



National Institute
on Drug Abuse
Advancing Addiction Science



*Lister Hill National Center for
Biomedical Communications*

Exploring opioid use through the Medicare dataset in collaboration with NIDA

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SPECIAL REPORT

The Role of Science in Addressing the Opioid Crisis

Nora D. Volkow, M.D., and Francis S. Collins, M.D., Ph.D.

Opioid misuse and addiction is an ongoing and rapidly evolving public health crisis, requiring innovative scientific solutions. In response, and in blood naloxone levels equivalent to those achieved with parenteral administration; it was approved by the Food and Drug Administration (FDA) in 2015. The NIH will continue to support research on the potential to use oral naloxone to reduce



Be Part of the Largest Annual Conference Addressing the Opioid Crisis

The National Rx Drug Abuse & Heroin Summit is where solutions are formulated, stakeholders convene, and change begins. Be part of the international discussion on addressing the opioid crisis by attending the 2017 Summit.

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Featured Speakers:



Thomas E. Price, M.D.,
Secretary,
U.S. Department of Health and Human Services (HHS)



William R. Brownfield
Assistant Secretary,
Bureau of International Narcotics and Law Enforcement Affairs,
U.S. Department of State



Vivek H. Murthy, M.D., MBA
19th United States Surgeon General



Francis Collins, M.D., Ph.D.,
Director,
National Institutes of Health (NIH)



Nora D. Volkow, M.D.,
Director,
National Institute on Drug Abuse (NIDA)
National Institutes of Health



Anne Schuchat, M.D.,
Acting Director,
Centers for Disease Control and Prevention (CDC)
Acting Administrator,
Agency for Toxic Substances and Disease Registry, Rear Admiral,
U.S. Public Health Service



Richard J. Baum
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Office of National Drug Control Policy (ONDCP)



Kana Enomoto
Acting Deputy Assistant Secretary
Substance Abuse and Mental Health Services Administration (SAMHSA)

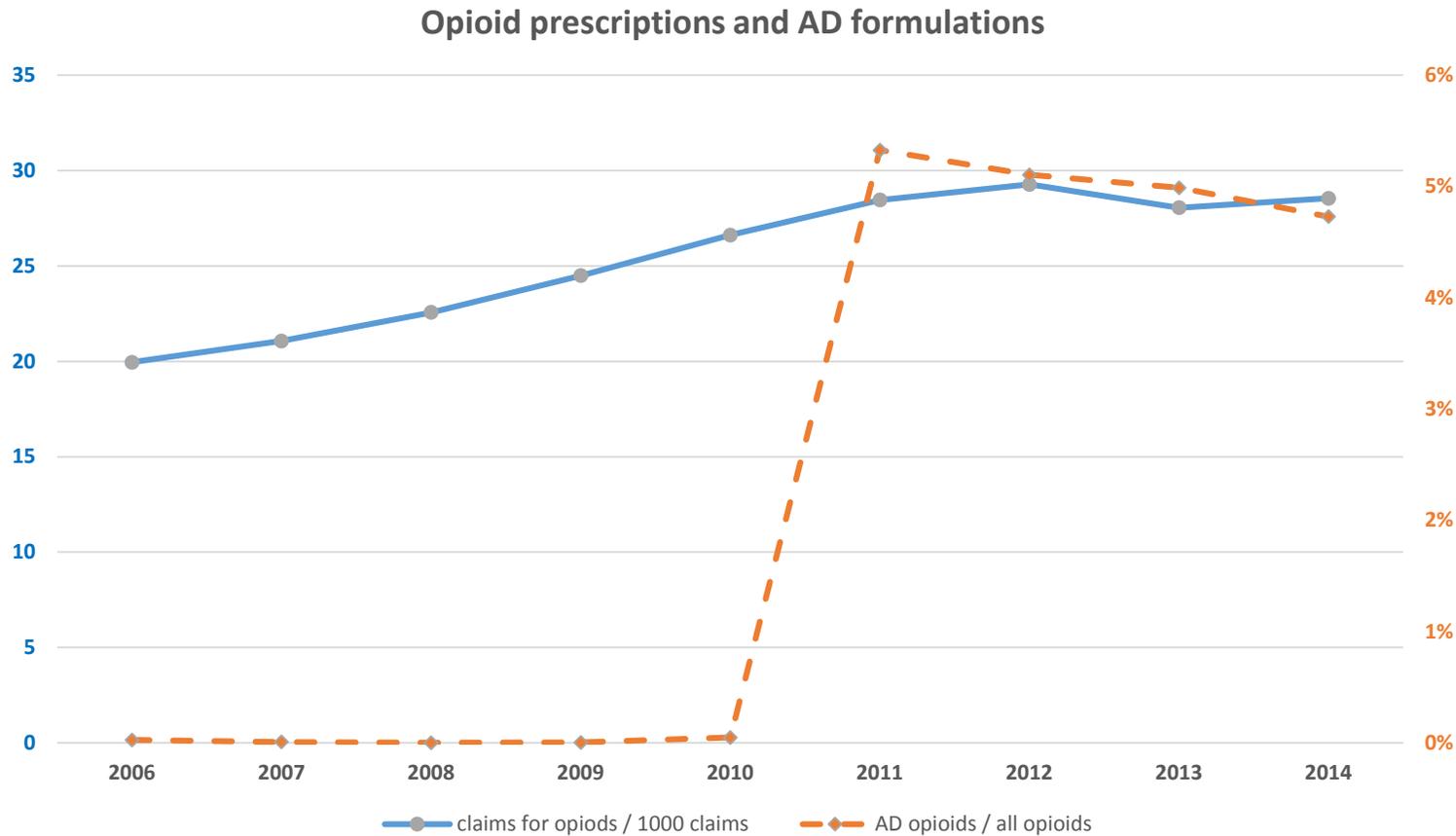
NLM activities related to opioid abuse

as of 4/13/2017

- RxNorm
 - Qualifier for abuse-deterrent formulations
 - Ingredients: morphine sulfate, oxycodone, and hydrocodone
 - Brand names: Arymo, Embeda, Hysingla, Morphabond, Oxycontin, and Xtampza
- Value Set Authority Center
 - 63 value sets related to “opioids,” including value sets for medications containing opioids and conditions associated with opioids

Do you have access to information related to the frequency with which ADF opiates are being prescribed? – Nora Volkow

