

Supplementary Appendix

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

Supplement to: Zhu W, Chernew ME, Sherry TB, Maestas N. Initial opioid prescriptions among U.S. commercially insured patients, 2012–2017. *N Engl J Med* 2019;380:1043-52. DOI: 10.1056/NEJMsa1807069

Supplementary Appendix for

“Initial Opioid Prescriptions in U.S. Commercial Health Insurance, 2012-2017”

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Appendix A: Comparison of BCBS Populations to the U.S. Privately Insured

2 Table S1: Summary Statistics of Privately Insured Populations Aged 15 and Older, 2012-2017

Appendix B

3 Opioid Ingredients and Morphine Milligram Equivalent (MME) Conversion Factors

Appendix C

4 Chronic and Acute Pain-Related Indications and Associated ICD-9 Codes

Appendix D: Supplementary Figures

8 Figure S1: Decomposition of Opioid Incidence by Prescriber and Patient Subgroups, July 2012 – December 2017

9 Figure S2: Incidence Rate of Opioid Prescriptions by Census Region, Gender, and Age Group, July 2012 – December 2017

10 Figure S3: Average Days’ Supply and MME/day of Initial Opioid Prescriptions, Overall and by Prescriber Specialty, Patient Indication, Census Region, Gender, and Age Group, July 2012 – December 2017

12 Figure S4: Share of Initial Opioid Prescriptions with High Duration (Days’ Supply >3, Days’ Supply >7), Overall and by Prescriber Specialty, Patient Indication, Census Region, Gender, and Age Group, July 2012 – December 2017

14 Figure S5: Share of Initial Opioid Prescriptions with High Dose (MME/day ≥ 50 , MME/day ≥ 90), Overall and by Prescriber Specialty, Patient Indication, Census Region, Gender, and Age Group, July 2012 – December 2017

Online Appendix A. Comparison of BCBS Populations to the U.S. Privately Insured

Table S1. Summary Statistics of Privately Insured Populations Aged 15 and Older, 2012-2017

	U.S. Privately Insured	BCBS Populations			
		All Eligibles (N=86,258,528)	Opioid-Naïve Eligibles (N=63,817,512)	Eligibles with Any Opioid (N=19,911,193)	Opioid-Naïve Eligibles with First Opioid (N=10,874,869)
Gender					
Female	51%	51%	51%	55%	54%
Age					
15-24	17%	18%	19%	7%	16%
25-34	16%	18%	17%	13%	17%
35-44	17%	19%	19%	19%	19%
45-54	19%	22%	22%	28%	22%
55-64	17%	21%	21%	30%	22%
65+	15%	3%	3%	3%	3%
Region					
Northeast	19%	19%	20%	16%	17%
Midwest	23%	22%	23%	22%	24%
South	35%	49%	47%	52%	48%
West	23%	10%	10%	11%	11%

Note: Statistics for "U.S. Privately Insured" come from the Annual Social and Economic Supplement fielded as part of the Current Population Survey (CPS), 2012-2017. Persons younger than 15 years old were excluded from the data.

The BCBS "All Eligibles" include enrollees who were 15 years and older, resided in the United States, and had primary medical and prescription drug coverage in a given month between July 2012 and December 2017. "Opioid-Naïve Eligibles" are "All Eligibles" who had been continuously enrolled for at least 6 months and had no recorded opioid prescription or diagnosis of opioid use disorder in the 6 months prior to a given month. "Eligibles with Any Opioid" are "All Eligibles" who received an opioid prescription during the study period. "Opioid-Naïve Eligibles with First Opioid" are "Opioid-Naïve Eligibles" who received their first opioid prescription during the study period.

Online Appendix B. Opioid Ingredients and Morphine Milligram Equivalent (MME) Conversion Factors

Opioid (strength in mg except where noted)	MME Conversion Factor
Buprenorphine, transdermal patch (MCG/HR)	12.6
Buprenorphine, tablet or film	30
Buprenorphine, film (MCG)	0.03
Butorphanol	7
Codeine	0.15
Dihydrocodeine	0.25
Fentanyl, buccal/SL tablet or lozenge/troche (MCG)	0.13
Fentanyl, film or oral spray (MCG)	0.18
Fentanyl, nasal spray (MCG)	0.16
Fentanyl, transdermal patch (MCG/HR)	7.2
Hydrocodone	1
Hydromorphone	4
Levomethadyl acetate	8
Levorphanol tartrate	11
Meperidine	0.1
Methadone	
>0, <= 20	4
>20, <=40	8
>40, <=60	10
>60	12
Morphine	1
Opium	1
Oxycodone	1.5
Oxymorphone	3
Pentazocine	0.37
Propoxyphene	0.23
Tapentadol	0.4
Tramadol	0.1

Note: This table shows a list of MME conversion factors compiled from multiple sources, including CDC,¹ CMS,² NCIPC,³ and the literature.⁴

Online Appendix C. Chronic and Acute Pain-Related Indications and Associated ICD-9 Codes

We follow a recent paper by Sherry and colleagues⁵ in defining pain-related indications as “those where prescription-strength pain medications might be needed to provide adequate relief, and where pain does not resolve promptly with treatment of the underlying pathologic process alone. This definition excludes conditions such as urinary tract infections, ear infections, and angina, because pain typically resolves promptly with treatment.” Chronic conditions are those lasting three months or longer, while acute conditions are those lasting less than three months.

ICD-9 Codes for All Chronic Painful Conditions:

Note: “*” indicates that all subcodes are included

Infectious Diseases:

003.23, 015.*, 053.12, 053.13, 056.71, 088.81, 135, 136.0, 136.1, 122.*, 137.3

Endocrine Disease:

249.60, 249.61, 249.70, 249.71, 250.60, 250.61, 250.62, 250.63, 250.70, 250.71, 250.72, 250.73, 251.5, 268.0, 268.1, 268.2

Nutrition:

266.0, 266.2

Joint Disease:

135, 274.0, 274.00, 274.02, 274.03, 274.9, 275.01, 275.02, 275.03, 275.49, 277.2, 277.30, 277.31

Cancer:

