Fun with Medicare Part D Data

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Medicare Part D

- **Optional. Different plans. About $100 per month.**
- **Currently about two thirds of Medicare recipients without HMO are enrolled.**
- **Information on name of drug, ID of prescriber, dose, number of days' supply, each time the script is filled or refilled.**

Limitations:

- **No diagnosis (indication) in Part D.**
- **Provider ID in Part D not the same as in Part A and B, so cannot link (without special permission)**

What you can do with Medicare Part D

- Policy stuff, like doughnut holes, out of pocket costs, implications for use
- Time trends in use, geographic variations, predictors of use
- Toxicity
- Drug Interactions
- Comparative effectiveness (maybe)

We could always do this with parenterally administered drugs, because they were reimbursed in the outpatient file.

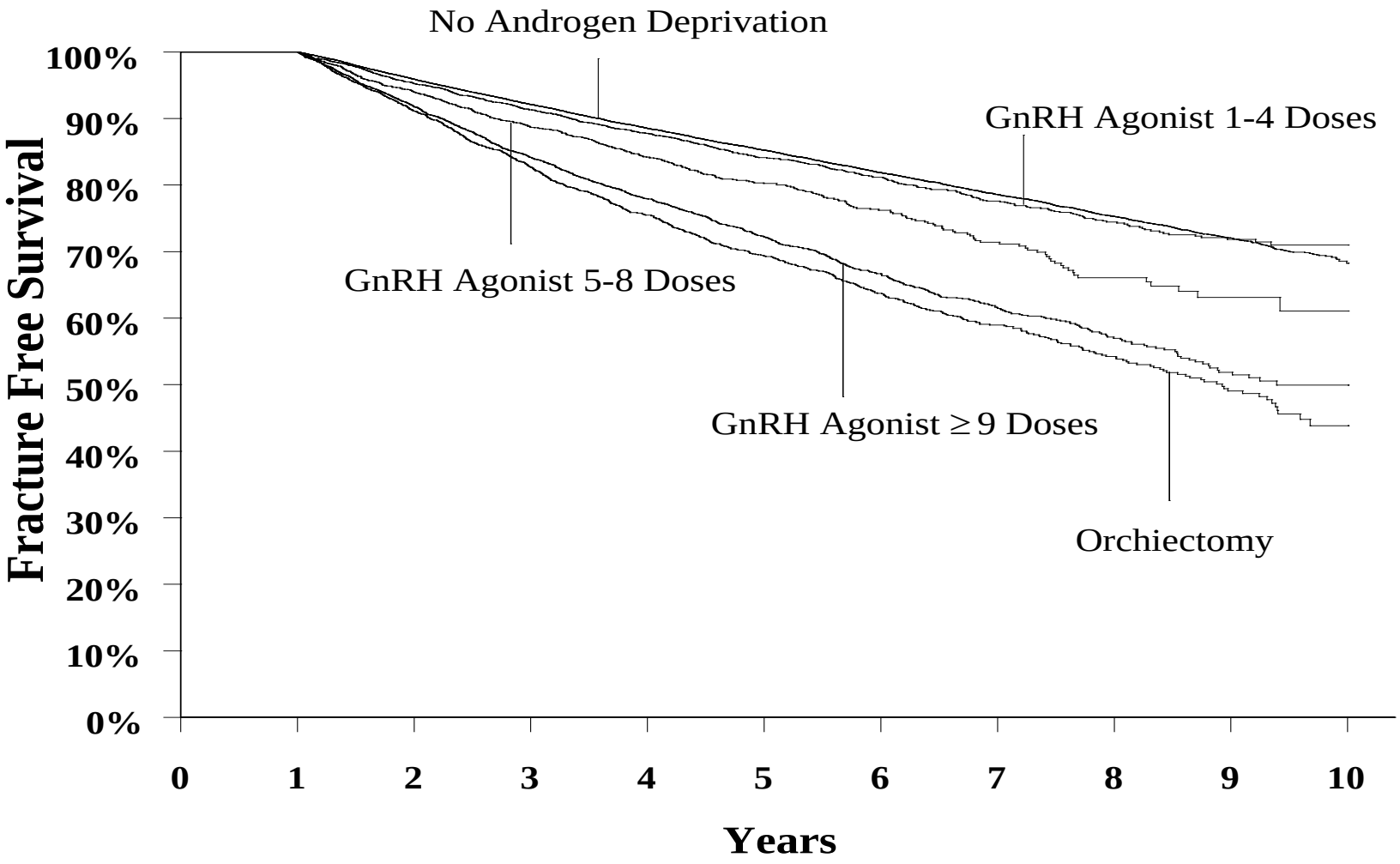
Chemotherapy, anti androgens, intravenous bisphosphonates
- who gets it, time trends, toxicity, role of provider

Comparative Toxicity Research: Assessing toxicities of therapies using observational data

- **Advantages:**
  - **Large representative sample allows estimation of toxicities in subgroups (e.g. very old, those with multiple comorbidities)**
  - **Ability to assess toxicity in "real world" rather than in setting of clinical trial with motivated patients, excellent monitoring, etc.**
  - **Ability to assess for rare toxicities and late toxicities.**
- **Disadvantages:**
  - **Selection bias**
  - **Under reporting of outcomes and covariates**
  - **Possible contamination by publicity (e.g. silicone breast implants)**

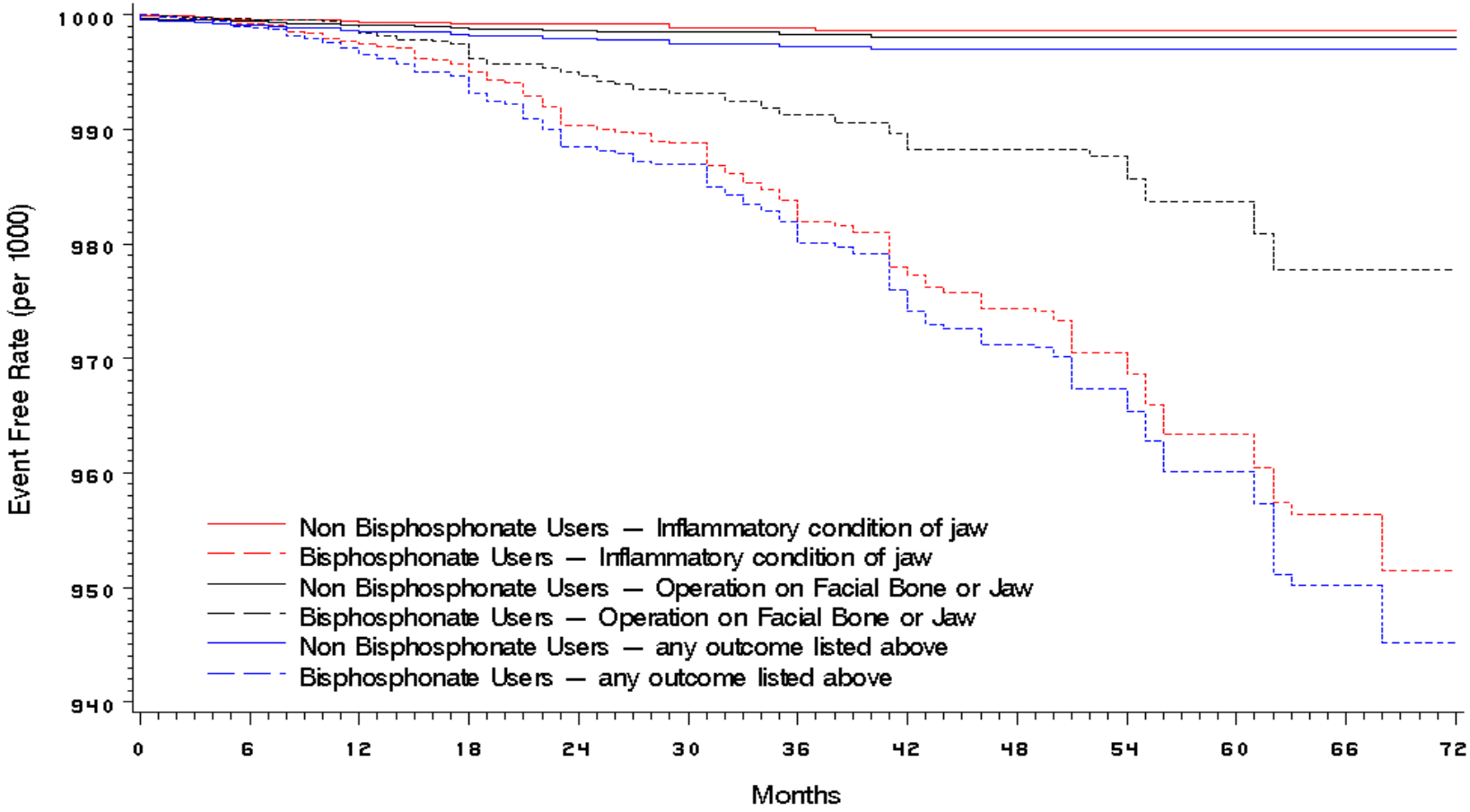
Late toxity: the example of anti-androgens for prostate cancer