Frequency of prescription in Medicare



Medicare dataset
Random 10% cohort of all Medicare beneficiaries (irrespective of Part D enrollment) sampled from 1999 to 2013. 4.8 M beneficiaries with Part D claims. Claims for years 2006-2014

Opioids found in the Medicare dataset (from ATC class = N02AA)
23088 | dihydrocodeine
3423 | Hydromorphone
7052 | Morphine
7676 | Opium
7804 | Oxycodone

NIDA questions

- 1. What is the range of opioid doses prescribed for chronic pain, the average dose, and what percentage of those patients are also prescribed concomitant selective serotonin reuptake inhibitors (SSRIs)?
- 2. Which clinical characteristics of patients admitted to emergency departments with a drug overdose predict those who are more likely to have
 - hospital re-admissions?
 - a greater likelihood of future drug overdoses?
- 3. What is the prevalence of opioid use disorder in patients who have been prescribed opioids for three or more months vs. in patients who have been prescribed opioids for less than three months, for chronic non-cancer pain.
- 4. Do we have mortality data on these patients?

Materials & Methods

LHC (new) MEDICARE dataset

- 20% random sample of Part D enrollees
 - 10.7 million beneficiaries (patients)
 - ~2.3 billion prescriptions
- Continuous enrollment (no gaps) between initial enrollment and end of study (death or 12/31/2015)
 - Required for outcomes research
 - 4.9 million beneficiaries (> 50% loss)
 - ~1 billion prescriptions
 - 41 million opioid prescriptions

Definitions – Opioids

- NDC codes -> RxNorm -> ATC classes
- 3 ATC classes
 - **N02A OPIOIDS**
 - N07BC Drugs used in opioid dependence
 - N01AH Opioid anesthetics
 - R05DA Opium alkaloids and derivatives [Respiratory system*]

Opioids present in the Medicare dataset

BUPRENORPHINE
BUTORPHANOL
CODEINE
DIHYDROCODEINE
FENTANYL
HYDROCODONE
HYDROMORPHONE
MEPERIDINE (PETHIDINE)
METHADONE
MORPHINE
NALBUPHINE
OPIUM
OXYCODONE
PENTAZOCINE
PROPOXYPHENE (DEXTROP.)
TAPENTADOL
TRAMADOL

N NERVOUS SYSTEM
N02 ANALGESICS
N02A OPIOIDS
 N02AA Natural opium alkaloids
 N02AB Phenylpiperidine derivatives
 N02AC Diphenylpropylamine derivatives
 N02AD Benzomorphan derivatives
 N02AE Oripavine derivatives
 N02AF Morphinan derivatives
 N02AG Opioids in combination with antispasmodics
 N02AJ Opioids in combination with non-opioid analgesics
 N02AX Other opioids

N NERVOUS SYSTEM
N01 ANESTHETICS
N01A ANESTHETICS, GENERAL
N01AH Opioid anesthetics

ATC code	Name
★ N01AH01	<u>fentanyl</u>
N01AH02	<u>alfentanil</u>
N01AH03	<u>sufentanil</u>
N01AH04	<u>phenoperidine</u>
N01AH05	<u>anileridine</u>
N01AH06	<u>remifentanil</u>
N01AH51	<u>fentanyl, combinations</u>

N NERVOUS SYSTEM
N07 OTHER NERVOUS SYSTEM DRUGS
N07B DRUGS USED IN ADDICTIVE DISORDERS
N07BC Drugs used in opioid dependence

ATC code	Name	DDD
★ N07BC01	<u>buprenorphine</u>	8
★ N07BC02	<u>methadone</u>	25
		25
N07BC03	<u>levacetylmethadol</u>	
N07BC04	<u>lofexidine</u>	1.4
N07BC05	<u>levomethadone</u>	
N07BC06	<u>diamorphine</u>	
N07BC51	<u>buprenorphine, combinations</u>	8

R RESPIRATORY SYSTEM
R05 COUGH AND COLD PREPARATIONS
R05D COUGH SUPPRESSANTS, EXCL. COMBI
R05DA Opium alkaloids and derivatives

ATC code	Name
★ R05DA01	<u>ethylmorphine</u>
★ R05DA03	<u>hydrocodone</u>
R05DA04	<u>codeine</u>
R05DA05	<u>opium alkaloids with morphine</u>
R05DA06	<u>normethadone</u>
R05DA07	<u>noscapine</u>
R05DA08	<u>pholcodine</u>
R05DA09	<u>dextromethorphan</u>
R05DA10	<u>thebacon</u>
R05DA11	<u>dimemorfan</u>
R05DA12	<u>acetyldihydrocodeine</u>
R05DA20	<u>combinations</u>

Definitions – Conditions

- Pain
 - All opioid prescriptions are assumed to be for pain
 - Minus mentions of opioid use disorder
- Non-cancer pain
 - Exclude all prescriptions after 2 occurrences of a cancer code
- Opioid use disorder
 - 304.0 Opioid type dependence
 - 304.7 Combinations of opioid type drug with any other drug dependence
- Opioid overdose
 - 305.5 Opioid abuse [under Nondependent abuse of drugs]
 - 965.0 Opiates and related narcotics [under Poisoning by analgesics, antipyretics, and antirheumatics]
 - Require an additional 304 (drug dependence) or 305 (nondependent abuse) code
- Death
 - MEDICARE mortality table

Results

Q 0 – cohort characteristics

VARIABLE	%	N
N		4,923,392
FEMALE	59.9	2,947,084
WHITE	80.5	3,965,169
BLACK	7.1	351,060
HISPANIC	5.7	278,918
ASIAN	2.9	143,196
OTHER	3.8	185,049
DUAL EVER	25.1	1,234,506
NON-DUAL LIS	3	146,238
NO COST-SHARING	72	3,542,648
LIVING IN RURAL AREA	22.2	1,091,270

2.4M patients with an opioid prescription for non-cancer pain (28.9M claims)

“Poor”

Q0 – cohort characteristics (chronic conditions)