140.*, 141.*, 142.*, 143.*, 144.*, 145.*, 146.*, 147.*, 148.*, 149.*, 150.*, 151.*, 152.*, 153.*, 154.*, 155.*, 156.*, 157.*, 158.*, 159.*, 160.*, 161.*, 162.*, 163.*, 164.*, 165.*, 166.*, 167.*, 168.*, 169.*, 170.*, 171.*, 172.*, 173.*, 174.*, 175.*, 176.3, 176.4, 177.*, 178.*, 179.*, 180.*, 181.*, 182.*, 183.*, 184.*, 185.*, 186.*, 187.*, 188.*, 189.*, 191.*, 192.*, 194.*, 195.*, 196.*, 197.*, 198.*, 199.*, 200.*, 201.*, 202.*, 203.*, 204.*, 205.*, 206.*, 207.*, 208.*, 209.*, 218.*, 235.*, 236.*, 237.*, 238.*, 239.*, 528.01, 357.3, V10.*, V58.0, V58.1*, 990

Immune Disorders:

279.50, 279.52, 279.53

Hematologic Disorders:

282.41, 282.60, 282.61, 282.63, 282.68, 286.0, 286.1, 289.1

Neurologic Disorders (including headache):

322.2, 332.0*, 336.0, 339.00, 339.02, 339.04, 339.09, 339.10, 339.12, 339.20, 339.22, 339.41, 339.42, 339.44, 339.89, 340, 341.0, 346.7*, 349.0, 353.*, 354.*, 355.*, 356.0, 356.2, 356.4, 356.8, 356.9, 357.1, 357.2, 357.4, 357.5, 357.6, 357.7, 357.81, 357.89, 357.9

Pain (cause unspecified):

338.0, 338.21, 338.22, 338.28, 338.29, 338.3 (NB this is cancer-related pain), 338.4, 780.96

Eye Disorders:

360.03

Ear Disorders:

380.02, 380.03, 380.14, 383.1, 383.20, 383.22, 383.9, 388.7*

Cardiovascular Disorders:

393, 443.1, 443.8*, 443.9, 446.0, 446.3, 446.4, 446.7, 447.6, 454.0, 454.1, 454.2, 454.8, 457.0, 457.1

GI Disorders:

522.6, 523.4*, 527.2, 528.3, 531.4*, 531.5*, 531.6*, 531.7*, 531.9*, 532.4*, 532.5*, 532.6*, 532.7*, 532.9*, 533.4*, 533.5*, 533.6*, 533.7*, 533.9*, 534.4*, 534.5*, 534.6*, 534.7*, 534.9*, 535.30, 535.31, 535.40, 535.41, 535.50, 535.51, 535.60, 535.61, 535.70, 535.71, 536.3, 536.8, 555.*, 556.0, 556.1, 556.2, 556.3, 556.5, 556.6, 556.8, 556.9, 558.1, 558.41, 558.42, 564.1, 569.41, 569.42, 569.82, 577.1, 577.2

GU Disorders:

588.0, 590.00, 590.01, 590.80, 590.81, 590.9, 595.1, 614.1, 614.2, 614.4, 614.7, 614.8, 614.9, 616.89, 616.9, 617.*

Skin Disorders:

686.01, 694.4, 695.81, 705.83, 707.*

MSK Disorders:

696.0, 710.0*, 710.1*, 710.3*, 710.4*, 710.5*, 711.1*, 711.2*, 711.3*, 711.4*, 711.5*, 711.6*, 711.7*, 711.8*, 712.*, 713.*, 714.0*, 714.1*, 714.2*, 714.3*, 714.4*, 714.89, 714.9*, 715.*, 716.0*, 716.1*, 716.3*, 716.5*, 716.6*, 716.8*, 716.9*, 717.*, 718.0*, 718.1*, 718.8*, 718.9*, 719.1*, 719.2*, 719.3*, 719.4*, 720.*, 721.*, 722.3*, 722.4*, 722.5*, 722.6*, 722.7*, 722.8*, 723.0*, 723.1*, 723.2*, 723.3*, 723.4*, 723.5*, 723.6*, 724.*, 725, 726.*, 727.0*, 727.2*, 727.3*, 728.1*, 728.81, 729.0, 729.1, 729.2, 729.3*, 729.4, 729.5, 730.1*, 730.2*, 730.3*, 730.7*, 731.2*, 733.7, 997.62, V13.4, V13.5*

Mental Disorders:

307.80, 307.81, 307.89

Miscellaneous:

V66.1, V66.2, V66.7, V67.1*, V67.2*, V68.01, V57.1

ICD-9 Codes for All Acute Painful Conditions:

Note: "*" indicates that all subcodes are included

Infectious Diseases:

003.24, 036.82, 040.0, 040.81, 053.20, 053.21, 053.22, 053.29, 053.71, 053.79, 053.8, 053.9, 054.10, 054.11, 054.12, 054.13, 054.19, 060.*, 061, 066.40, 066.49, 072.0, 072.3, 074.1, 074.20, 074.21, 074.23, 095.5, 095.7, 099.3, 101, 112.84, 117.5, 136.0, 136.5, 321.2

Endocrine Disease:

245.0, 245.1, 277.1

Joint Disease:

136.1, 274.01

Immune Disorders:

279.51,

Hematologic Disorders:

282.42, 282.62, 282.64, 282.69

Neurologic Disorders:

321.4, 322.0, 322.1, 322.9, 324.0, 324.1, 324.9, 325, 339.01, 339.03, 339.05, 339.11, 339.21, 339.3, 339.43, 339.81, 339.82, 339.83, 339.84, 339.85, 341.20, 341.21, 341.22, 346.00, 346.01, 346.02, 346.03, 346.1*, 346.2*, 346.3*, 346.4*, 346.5*, 346.6*, 346.8*, 346.9*, 350.1, 350.2, 357.0, 357.82, 359.4, 359.5, 359.6, 359.7*, 359.8*, 359.9*, 430, 431.*, 432.*, 437.4, 437.6

Pain (cause unspecified):

338.11, 338.12, 338.18, 338.19

Eye Disorders:

360.11, 360.12, 376.02, 376.03, 379.91

Ear Disorders:

383.*, 383.21

Cardiovascular Disorders:

390, 391, 415.1*, 420.*, 422.*, 429.0, 444.2*, 444.8*, 444.9, 445.*, 449, 451.*, 453.0, 453.1, 453.4*, 453.82, 453.83, 453.84, 453.89, 457.2

GI Disorders:

