders with crisis, unspecified	D57.819

Table S4. Milliman's MedInsight Health Waste Calculator Specifications for Low-Value Opioids for Acute Low Back Pain

Starting Population	All claims for those aged ≥ 18 years who received an opioid prescription during the acute timeframe (< 28 days) for low back pain between 2019-2021.
Classified as Clinically Appropriate	Claims for patients with a diagnosis of cancer or sickle cell anemia. Claims for patients with an indication of a trial of other options before the prescription (e.g., getting non-steroidal anti-inflammatories within a specified timeframe before the opioid prescription).
Classified as Low-value	All remaining.

Other studies have applied this methodology to evaluate low-value opioid utilization.¹⁻³

Table S5. Unadjusted Rate of Annual Opioids Prescribed for Acute Low Back Pain and Percentage of Total Opioids Characterized as Low-value in a Virginia Cohort (2019-2021)

	<i>Prescription Claims per 1000 Patients</i> ^a			
	2019	2020	2021	2019 to 2021 ^c
Total	210.1	174.7	146.5	177.1
Low-value	155.0	130.0	107.5	130.8
Clinically Appropriate	55.1	44.7	39.0	46.3
	<i>Percentage of Low-value</i> ^b			
	73.8%	74.3%	73.3%	73.9%

^a Annual opioid utilization rate (number of prescription claims divided by total number of patients multiplied by 1000)

^b Percentage (or proportion) of annual opioid utilization for acute LBP that were characterized as low-value

^c The three-year mean (2019-2021)

Table S6. Unadjusted Rate of Total Annual Utilization of Opioids for Acute Low Back Pain and Percentage of Total Utilization Characterized as Low-value in Virginia by Demographic Characteristic (2019-2021)

	<i>Prescription Claims per 1000 Patients ^a (Low-value Percentage) ^b</i>			
Year	2019	2020	2021	2019 to 2021 ^c
Age (Years)				
18-39	56.2 (72.4)	40.1 (72.9)	27.0 (71.2)	41.1 (72.2)
40-64	342.2 (76.5)	293.7 (77.2)	228.8 (75.7)	288.2 (76.5)
65-79	203.1 (71.9)	171.6 (72.0)	164.0 (72.0)	179.6 (71.9)
80+	146.2 (66.7)	111.6 (68.8)	104.9 (67.1)	120.9 (67.5)
Biological Sex				
Female	229.5 (74.3)	190.4 (74.9)	161.9 (73.7)	193.9 (74.2)
Male	184.8 (73.0)	154.5 (73.8)	126.5 (72.9)	155.3 (73.2)
Rurality				
Rural	373.6 (76.2)	310.0 (76.1)	274.6 (75.7)	319.4 (76.0)
Non-Rural	188.7 (73.1)	156.2 (74.0)	130.3 (72.8)	158.4 (73.3)
Payer				
Commercial	103.6 (73.1)	79.4 (74.0)	65.1 (72.7)	82.7 (73.3)
Medicaid	196.7 (71.0)	104.4 (70.9)	57.4 (70.0)	119.5 (70.6)
Medicare Advantage	287.6 (74.3)	252.3 (74.9)	235.6 (73.8)	258.5 (74.3)

^a Annual opioid utilization rate (number of opioid prescription claims in each demographic characteristic group divided by the number of patients in each demographic characteristic group multiplied by 1000).

^b The percentage (or proportion) of annual opioid utilization characterized as low-value.

^c The three-year mean (2019-2021). Percentages may not total 100 due to rounding.