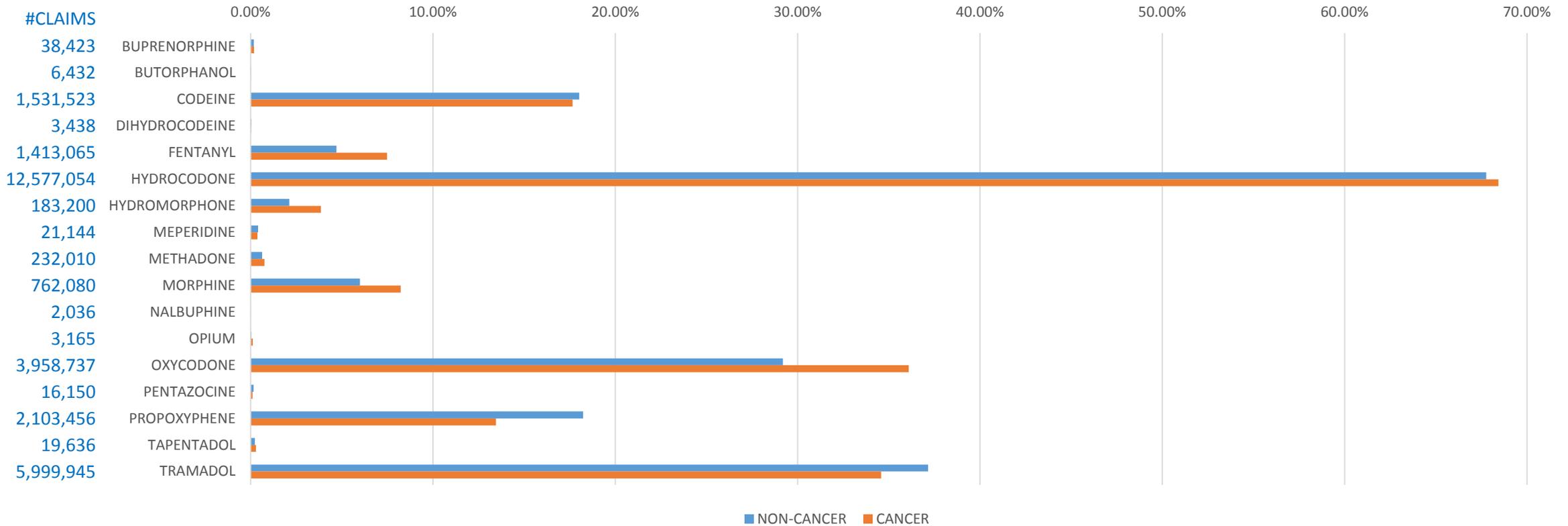
Chronic condition	%	#
HYPERTENSION	80.2	3,948,229
HYPERLIPIDEMIA	74.6	3,671,837
CATARACT	66.3	3,263,858
ANEMIA	56.6	2,787,065
RHEUMATOID ARTHRITIS/OSTEOARTHRITIS	55.6	2,736,185
ISCHEMIC HEART DISEASE	50.1	2,467,771
DIABETES	37.4	1,842,220
HEART FAILURE	33.2	1,633,764
DEPRESSION	32.7	1,611,324
CHRONIC KIDNEY DISEASE	31.7	1,561,233
COPD	29	1,428,327
HYPOTHYROIDISM	28.1	1,382,054
PERIPHERAL VASCULAR DISEASE	26.5	1,306,033
MAJOR DEPRESSIVE AFFECTIVE DISORDER	25.4	1,249,669
OSTEOPOROSIS	24.3	1,196,185
ALZHEIMER'S DISEASE OR SENILE DEMENTIA	23.5	1,158,541
GLAUCOMA	23.3	1,145,719
FIBROMYALGIA, CHRONIC PAIN AND FATIGUE	20.9	1,028,868
ANXIETY DISORDERS	20.8	1,025,539
ATRIAL FIBRILLATION	19.5	960,809
STROKE/TRANSIENT ISCHEMIC ATTACK	18.9	931,336
HYPERPLASIA	17.9	880,967
OBESITY	15.5	765,115
ASTHMA	14.4	709,721
PRESSURE ULCERS AND CHRONIC ULCERS	13.4	659,134
SENSORY - DEAFNESS AND HEARING IMPAIRMENT	13.3	653,307
TOBACCO USE DISORDERS	10	489,964

NIDA questions

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Q 1a – opioid prescriptions (overall, cancer vs. non-cancer pain)