455.1, 455.4, 455.7, 522.1, 522.4, 522.5, 522.7, 523.3*, 525.11, 526.5, 527.3, 528.00, 528.02, 528.09, 530.10, 530.12, 530.13, 530.19, 530.20, 530.21, 530.4, 530.7, 531.0*, 531.1*, 531.2*, 531.3*, 532.0*, 532.1*, 532.2*, 532.3*, 533.0*, 533.1*, 533.2*, 533.3*, 534.0*, 534.1*, 534.2*, 534.3*, 535.00, 535.01, 536.41, 537.3, 538, 540.*, 541.*, 542.*, 550.0*, 550.1*, 551.*, 552.*, 557.0, 558.2, 558.3, 558.9, 560.1, 560.2, 560.81, 560.89, 560.9, 562.01, 562.03, 562.11, 562.13, 566, 567.*, 569.3, 569.5, 569.61, 569.71, 569.83, 572.0, 572.1, 573.4, 574.0*, 574.1*, 574.3*, 574.4*, 574.51, 574.7*, 574.8*, 574.91, 575.0, 575.10, 575.12, 575.2, 575.3, 575.4, 576.1, 576.2, 576.3, 577.0, 578.*

GU Disorders/Pregnancy:

590.10, 590.11, 590.2, 591, 592.*, 596.6, 596.81, 599.0, 599.6, 599.60, 599.69, 601.2, 607.3, 608.2*, 611.0, 611.71, 614.5, 616.5*, 616.81, 620.5, 629.3*, 633.*, 639.0, 664.0*, 664.1*, 664.2*, 664.3*, 664.4*, 664.6*, 664.8*, 664.9*, 665.0*, 665.1*, 665.3*, 665.4*, 665.5*, 665.8*, 665.9*, 673.*, 674.1*, 674.2*, 674.3*

Skin Disorders:

682.*, 683, 695.2

MSK Disorders:

711.0*, 711.9*, 716.2*, 716.4*, 718.2*, 718.3*, 722.0*, 722.1*, 722.2*, 727.6*, 728.0, 728.83, 728.85, 728.86, 728.88, 729.7*,
729.82, 730.0*, 730.8*, 730.9*, 733.1*, 733.4*, 733.6*, 733.93, 733.94, 733.95, 733.96, 733.97, 733.98, 784.0, 784.1, 784.92, 786.5*,
788.0, 788.20, 788.29, 789.0*, 789.6*, 789.7, 800-897.*, 920.*, 921.0, 921.1, 922.*, 923.*, 924.*, 925-949.*, 953.*, 954.8, 954.9,
955-957.*, 958.9*, 959.*, 997.41, V43.6*

Respiratory Disorders:

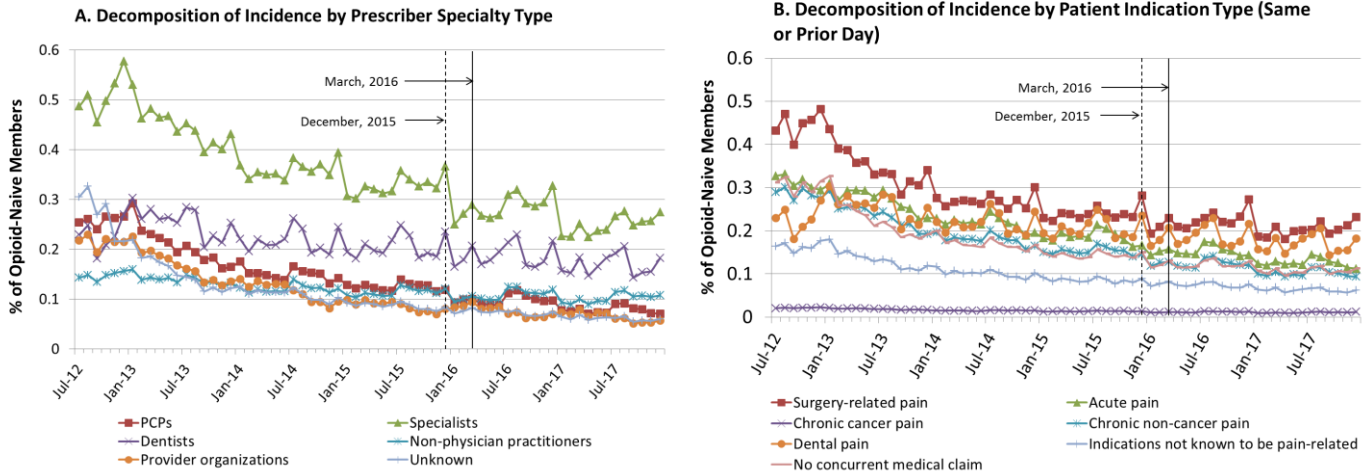
475, 478.11, 478.21, 478.22, 478.24, 478.71, 511.0 511.1, 517.3, 519.2

Miscellaneous:

V64.4*, V66.0, V66.4, V67.0*, V67.4*, V50.*, V51.*, V54.*, V58.4*, V58.7*

Online Appendix D. Supplementary Figures

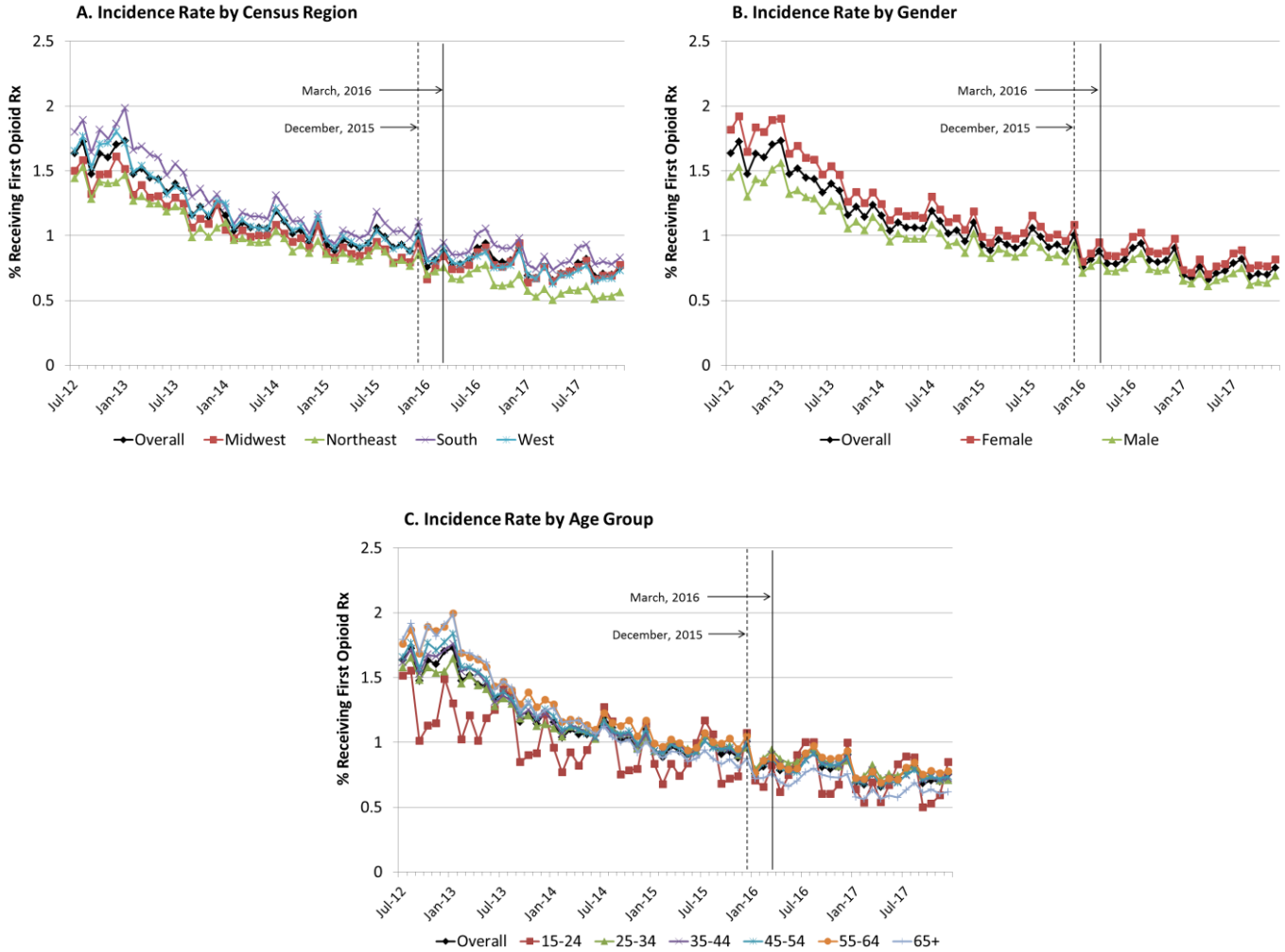
Figure S1. Decomposition of Opioid Incidence by Prescriber Specialty Type and Patient Indication Type, July 2012 – December 2017.



Note:

Figures show the percent of opioid-naïve enrollees receiving first opioid prescriptions that fall in each of the prescriber and patient categories (i.e., the sum of incidence by specialty or patient indication in a given month equals the total incidence for the month). The denominator is eligible enrollees who had been continuously enrolled for at least 6 months and had no recorded opioid prescription or diagnosis of opioid use disorder during those 6 months. Prescribers were classified into specialty types based on the National Provider Identifier Taxonomy file in the National Plan and Provider Enumeration System. Patients’ indications for opioid therapy were identified from the ICD-9 diagnosis and type of service codes associated with any office or hospital visit that occurred on the day of or the day prior to the date the prescription was filled. See text for more details on the construction of these categories. The dashed (solid) vertical line represents December 2015 (March 2016), when the CDC issued draft (final) opioid prescribing guidelines.

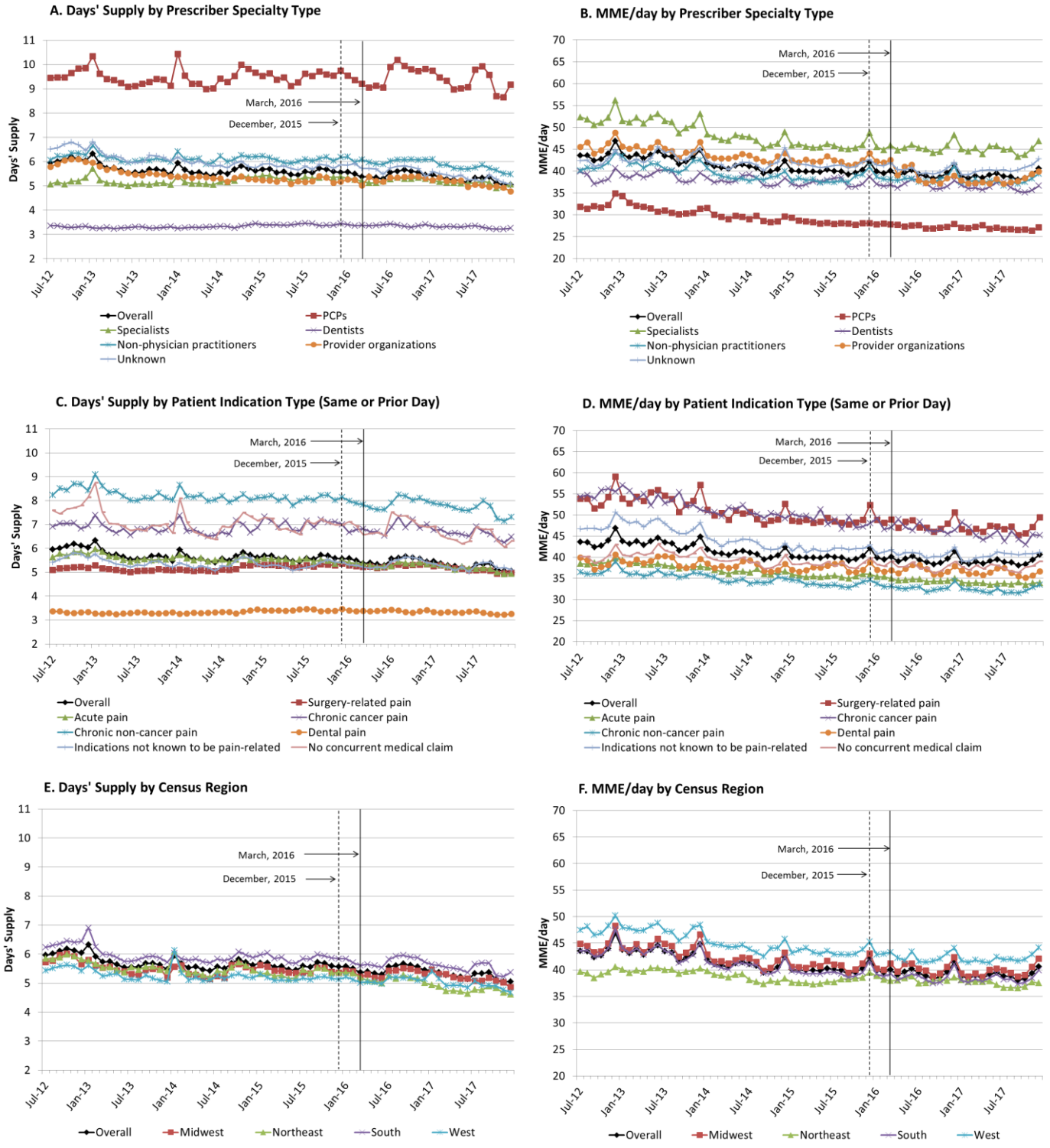
Figure S2. Incidence Rate of Opioid Prescriptions by Census Region, Gender, and Age Group, July 2012 – December 2017.