- GnRH agonists were overused in the 1990's and early 2000's in men with prostate cancer.
- Androgens promote bone integrity.
- Does GnRH agonist use lead to increased fractures?



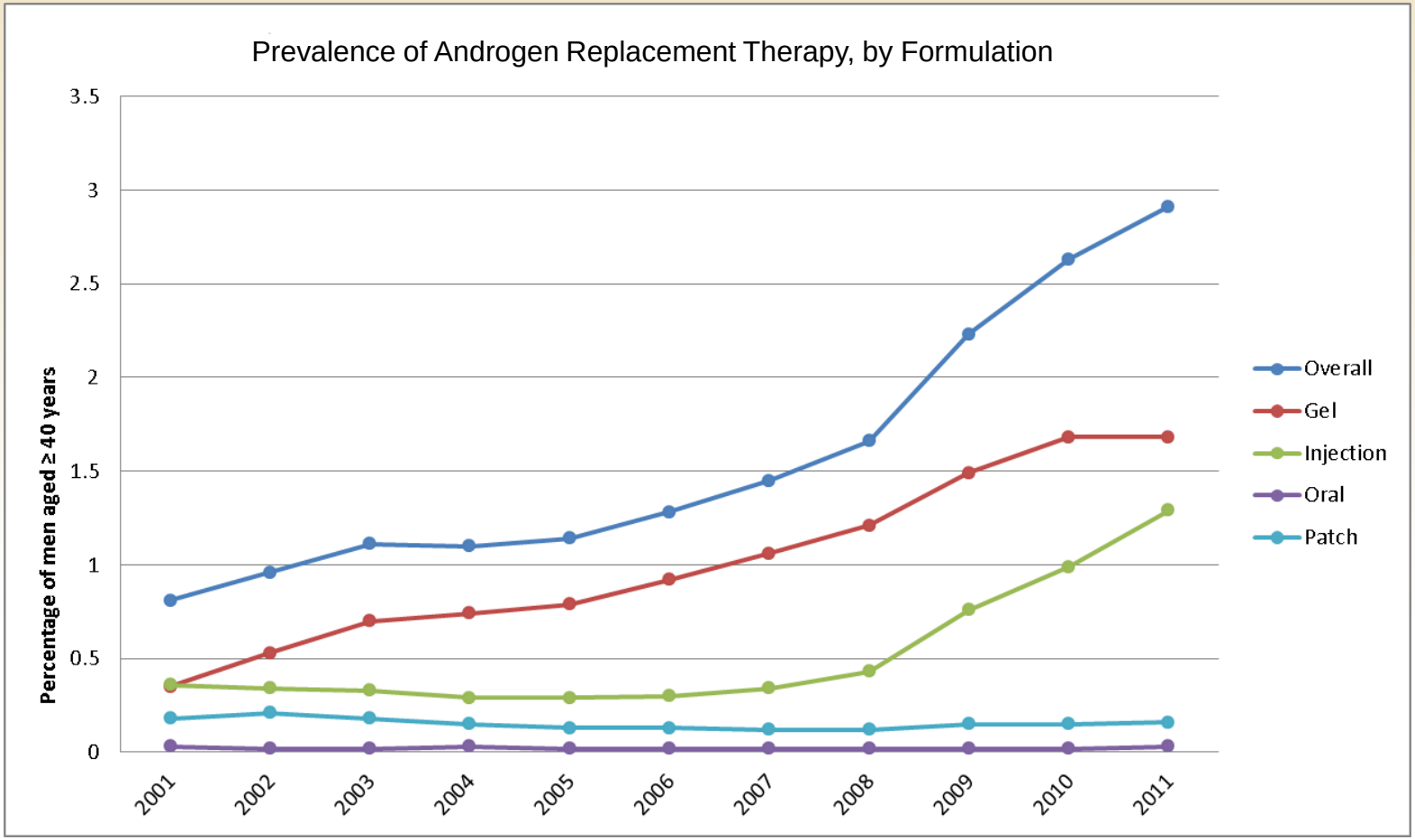
(from Shahinian et al., New Engl J Med 2005; 352:154-64)

Survival free of jaw toxicity after IV bisphosphonates in 14,349 users vs. 28,698 matched controls



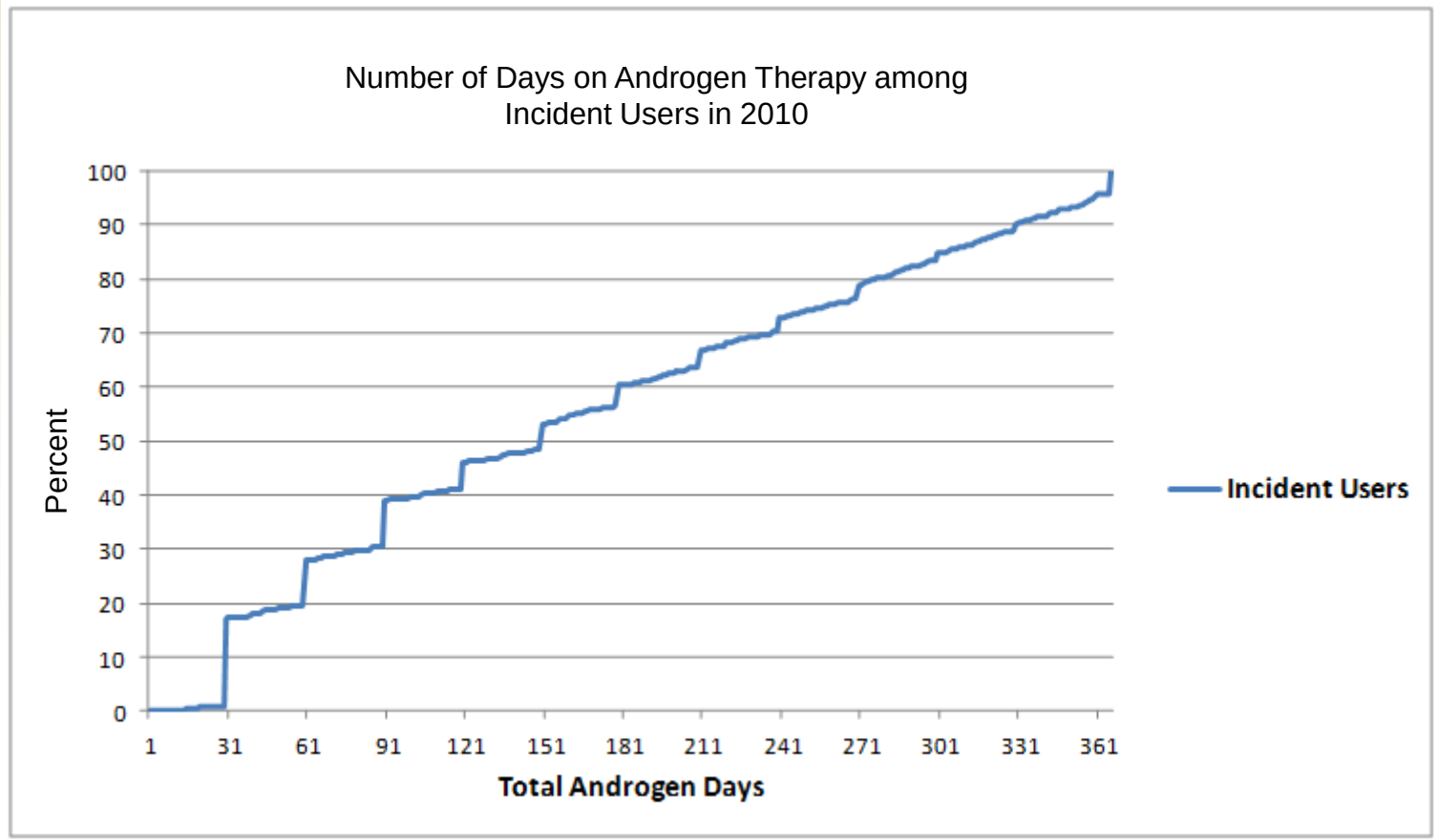
(from Wilkinson et al, J. Natl. Cancer Inst, 2007;Jul 4; 99(13):1016-24)