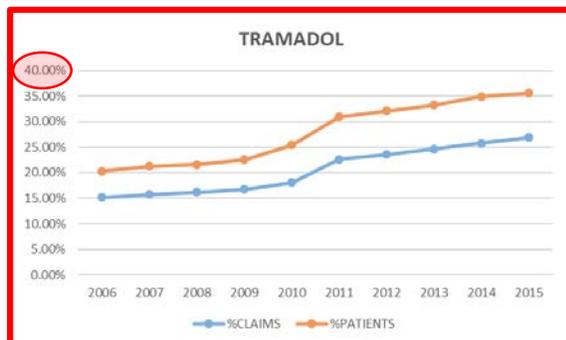
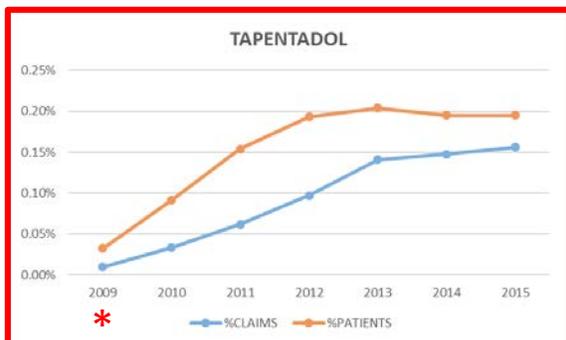
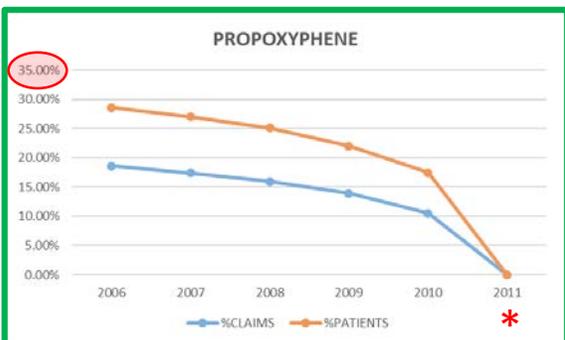
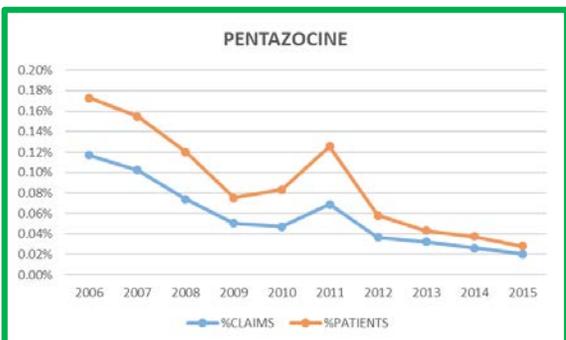
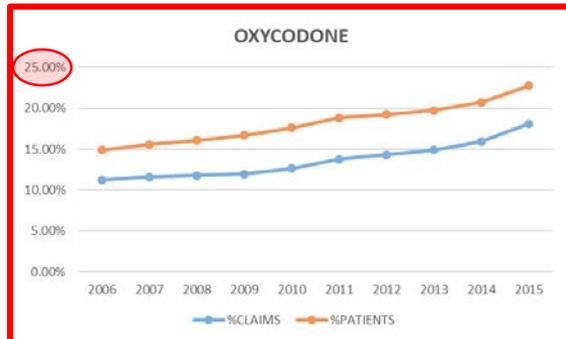
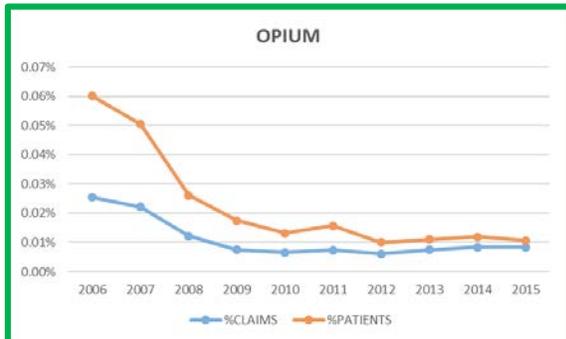
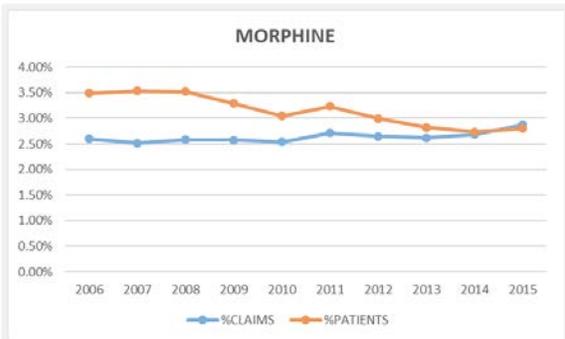
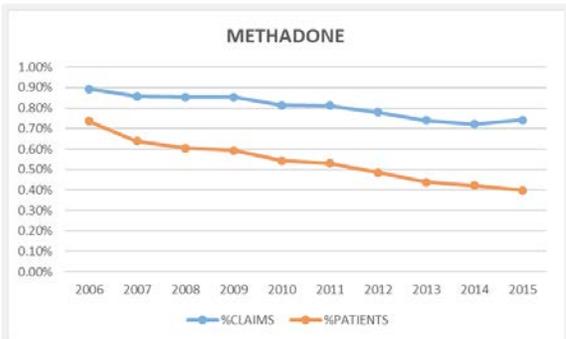
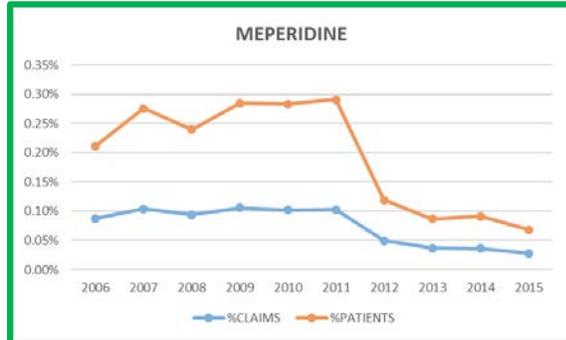
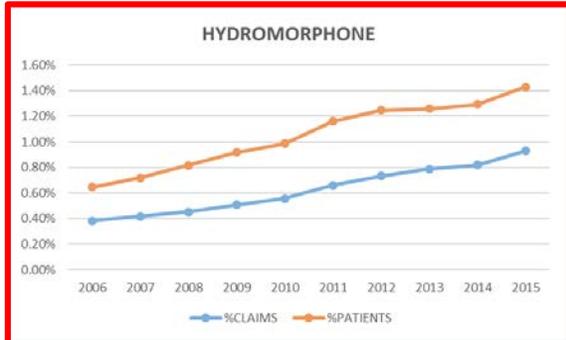
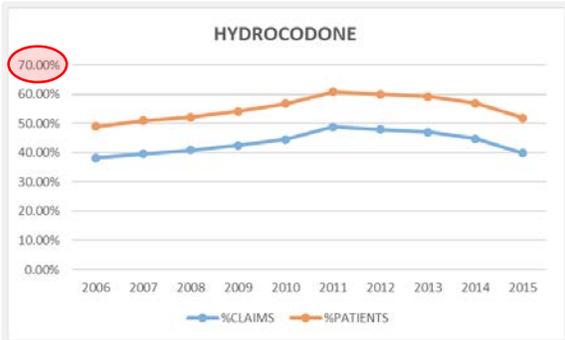
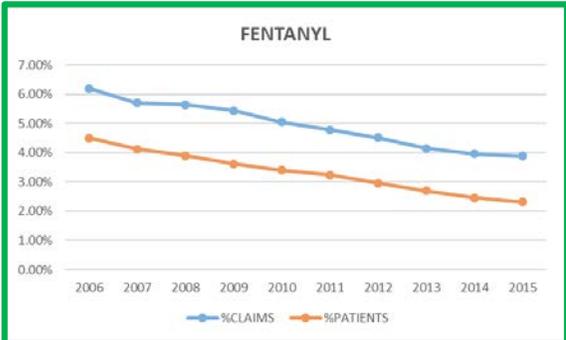
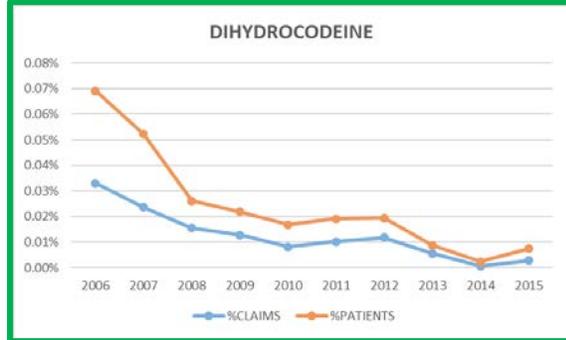
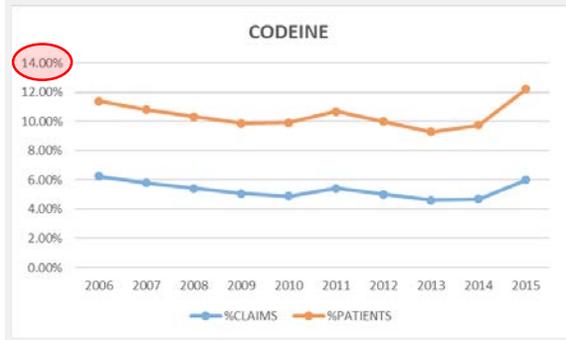
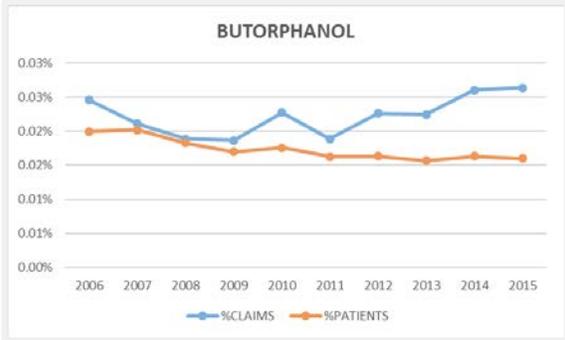
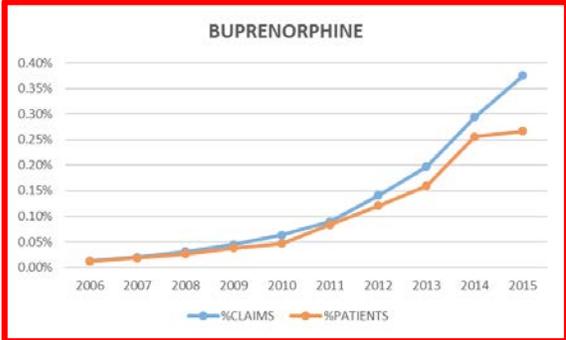
Proportion of patients with opioid prescription (by drug)