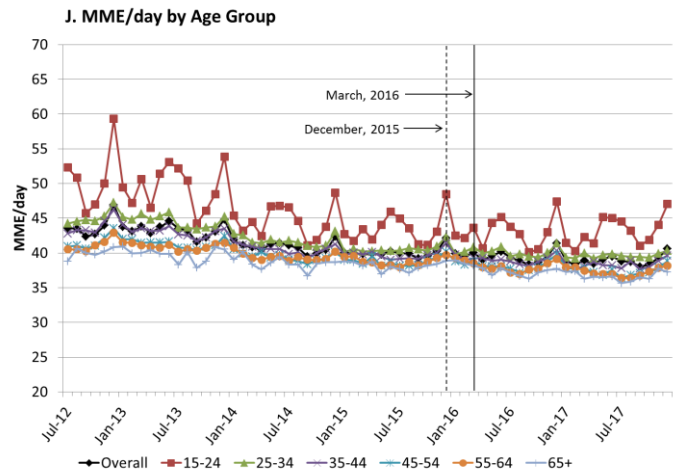
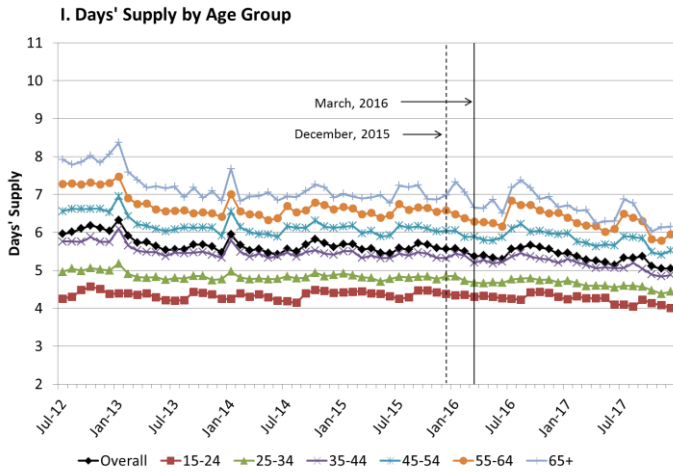
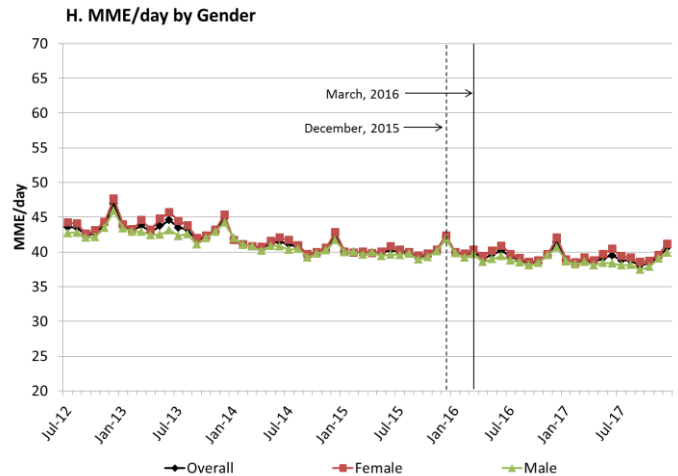
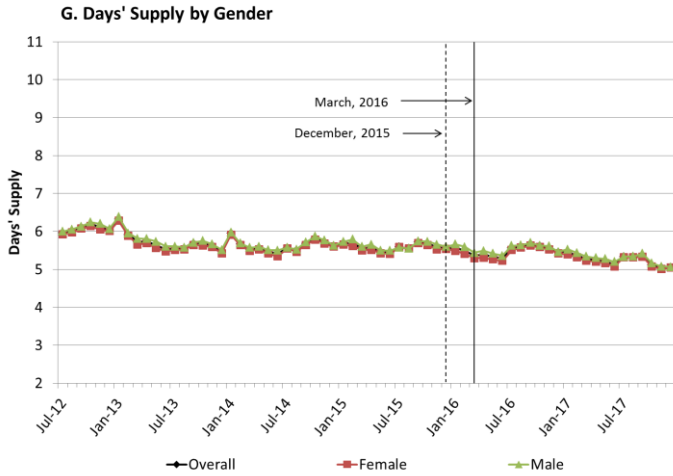


Note:

Figure shows the monthly rate of opioid-naïve enrollees receiving first opioid prescriptions by Census region, gender, and age group. The denominator is enrollees who were 15 years and older in a given region, gender or age group category and had primary medical and prescription coverage in each month, and also had been continuously enrolled for at least 6 months and had no recorded opioid prescription or diagnosis of opioid use disorder during those 6 months. Census region was grouped from patients' zip-codes of the month in which initial opioids were prescribed. The dashed (solid) vertical line represents December 2015 (March 2016), when the CDC issued draft (final) opioid prescribing guidelines.

Figure S3. Average Days' Supply and MME/day of Initial Opioid Prescriptions, Overall and by Prescriber Specialty, Patient Indication, Census Region, Gender, and Age Group, July 2012 – December 2017.