Table S7. Rate Regression Effects for Low-value Utilization of Opioids for Acute Low Back Pain in Virginia (2019-2021)

<i>Term</i>	<i>IRR (95% CI)</i>	<i>Estimate</i>	<i>Std. Error</i>	<i>Z (Wald)</i>	<i>P-Value</i>
Year (Since 2019)	0.906 (0.860, 0.955)	-0.098	0.027	13.32	<.001***
DiD (False) vs. ^a	1.0	0.0			
DiD (True)	0.796 (0.687, 0.921)	-0.228	0.075	9.33	0.002*
Rurality (Non-Rural) vs. ^a	1.0	0.0			
Rurality (Rural)	1.738 (1.297, 2.329)	0.055	0.149	13.69	<.001***
DiD x Rurality (Non-Rural) vs. ^b	1.0				
DiD x Rurality (Rural)	1.017 (0.954, 1.085)	0.017	0.033	0.27	0.060
Payer (Commercial) vs. ^a	1.0	0.0			
Payer (Medicaid)	1.992 (1.504, 2.639)	0.689	0.144	23.06	<.001***
Payer (MA)	5.268 (4.104, 6.762)	1.662	0.127	170.25	<.001***
DiD x Payer (Commercial) vs. ^b	1.0				
DiD x Payer (Medicaid)	0.552 (0.477, 0.639)	-0.594	0.075	63.54	<.001***
DiD x Payer (MA)	1.195 (1.068, 1.337)	0.178	0.057	9.62	0.002**
Rurality x Payer (Commercial) vs. ^c	1.0				
Rurality x Payer (Medicaid)	1.012 (0.693, 1.478)	0.012	0.193	0.00	0.950
Rurality x Payer (MA)	0.747 (0.561, 0.994)	-0.291	0.146	4.00	0.046*
Months (Jan-Feb) vs. ^a	1.0	0.0			
Months (Mar-April)	1.063 (1.039, 1.088)	0.062	0.012	26.34	<.001***
Months (May-Jun)	1.059 (1.032, 1.086)	0.057	0.013	19.45	<.001***
Months (Jul-Aug)	1.036 (1.002, 1.071)	0.035	0.017	4.31	0.038*
Months (Sep-Oct)	1.020 (0.985, 1.057)	0.020	0.018	1.23	0.267
Months (Nov-Dec)	0.969 (0.937, 1.002)	-0.031	0.017	3.37	0.066
DiD x Months (Jan-Feb) vs. ^b	1.0				
DiD x Months (Mar-April)	0.995 (0.973, 1.017)	-0.005	0.011	0.21	0.650
DiD x Months (May-Jun)	0.987 (0.961, 1.014)	-0.013	0.014	0.87	0.351
DiD x Months (Jul-Aug)	1.058 (1.024, 1.093)	0.056	0.017	11.46	<.001***
DiD x Months (Sep-Oct)	1.030 (0.992, 1.070)	0.029	0.019	2.33	0.127
DiD x Months (Nov-Dec)	0.959 (0.929, 0.990)	-0.042	0.016	6.50	0.011*
Age (18-39 years) vs. ^a	1.0	0.0			
Age (40-64 years)	4.437 (3.893, 5.058)	1.490	0.067	497.59	<.001***
Age (65-79 years)	1.073 (0.890, 1.295)	0.071	0.096	0.55	0.459
Age (80+ years)	0.661 (0.538, 0.810)	-0.415	0.104	15.81	<.001***
Sex (F) vs. ^a	1.0	0.0			
Sex (M)	0.729 (0.653, 0.813)	-0.316	0.056	31.95	<.001***
Rurality x Sex (F) vs. ^c	1.0				
Rurality x Sex (M)	1.253 (1.097, 1.431)	0.226	0.068	11.03	<.001***

Abbreviations: MA = Medicare Advantage; F = Female; M = Male; CI = Confidence Interval

^a Incidence rate ratios (IRRs) represent multiplicative changes in opioid prescribing rates per 1,000 patients associated with each covariate relative to the reference category, with 95% confidence intervals.

^b Interaction terms which include the DiD term (DiD x Rurality, DiD x Payer) represent difference-in-differences effects on the multiplicative scale. Specifically, these IRRs indicate how the pandemic-associated change in prescribing rates differs across subgroups relative to the reference category..

^c Cross-sectional interaction terms (e.g., Rurality x Payer) represent multiplicative effect modification. For example, Rurality x Payer compares the rural-nonrural rate ratio across payer types.

* denotes a p-value of <.05, ** denotes a p-value <.01, and *** denotes a p-value <.001

References

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