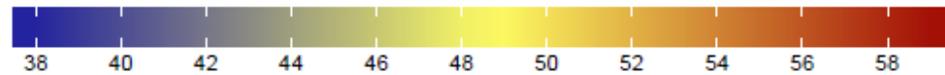
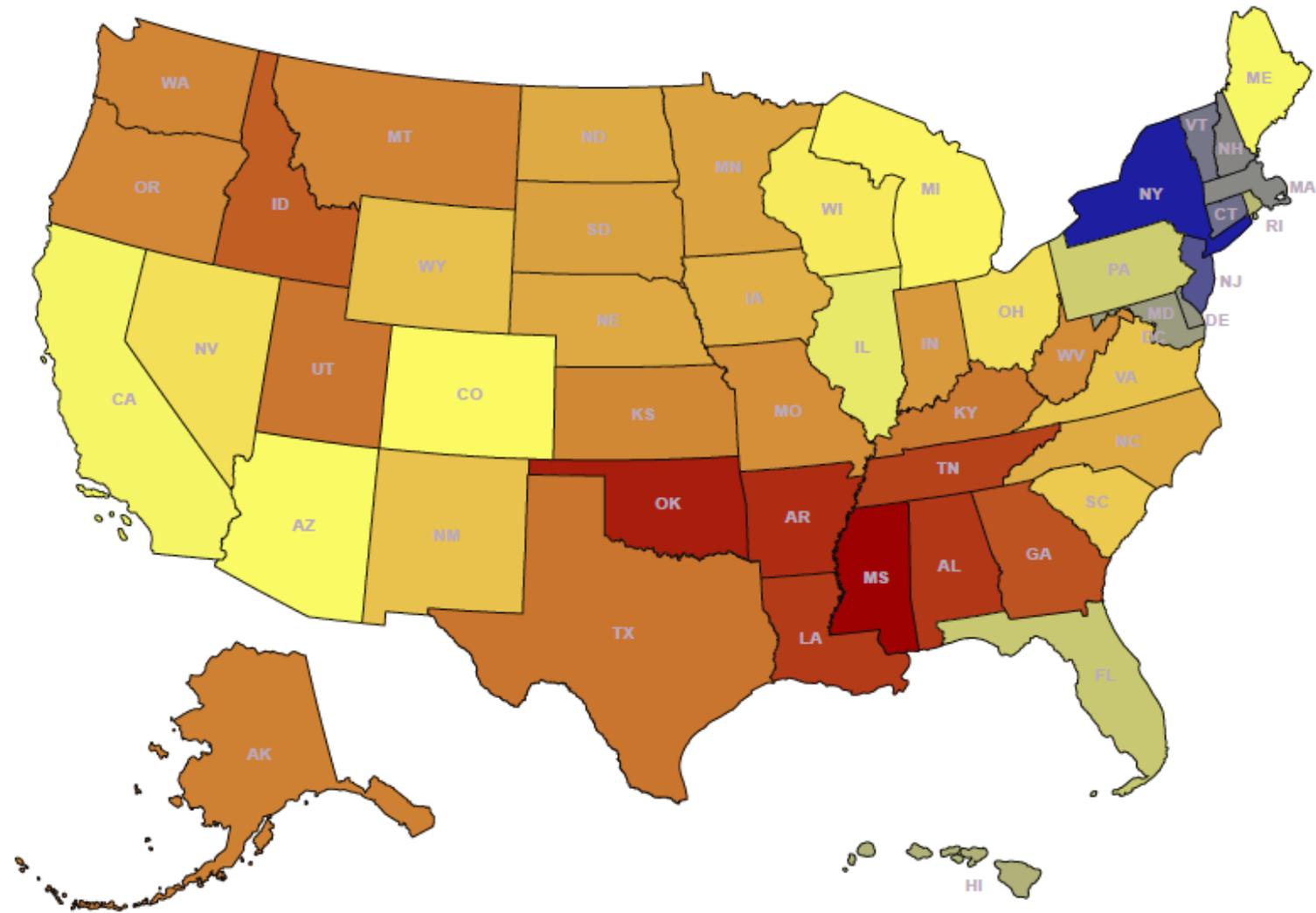
28,871,494 claims
2,436,397 patients

11,504,312 claims
1,118,652 patients

* 856,656 claims
post-ODU excluded



Opioid users per 100 eligible PD beneficiaries, 2006–2015.