Note:

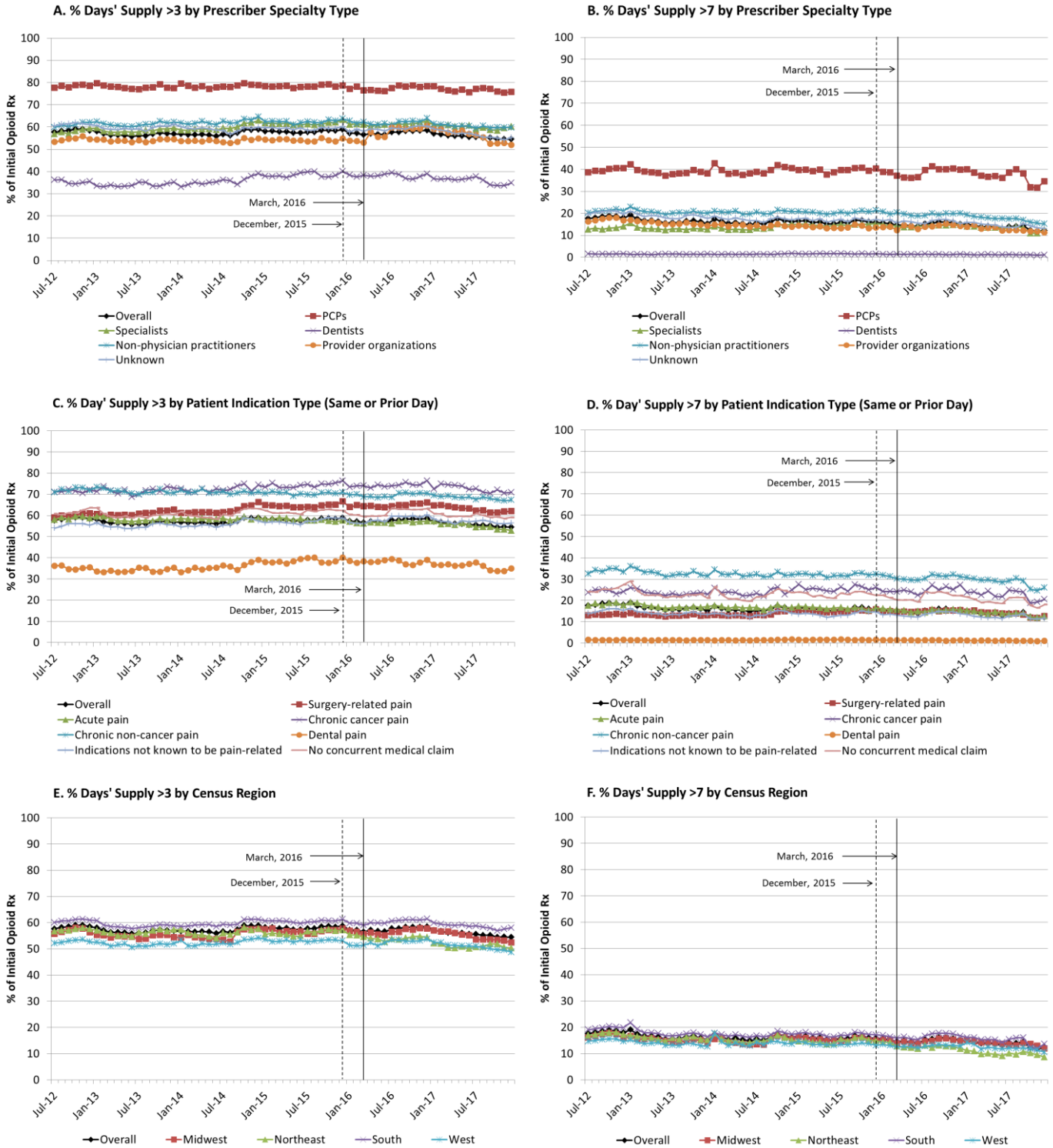
Sample is 10,874,869 first-time opioid users who were 15 years and older, resided in the United States, had primary medical and prescription coverage in each month, and also had been continuously enrolled for at least 6 months and had no recorded opioid prescription or diagnosis of opioid use disorder during those 6 months.

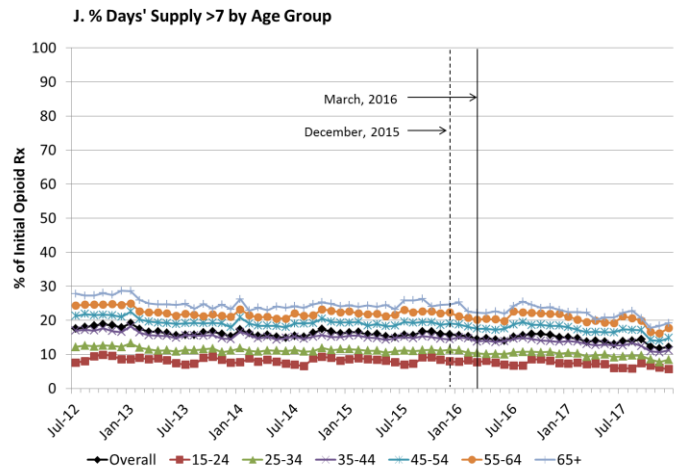
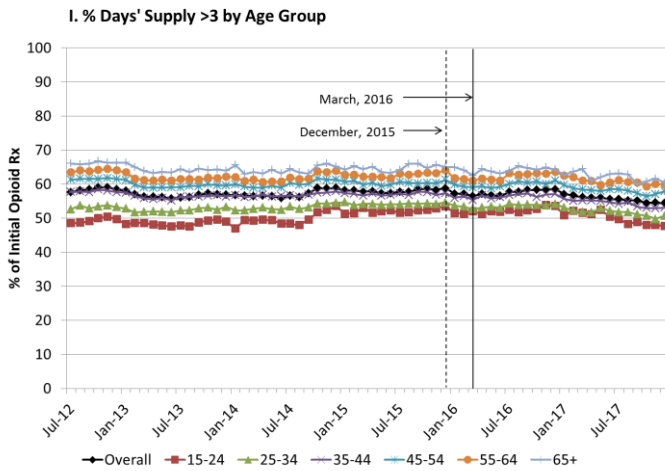
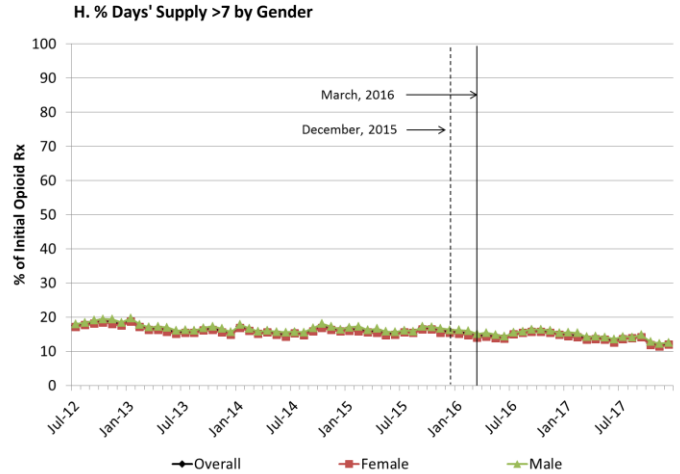
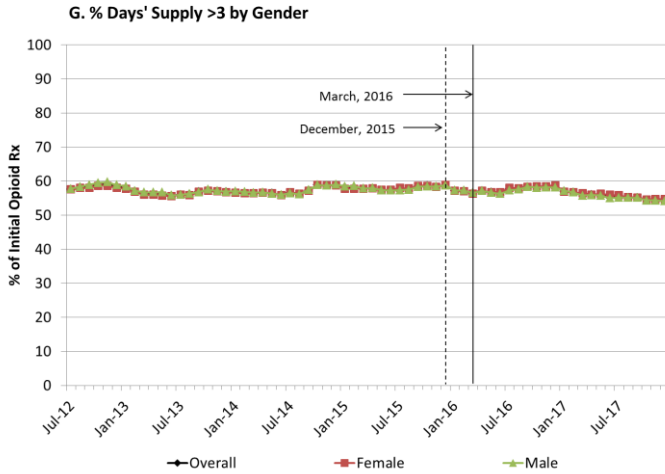
Prescribers were classified into specialty types based on the National Provider Identifier Taxonomy file in the National Plan and Provider Enumeration System. Patients' indications for opioid therapy were identified from the ICD-9 diagnosis and type of service codes associated with any office or hospital visit that occurred on the date of or the day prior to the date the prescription was filled. Census region was grouped from patients' zip-codes of the month in which initial opioids were prescribed. See text for more details on the construction of these categories.