Drug data in United Health claims: The change in prevalence of androgen use over time in the use of different androgen formulations. Gel formulations were the most popular and increased the most, followed by injections. Use of oral androgens and patches was low and showed no increase over time.



(Baillargeon et al. JAMA Int Med 2013)

The total days on androgen therapy was estimated using incidence cohort from 2010. The cohort of incident androgen users was identified by selecting all androgen users who initiated androgen treatment at any time in 2010, had not received a prescription for androgen in the prior 12 months and had 12 months of continuous coverage before and after their androgen treatment start date. Total androgen days were assessed in the 12 months following the first prescription for androgen.



(Baillargeon et al. JAMA Int Med 2013)

An example of drug interaction: sulfonylureas and antiobiotics

- Sulfonylureas are commonly used to treat type 2 diabetes.
- A number of antibiotics interact with sulfonylureas, by interfering with their absorption or metabolism, or by stimulating insulin release.
- No data exist on the prevalence of and risk factors for hypoglycemia after an older patient on a sulfonylurea is prescribed an antibiotic.

Approach

- **Part D Medicare for Texas for all patients who filled a prescription for glypizide or glyburide (n= 140,174) in 2009.**

- **We then identified any instance of a patient filling a prescription for an antibiotic which overlapped with the prescription for sulfonylurea.**

- **The outcomes were:**
  1. **Any emergency room visit or hospitalization for hypoglycemia within 14 days of the antibiotic prescription.**
  2. **Medicare costs from those ER visits and hospitalizations.**

- **We assessed those outcomes after prescription of antibiotics known to interact with sulfonylureas, using non-interacting antibiotics as a reference.**

(Parekh et al. JAMA Int Med 2014)

Antibiotics thought to interact with sulfonylureas and those with no interaction

Interacting Antibiotics	Potential Mechanism
Ciprofloxacin	Stimulates pancreatic beta cells
Clarithromycin	Inhibits intestinal p-glycoprotein
Fluconzole	CYP2C9 inhibitor
Levofloxacin	Stimulates beta cells and possibly inhibits intestinal P-glcoprotein
Metronidazole	CYP2C9 inhibitor
Sulfamethoxazole/Trimethiprim	CYP2C9 inhibitor

Non-interacting: Amoxicillin, Azithromycin, Cefdinir, Cefuroxime, Cephalexin, Clindamycin, Doxycycline, Nitrofurantoin, Penicillin

Adjusted odds of hospitalization or emergency room visits for hypoglycemia within 14 days of antimicrobial exposure

		Glyburide users	
Antimicrobial	Ref=Azithromycin	Ref=Amoxicillin	Ref=Cephalexin
Ciprofloxacin	1.41 (0.92, 2.15)	1.76 (1.13, 2.73)	1.81 (1.12, 2.95)
Clarithromycin	4.17 (1.89, 9.20)	5.22 (2.31, 11.78)	5.38 (2.33, 12.42)
Fluconazole	1.15 (0.52, 2.53)	1.44 (0.64, 3.22)	1.48 (0.65, 3.41)
Levofloxacin	2.35 (1.59, 3.49)	2.95 (1.93, 4.50)	3.04 (1.91, 4.82)
Metronidazole	1.72 (0.73, 4.05)	2.16 (0.91, 5.12)	2.22 (0.91, 5.40)
Moxifloxacin	1.37 (0.60, 3.09)	1.71 (0.74, 3.94)	1.76 (0.75, 4.16)
Sulfamethoxazole / Trimethoprim	2.78 (1.84, 4.18)	3.47 (2.27, 5.32)	3.58 (2.25, 5.69)

All models were adjusted for age, gender, ethnicity, Medicaid eligibility at the year of antimicrobial use, comorbidity, any emergency department visit due to hypoglycemia, any acute hospitalization in the prior year, nursing facility residence, and the indication for antimicrobial use.

(Parekh et al. JAMA Int Med 2014)

Association of patient characteristics and antimicrobial exposure with hypoglycemic events among glipizide or glyburide users (Part 1)

	Odds Ratio(95% CI)	Number Needed to Harm (95% CI**)
Antimicrobial*		
Ciprofloxacin	1.62 (1.33, 1.97)	334 (223, 595)
Clarithromycin	3.96 (2.42, 6.49)	71 (43, 157)
Fluconazole	0.92 (0.52, 1.61)	-
Levofloxacin	2.60 (2.18, 3.10)	131 (107, 168)
Metronidazole	2.11 (1.28, 3.47)	187 (92, 457)
Moxifloxacin	1.13 (0.65, 1.98)	-
Co-trimoxazole	2.56 (2.12, 3.10)	133 (107, 180)
Non-interacting antimicrobials†	1.00	
Age at antimicrobial use (years)		
66-70	1.00	
71-75	1.37 (1.12, 1.69)	
76-80	1.66 (1.35, 2.04)	
81-85	2.02 (1.63, 2.50)	
86+	2.03 (1.61, 2.55)	
Race/ethnicity		
Non-Hispanic White	1.00	
Black	1.80 (1.47, 2.19)	
Hispanic	1.33 (1.13, 1.56)	
Other	0.86 (0.56, 1.33)	

Association of patient characteristics and antimicrobial exposure with hypoglycemic events among glipizide or glyburide users (Part 2)

	Odds Ratio (95% CI)
Medicaid Eligibility at the year of antimicrobial use	
No	**1.00**
Yes	**1.09 (0.94, 1.27)**
Charlson comorbidity index	
0	**1.00**
1	**1.14 (0.94, 1.39)**
2	**1.33 (1.11, 1.66)**
3+	**1.76 (1.45, 2.13)**
Prior ED visit for hypoglycemia in prior year (Yes vs. No)	**4.02 (3.32, 4.86)**
Prior hospitalization for any cause in prior year (Yes vs. No)	**1.32 (1.14, 1.54)**

The analyses also controlled for the indication for the antibiotic prescription.