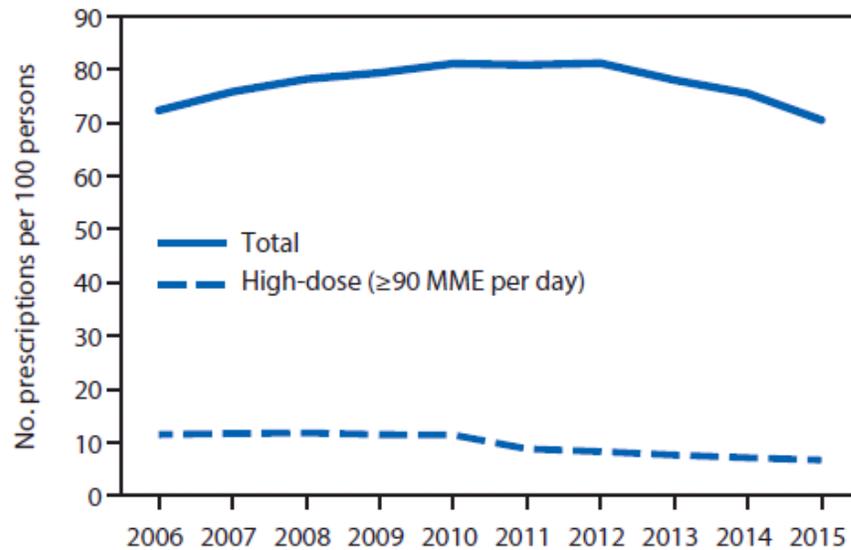
Q 1a – opioid doses prescribed for chronic pain (non-cancer pain)

28,871,494 claims
2,436,397 patients
(excluding outliers)

INGREDIENT	#CLAIMS	#PATIENTS	MIN	MAX	STD.DEV	MEAN	MODE	MEDIAN	MEDIAN as MME
BUPRENORPHINE	38,423	4,373	0.00	160.00	9.16	8.44	0.00	6.00	180.00
BUTORPHANOL	6,432	628	0.28	75.00	4.96	4.23	1.67	2.50	17.50
CODEINE	1,531,523	439,118	3.00	1080.00	105.34	160.98	120.00	128.57	19.29
DIHYDROCODEINE	3,438	1,120	9.09	480.00	61.00	114.90	128.00	106.67	26.67
FENTANYL	1,413,065	114,755	0.00	25.00	0.18	0.02	0.01	0.01	0.00
HYDROCODONE	12,577,054	1,651,038	0.63	2160.00	37.59	32.78	30.00	30.00	30.00
HYDROMORPHONE	183,200	51,602	0.13	2500.00	17.95	16.90	12.00	12.50	50.00
MEPERIDINE	21,144	9,816	2.50	1600.00	187.19	256.04	200.00	200.00	20.00
METHADONE	232,010	15,230	1.25	714.29	38.55	36.66	30.00	30.00	240.00
MORPHINE	762,080	145,971	0.13	4500.00	299.78	143.28	30.00	60.00	60.00
NALBUPHINE	2,036	217	3.33	240.00	36.68	42.84	10.00	40.00	
OPIUM	3,165	1,040	2.50	900.00	96.04	75.22	60.00	39.33	39.33
OXYCODONE	3,958,737	711,297	0.63	2700.00	39.26	40.61	20.00	30.00	45.00
PENTAZOCINE	16,150	4,017	7.50	900.00	123.47	194.35	150.00	150.00	55.50
PROPOXYPHENE	2,103,456	444,022	12.50	1800.00	225.30	438.71	400.00	400.00	
TAPENTADOL	19,636	5,716	14.29	3000.00	139.87	253.69	200.00	200.00	80.00
TRAMADOL	5,999,945	905,307	9.38	5333.33	106.14	198.63	200.00	200.00	20.00