MME/day denotes Morphine Milligram Equivalents per day.

The dashed (solid) vertical line represents December 2015 (March 2016), when the CDC issued draft (final) opioid prescribing guidelines.

Figure S4. Share of Initial Opioid Prescriptions with High Duration (Days' Supply >3, Days' Supply >7), Overall and by Prescriber Specialty, Patient Indication, Census Region, Gender, and Age Group, July 2012 – December 2017.





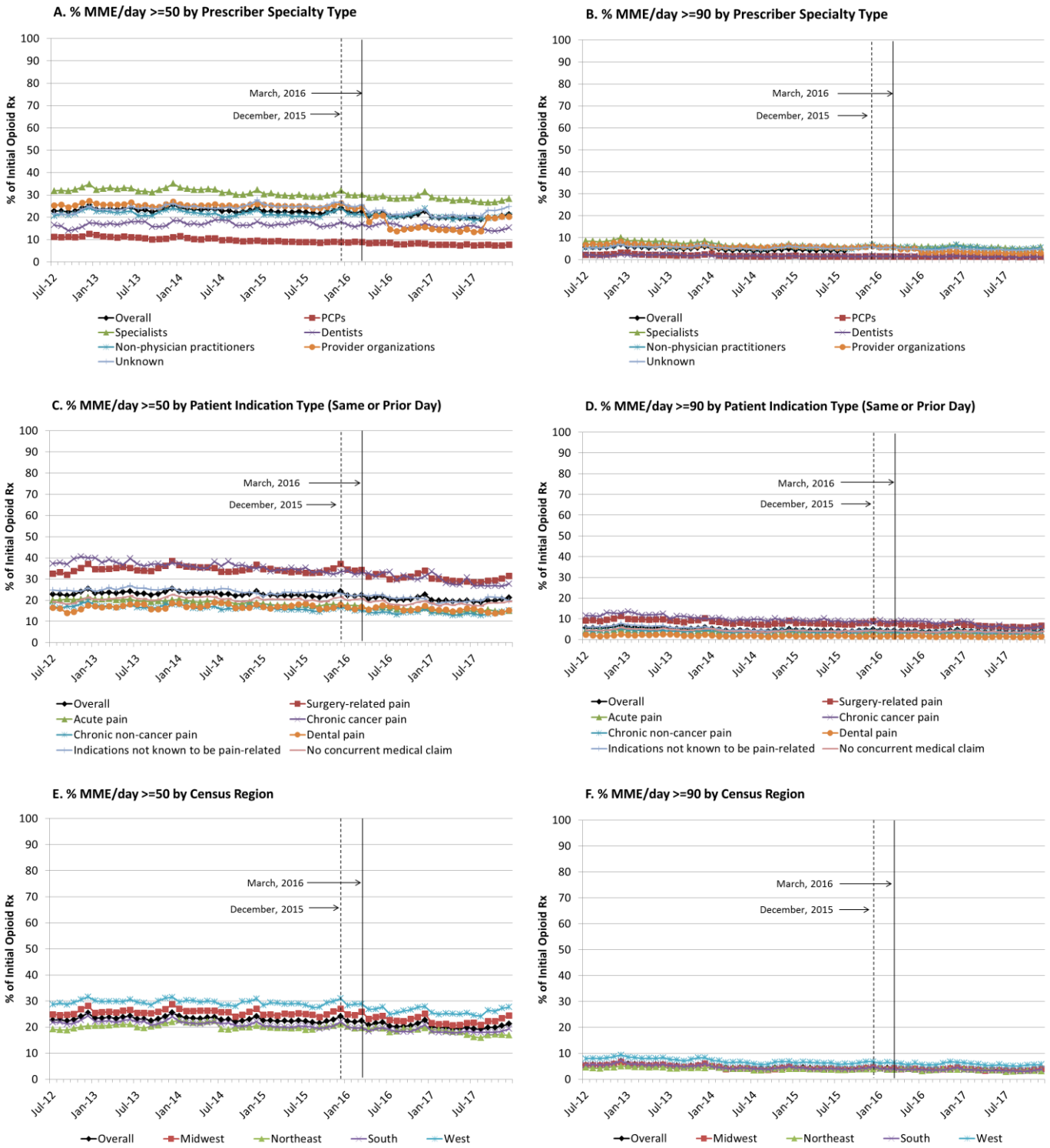
Note:

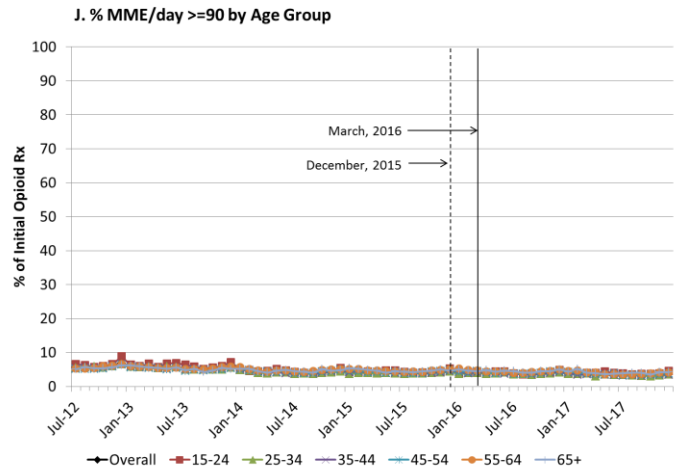
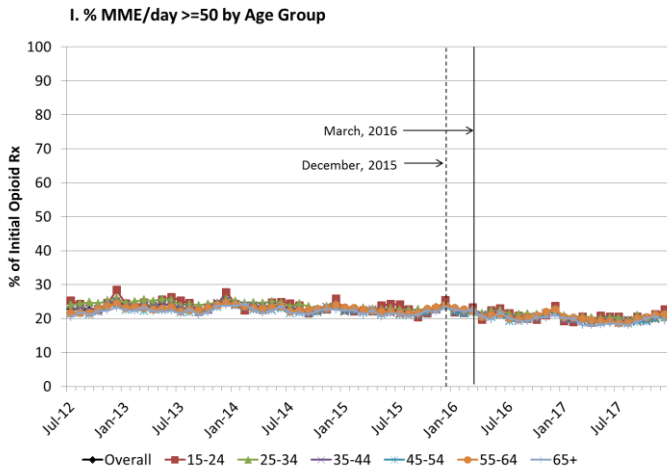
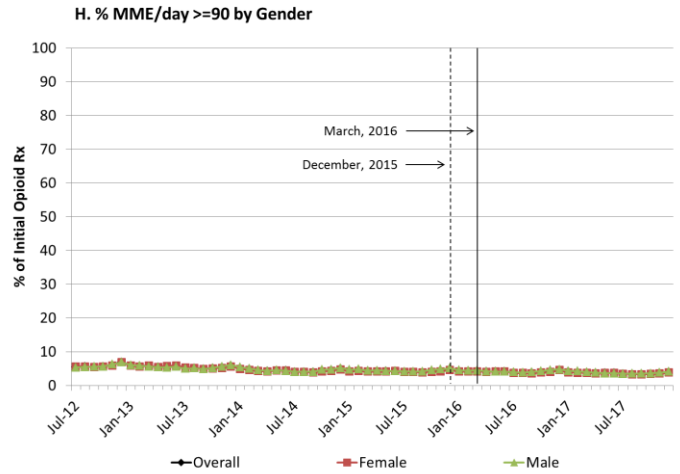
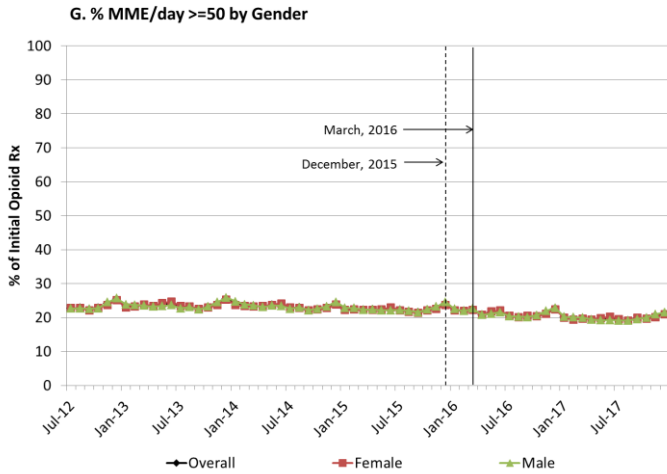
Sample is 10,874,869 first-time opioid users who were 15 years and older, resided in the United States, had primary medical and prescription coverage in each month, and also had been continuously enrolled for at least 6 months and had no recorded opioid prescription or diagnosis of opioid use disorder during those 6 months.

Prescribers were classified into specialty types based on the National Provider Identifier Taxonomy file in the National Plan and Provider Enumeration System. Patients' indications for opioid therapy were identified from the ICD-9 diagnosis and type of service codes associated with any office or hospital visit that occurred on the date of or the day prior to the date the prescription was filled. Census region was grouped from patients' zip-codes of the month in which initial opioids were prescribed. See text for more details on the construction of these categories.

The dashed (solid) vertical line represents December 2015 (March 2016), when the CDC issued draft (final) opioid prescribing guidelines.

Figure S5. Share of Initial Opioid Prescriptions with High Dose (MME/day ≥ 50 , MME/day ≥ 90), Overall and by Prescriber Specialty, Patient Indication, Census Region, Gender, and Age Group, July 2012 – December 2017.





Note:

Sample is 10,874,869 first-time opioid users who were 15 years and older, resided in the United States, had primary medical and prescription coverage in each month, and also had been continuously enrolled for at least 6 months and had no recorded opioid prescription or diagnosis of opioid use disorder during those 6 months.

Prescribers were classified into specialty types based on the National Provider Identifier Taxonomy file in the National Plan and Provider Enumeration System. Patients' indications for opioid therapy were identified from the ICD-9 diagnosis and type of service codes associated with any office or hospital visit that occurred on the date of or the day prior to the date the prescription was filled. Census region was grouped from patients' zip-codes of the month in which initial opioids were prescribed. See text for more details on the construction of these categories.

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The dashed (solid) vertical line represents December 2015 (March 2016), when the CDC issued draft (final) opioid prescribing guidelines.

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4. Jeffery MM, Hooten WM, Henk HJ, et al. Trends in opioid use in commercially insured and Medicare Advantage populations in 2007-16: retrospective cohort study. *Bmj* 2018;362.
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