Prevalence of overlapping use of the five antimicrobials associated with hypoglycemia among glypizide or glyburide users in 2007 and 2009

Antimicobial	Glypizide and Glyburide users	
	2007 (N= 136, 160)	2009 (N=140, 174)
	Number (%) prescribed an antimicrobial	
Ciprofloxacin	16,661 (12.24)	18,149 (12.95)
Clarithromycin	1,942 (1.43)	1,757 (1.25)
Levofloxacin	14,186 (10.42)	13,458 (9.60)
Metronidazole	2,967 (2.18)	3,305 (2.37)
Co-trimoxazole	13,017 (9.56)	14,347 (10.24)
Any of the above	38,048 (27.94)	39,631 (28.27)

Other outcomes

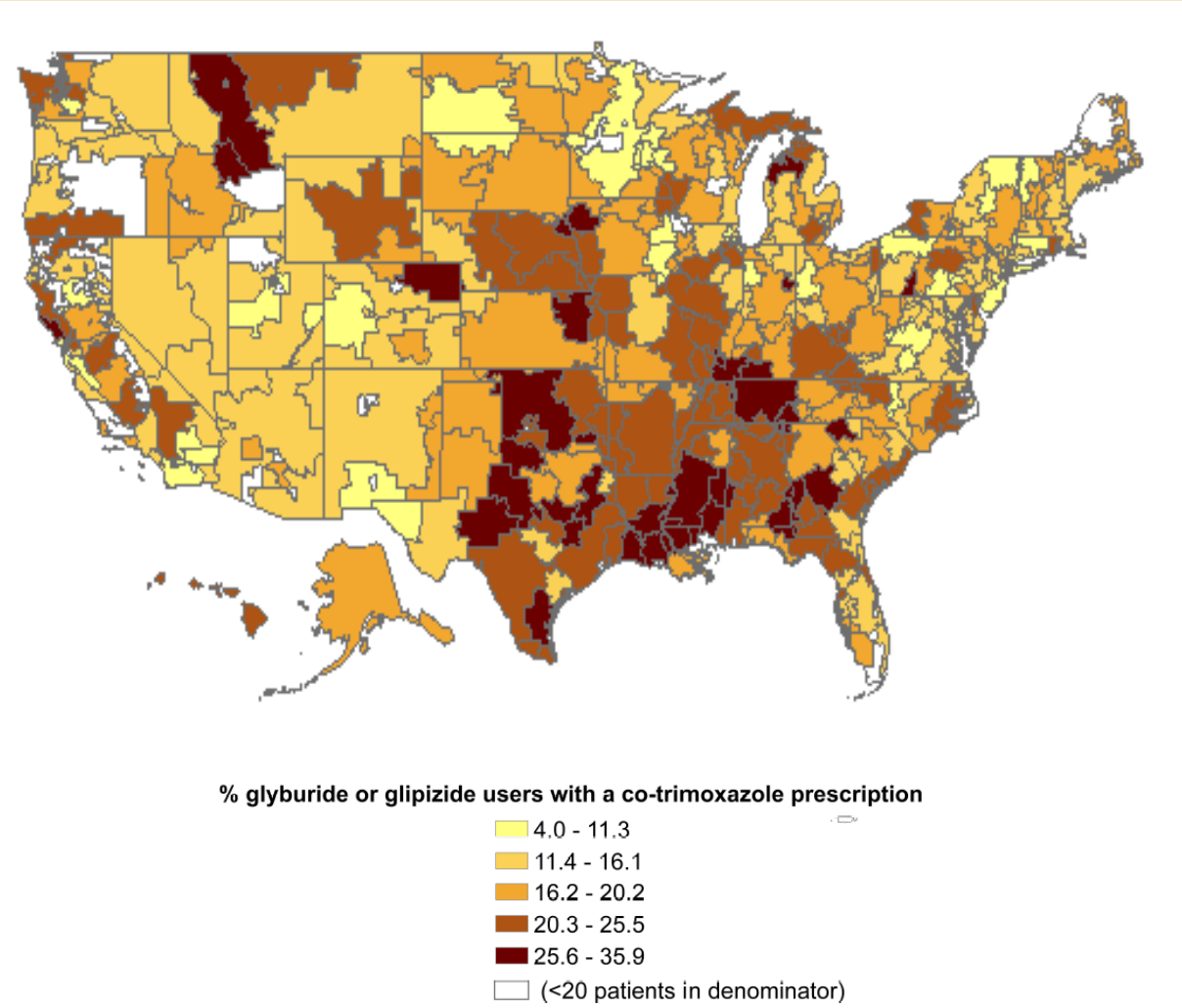
- **There were 9 deaths during hospitalization for hypoglycemia after prescription of an interacting antibiotic (54,028 episodes) vs. 3 deaths after a non-interacting antibiotic (74,481 episodes), p=0.021.**
- **Medicare costs associated with increased risk of ER or hospitalization totaled $2,124,000, or $30.54 for each of the 69,537 prescriptions filled for an interacting antibiotic by the 140,174 patients on sulfonylureas.**
- **13.2% of all ER visits and hospitalizations for hypoglycemia in patients on sulfonylureas were preceded by a prescription for one of the five interacting antibiotics.**

(Parekh et al. JAMA Int Med 2014)

Conclusion

- **A high proportion (28%) of older patients taking sulfonylureas are prescribed an interacting antibiotic each year.**
- **This practice is associated with increased ER visits, hospitalizations, and deaths from hypoglycemia, as well as increased costs to Medicare.**
- **Some inexpensive antibiotics (e.g., sulfamethoxazole/trimethoprim) are not so inexpensive when given to patients on sulfonylureas, after accounting for the downstream costs of treating hypoglycemia.**

Geographic variation in the proportion of patients received a co-trimoxazole prescription in 2008-2009 for older diabetic patients taking glyburide or glipizide in the United States, by hospital referral region.



Tan et al., J. Gerontol 2014

Hospital referral region (HRR) characteristics and their association with the rate of co-prescription of co-trimoxazole and glyburide/glipizide.

HRR-level Characteristics*	Mean (SD)	Correlation Coefficient (P value)†
% of glyburide or glipizide users with a co-trimoxazole prescription	17.9 (5.8)	—
Number of primary care physicians per 100,000 residents$	70.5 (12.0)	-0.23 (P < 0.001)
% of all oral prescriptions that were antibiotics, 2008-2010§	4.1 (0.4)	0.26 (P < 0.001)
% of all antibiotics prescribed that were co-trimoxazole, 2008-2010§	9.0 (1.5)	0.46 (P < 0.001)

Tan et al., J. Gerontol 2014

Looking at drug interactions at level of the PCP

Step 1: 2,857,475 'TX' BENE_IDs in 2007

⇩

Step 2: 1,360,154 (47.60% from previous step) BENE_IDs with completely (12 months) Part D enrollment

⇩

Step 3: 159,596 (11.73% from previous step) BENE_IDs with sulfonylurea prescriptions (with 1,146,377 sulfonylurea prescriptions)

⇩

Step 4: 143,296 (89.79% from previous step) BENE_IDs with sulfonylurea prescriptions prescribed by 'TX' prescribers (with 983,447 sulfonylurea prescriptions, 85.79% from the 1,146,377 sulfonylurea prescriptions in last step)

⇩

Step 5: Assign the plurality Prescriber there are 10,829 Prescribers (84.12% from 12,873 prescribers) 139,969 beneficiaries Note: there are 3,327 (2.32% from 143,296) BENE_IDs with ties, exclude these BENE_IDs