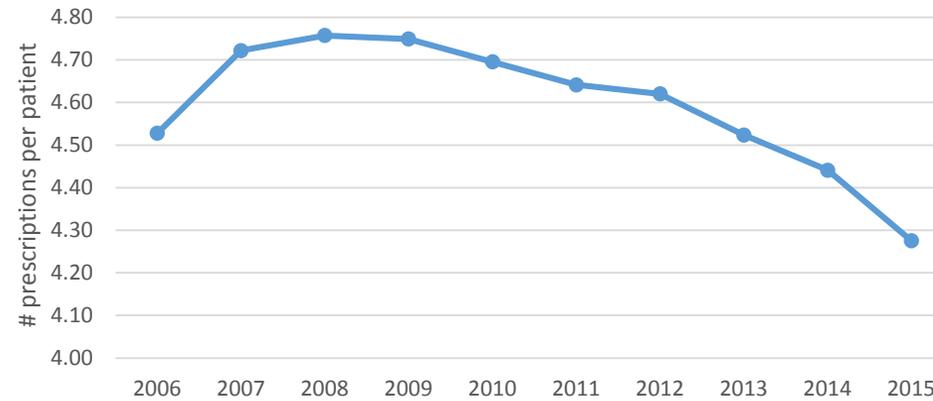
MMWR / July 7, 2017 / Vol. 66 / No. 26

Annual prescribing rate

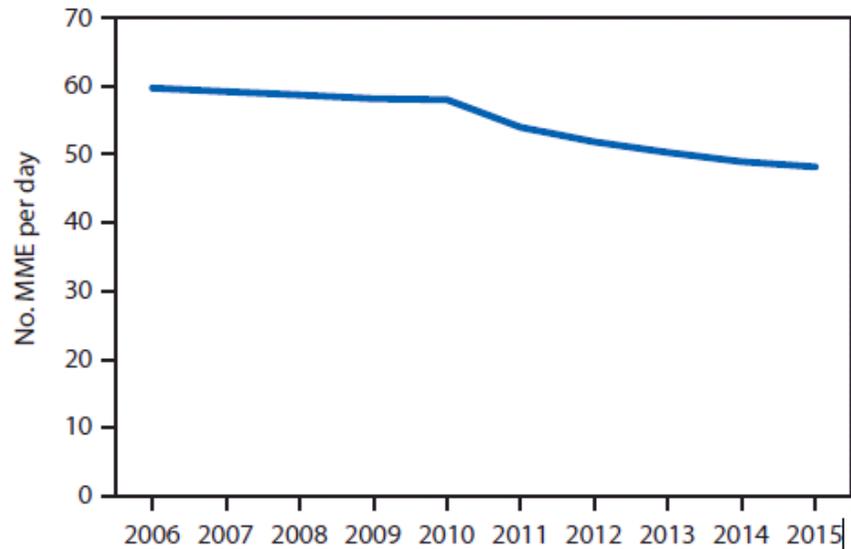


Medicare data

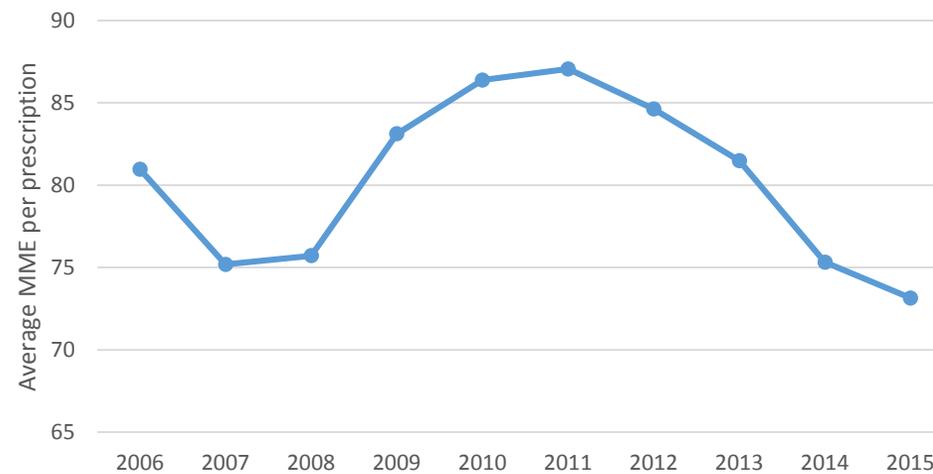
Annual prescribing rate [among opioid patients]



Average daily MME per prescription



Average daily MME per prescription



NIDA questions

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Q 2 – predictors of readmission/future overdose

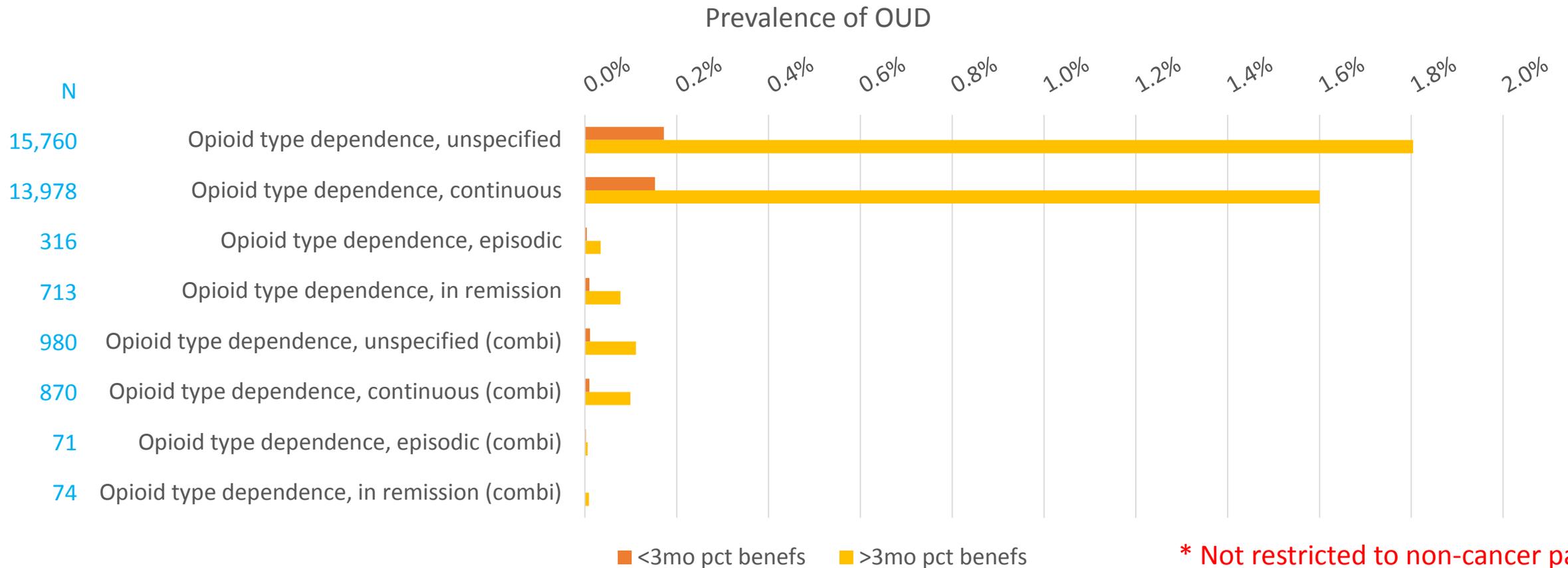
PREDICTORS FOR READMISSION/FUTURE OPIOID OVERDOSE POST EMERGENCY DEPARTMENT ADMISSION WITH A DRUG OVERDOSE

	30-DAY READMISSION 2,259 OUT OF 8,798 WERE READMITTED IN		3,032 OUT OF 8,798 WERE READMITTED IN 60 DAYS		971 OUT OF 8,798 HAD SUBSEQUENT RX OVERDOSE	
		P-VALUE		P-VALUE		P-VALUE
AGE AT THE FIRST ADMISSION TO ER	0.98	<.0001	0.98	<.0001	0.92	<.0001
FEMALE	0.91	0.1968	0.84	0.0118	0.66	<.0001
BLACK	1.11	0.2317	1.15	0.0966	1.56	<.0001
HISPANIC	0.99	0.9049	1.11	0.3264	1.40	0.0164
ASIAN	0.91	0.7083	1.21	0.3827	0.83	0.6449
OTHER	1.11	0.641	1.11	0.6068	0.86	0.6244
DUAL EVER	0.91	0.1046	0.92	0.1178	1.65	<.0001
NON-DUAL LIS	1.11	0.4712	0.98	0.9123	1.06	0.8198
LIVING IN RURAL AREA	1.26	0.0002	1.18	0.0047	0.74	0.0019
AMI	1.46	<.0001	1.43	<.0001	0.71	0.0252
DEPRESSION	0.89	0.2931	0.88	0.1931	1.40	0.0118
LUNG CANCER	1.18	0.1726	1.22	0.0768	0.52	0.0033
ANEMIA	1.17	0.018	1.26	0.0002	1.02	0.8439
BIPOLAR DISORDER	1.53	<.0001	1.50	<.0001	1.08	0.5326
MAJOR DEPRESSIVE AFFECTIVE DISORDER	1.50	<.0001	1.42	0.0001	0.89	0.3754
PERSONALITY DISORDERS	1.49	0.0023	1.57	0.0004	1.82	0.0015
EPILEPSY	1.19	0.072	1.27	0.0082	0.96	0.7902
FIBROMYALGIA, CHRONIC PAIN AND FATIGUE	1.19	0.0024	1.27	<.0001	1.20	0.0266
VIRAL HEPATITIS (GENERAL)	1.29	0.0074	1.25	0.0119	1.49	0.0004
LEUKEMIAS AND LYMPHOMAS	1.50	0.0071	1.37	0.0306	0.47	0.0269
MIGRAINE AND OTHER CHRONIC HEADACHE	0.95	0.5877	1.02	0.7961	1.39	0.0103
MOBILITY IMPAIRMENTS	1.01	0.8752	1.02	0.8348	0.70	0.0187
TOBACCO USE DISORDERS	1.18	0.0069	1.18	0.003	1.31	0.0008