⇩

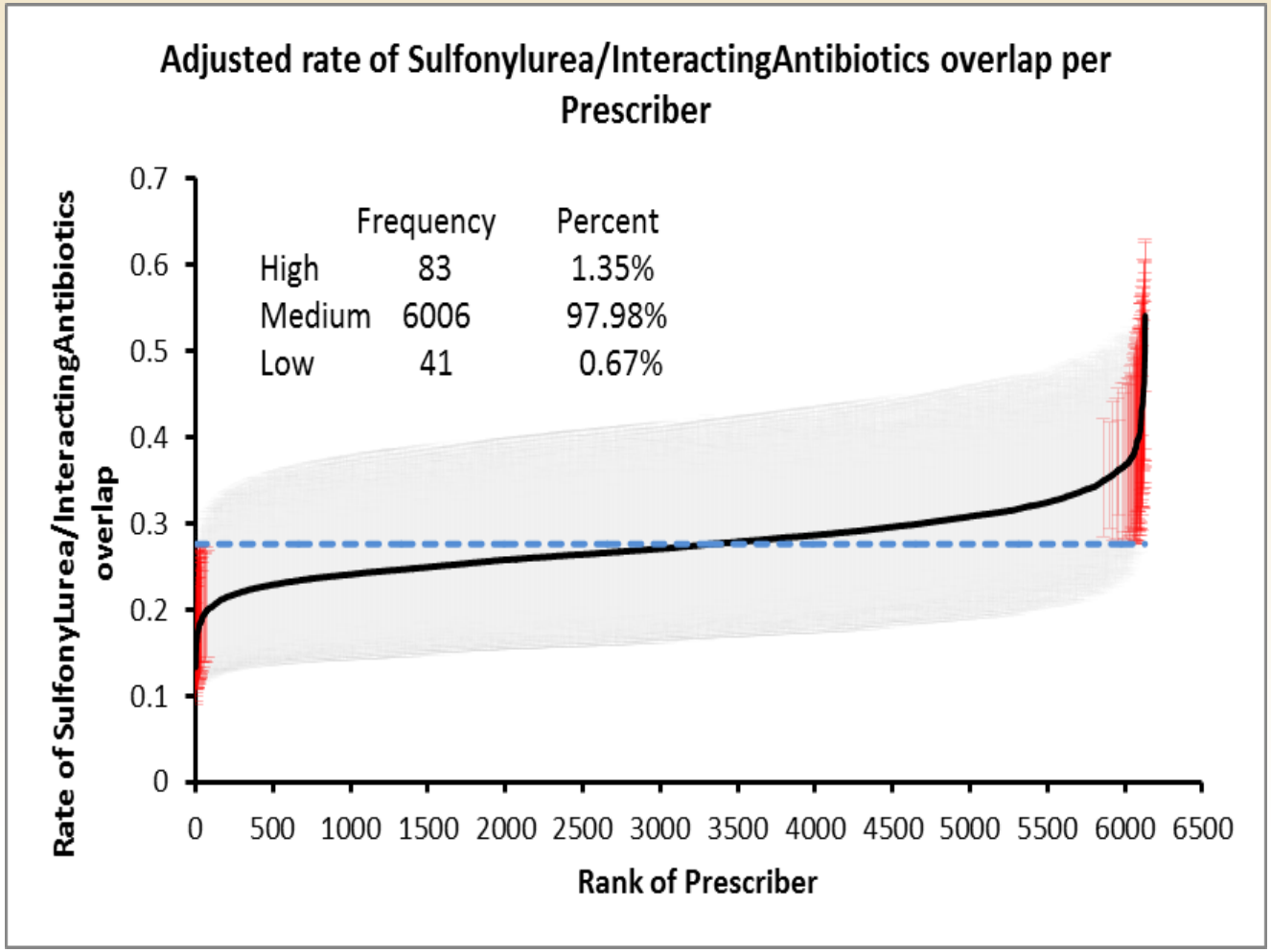
Step 6: Only keep the Prescribers with at least 10 beneficiaries. 118,925 (82.99% from previous step) beneficiaries left, 4,303 (39.74% from previous step) prescribers left

⇩

Step 7: Based on data in step 6, pick up all Prescribers with patients taking any antibiotics as denominator, all Prescribers with patients who were prescribed an interacting antibiotics as numerator . Note: exclude the prescribers with no overlap between sulfonylureas and antibiotics. Total 4,299 prescribers.

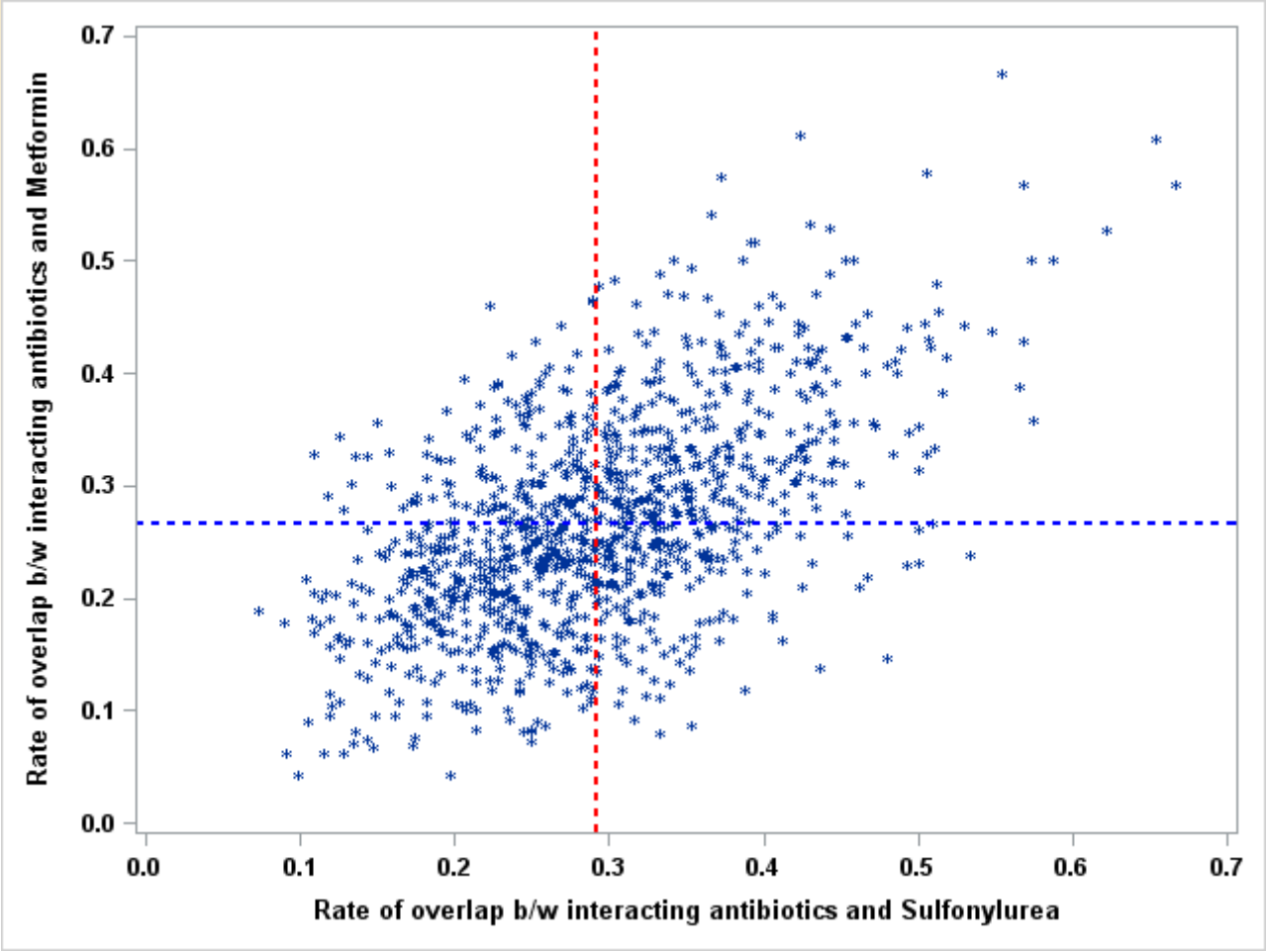
⇩

Step 8: Restrict the prescribers (in step 6) with at least 10 patients both on sulfonylurea and any antibiotics. 2,774 (25.62% from 10,829) prescribers left, 97,980 (70% from 139,969) beneficiaries left



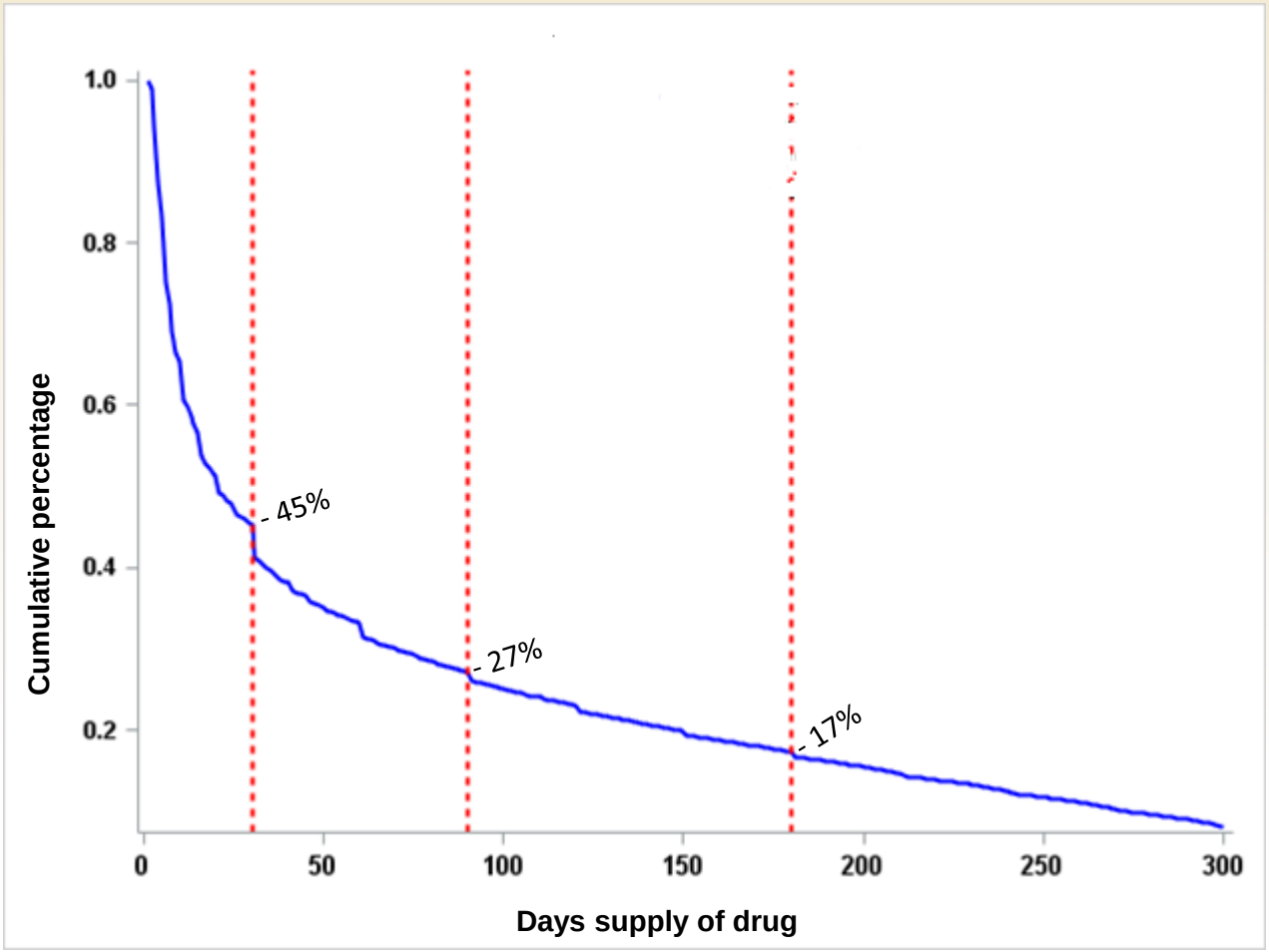
ICC = approximately 0.02

The correlation between the overlap rate on interacting-antibiotics/sulfonylurea and overlap rate on interacting-antibiotics/metformin



Prescriptions for Opiods: Variation among Physicians

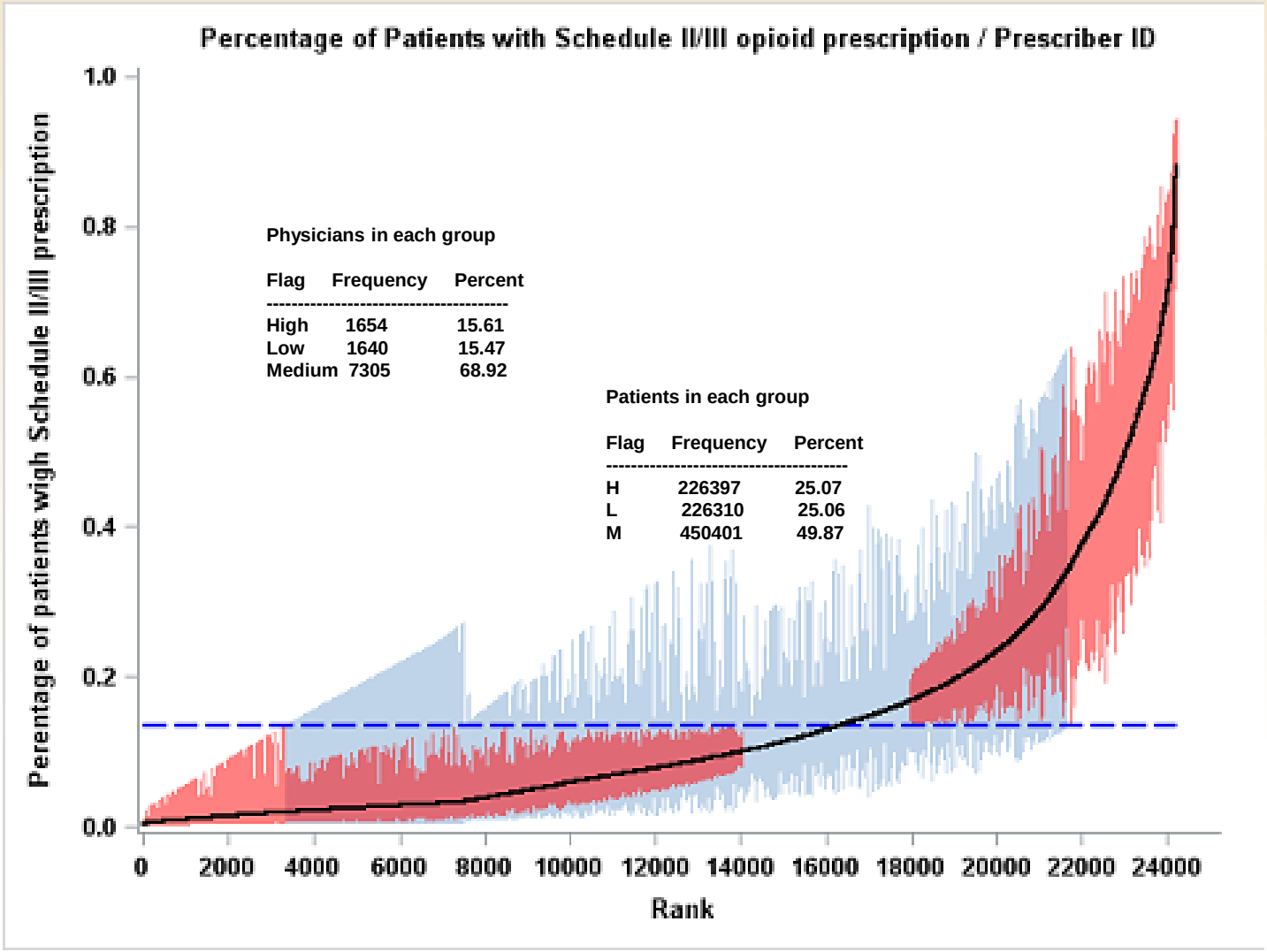
steps	# of beneficiaries	% from last step
Beneficiaries 66 years or older on Jan 1, 2009	2,316,082	
Beneficiaries from last step are in 'TX'	2,203,548	95.14%
Continuous Part A&B in 2008,2009 no HMO in 2008, 2009 continuous enrollment in Part D in 2009	709,021	32.18%
Beneficiaries in previous step with no cancer history in 2008	624,680	88.10%
Beneficiaries with at least one prescription	588,432	94.20%
Exclude the beneficiaries with no information in SEX, EDUCATION and AREA	562,480 (24,194 prescriber IDs)	99.91%
Beneficiaries received a prescription from a prescriber who wrote prescriptions for at least 10 beneficiaries. (constricted prescriber ID in Texas) (cohort)	563,005 (24,194 prescriber IDs)	95.68%
Beneficiaries with at least one opiod prescription	200,075	35.54%