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Q 3 – prevalence of opioid use disorder after ≥ 3 months vs. < 3 months of opioids

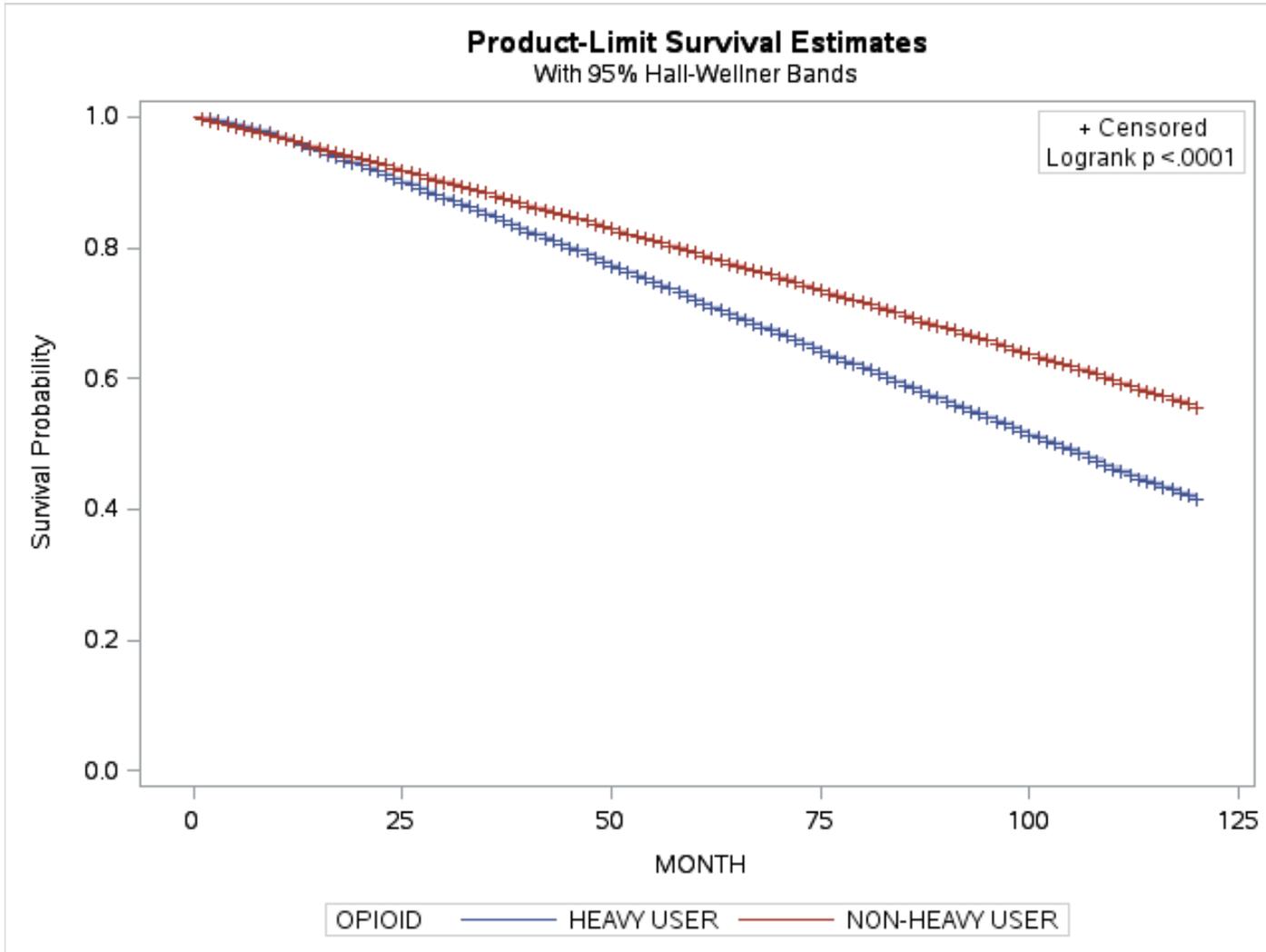


* Not restricted to non-cancer pain; Includes outliers; all beneficiaries

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Q 4 – mortality in OUD patients (light vs. heavy users)



2. ADJUSTED - COX PH REGRESSION

	REFERENCE	WALD	HR (95% CI)
OPIOID HEAVY USERS	NON-HEAVY USERS	4119.76	1.24(1.23,1.25)
AGE		434828.34	1.12(1.12,1.12)
FEMALE	MALE	10268.91	0.72(0.72,0.73)
BLACK	WHITE	246.27	1.08(1.07,1.09)
HISPANIC	WHITE	764.50	0.84(0.83,0.85)
ASIAN	WHITE	2552.37	0.60(0.59,0.61)
OTHER	WHITE	19.50	0.94(0.92,0.97)

Future work

Future work

- Refine the analysis
 - Multiple episodes of overdose
 - Obesity status
- Integrate ICD10-CM codes for conditions (2015Q4 and after)
- Manuscript in preparation for a clinical journal
 - “High incidence of adverse events in Medicare beneficiaries prescribed opioids for non-cancer pain”

Acknowledgments



- Nora Volkow
- Betty Tai
- Udi Ghitza
- Carlos Blanco