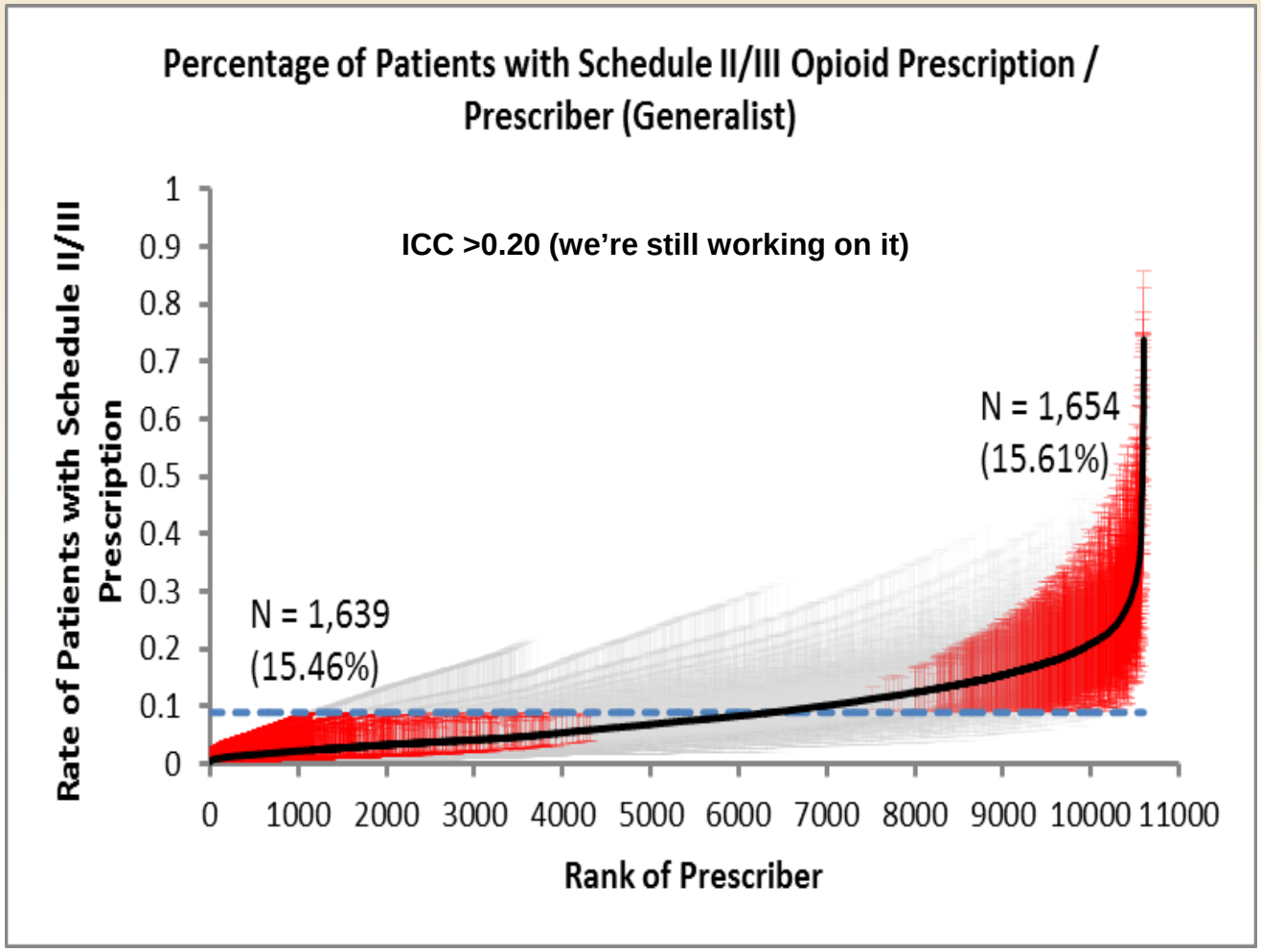

1.0
0.8
0.6
0.4
0.2
Cumulative percentage
45%
27%
17%
0
50
100
150
200
250
300
Days supply of drug

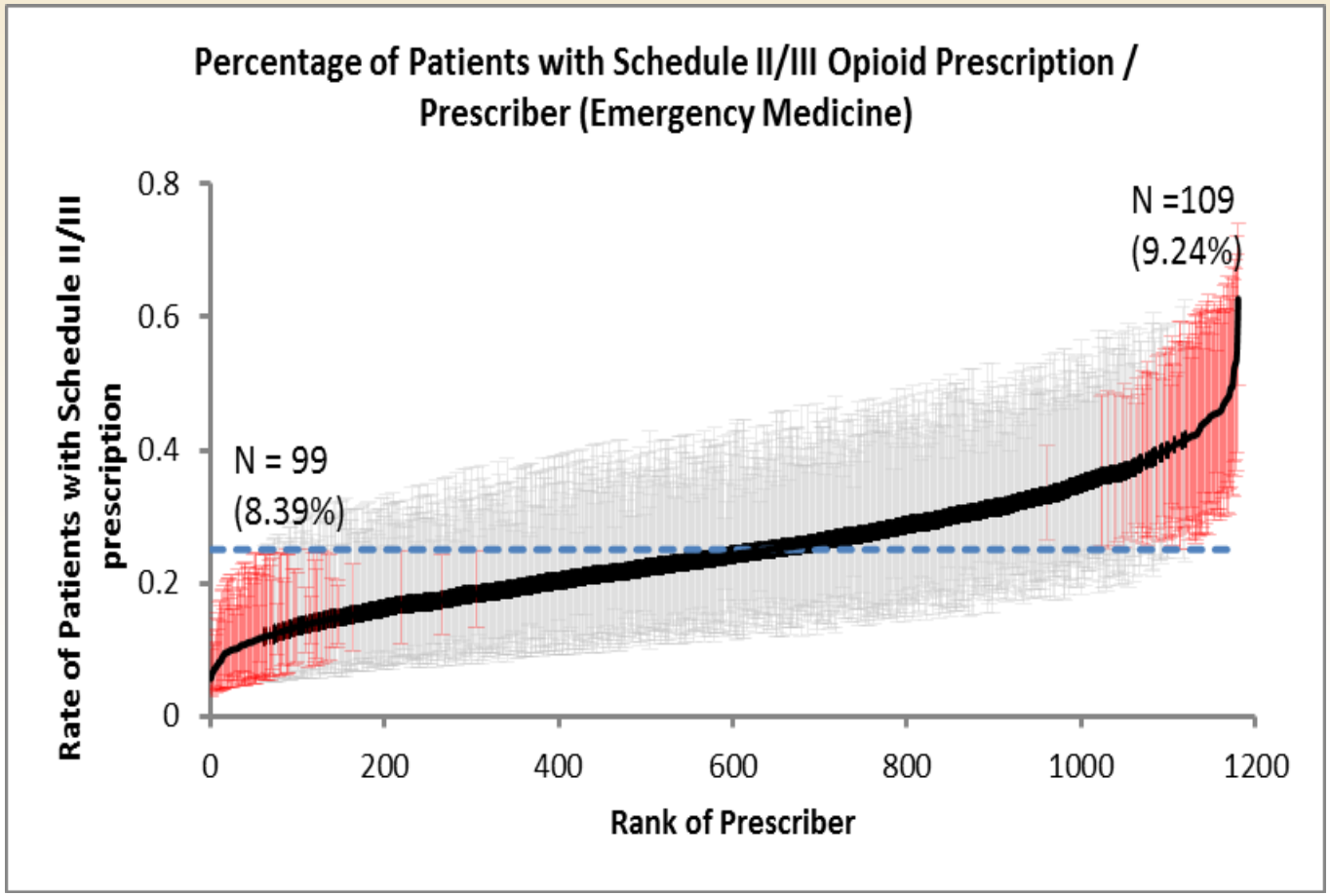
Drug	Percentage of prescriptions using drug
Oxycodone, Hydrocodone, Codeine	91.01%
Fentanyl, Morphine, Meperidine, Opim	7.17%
Methadone	1.34%
Hydromorphone	0.36%
Others	0.12%

Beneficiary characteristics associated with receiving opioid script.

Patient Characteristic	with opioid prescription	
	N1 (% having opioid prescription)	OR (95% CI) of having opioid prescription
All	562,480 (35.54%)	
Age		
66-69	130,300 (34.81%)	Reference
70-74	144,802 (35.06%)	0.970 (0.954-0.985)
75-79	114,569 (35.79%)	0.953 (0.937-0.969)
80-84	88,809 (36.34%)	0.935 (0.918-0.952)
>=85	84,000 (36.30%)	0.878 (0.862-0.894)
Race		
Non_Hispanic White	385,151 (35.12%)	1.146 (1.121-1.172)
Non_Hispanic Black	41,464 (39.71%)	Reference
Hispanic	118,409 (36.82%)	0.897 (0.875-0.918)
Comorbidity Score		
0	296,018 (30.06%)	Reference
1	142,421 (36.99%)	1.341 (1.323-1.359)
2	62,331 (43.86%)	1.753 (1.722-1.785)
>=3	61,710 (50.07%)	2.233 (2.192-2.274)
Quartile of Education		
Q1 (low)	141,487 (36.48%)	Reference
Q2	145,226 (37.47%)	1.085 (1.067-1.104)
Q3	141,314 (35.95%)	1.065 (1.046-1.083)
Q4 (high)	134,453 (32.02%)	0.967 (0.950-0.985)
Medcaid		
YES	171,516 (41.93%)	1.496 (1.474-1.518)
NO	390,964 (32.73%)	Reference
Gender of Patients		
Female	374,086 (37.82%)	Reference
Male	188,394 (31.01%)	0.747 (0.738-0.756)

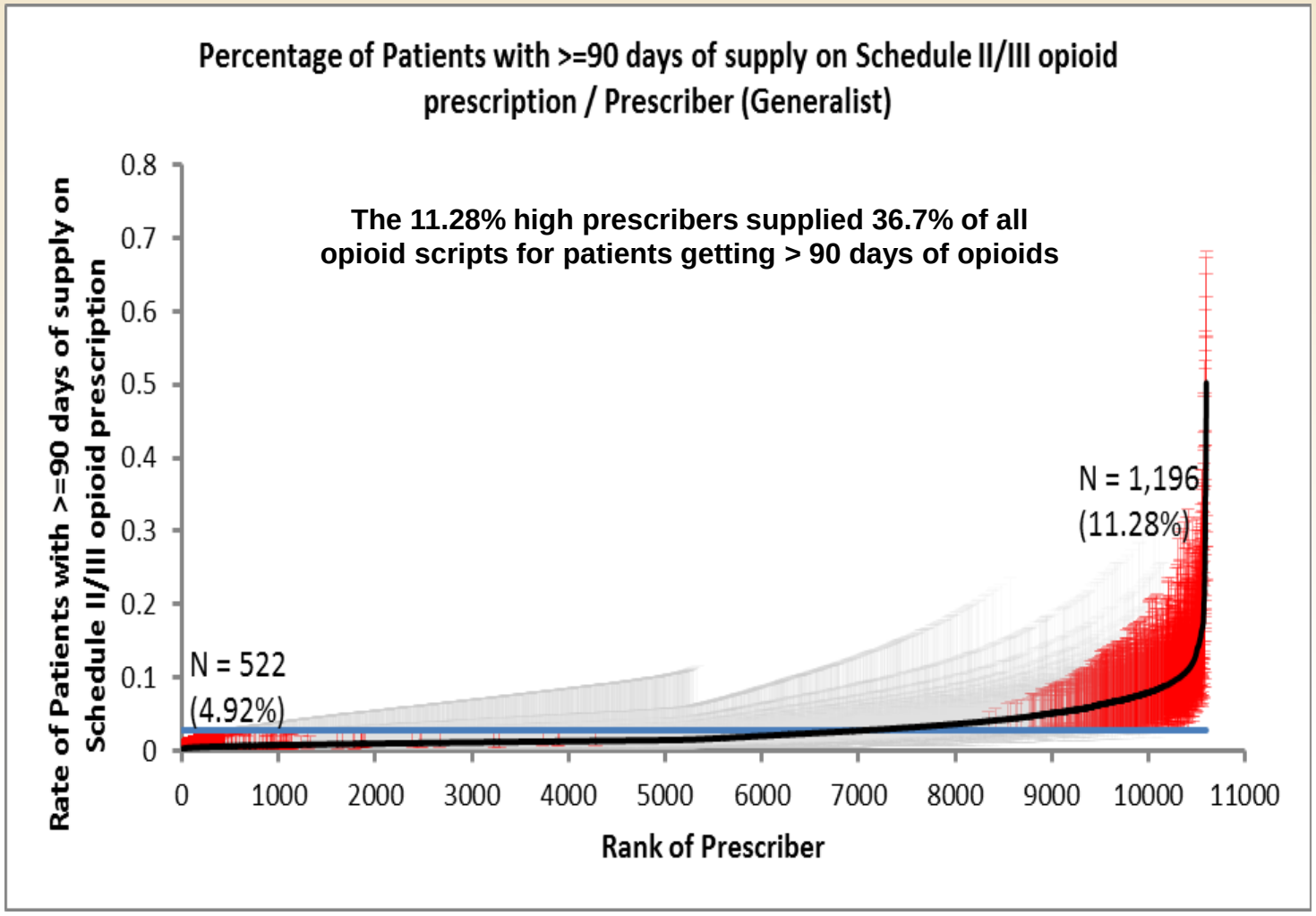

Percentage of Patients with Schedule II/III opioid prescription / Prescriber ID
Perentage of patients wigh Schedule II/III prescription
1.0
0.8
0.6
0.4
0.2
0.0
0
2000
4000
6000
8000
10000
12000
14000
16000
18000
20000
22000
24000
Rank
Physicians in each group
Flag Frequency Percent
High 1654 15.61
Low 1640 15.47
Medium 7305 68.92
Patients in each group
Flag Frequency Percent
H 226397 25.07
L 226310 25.06
M 450401 49.87

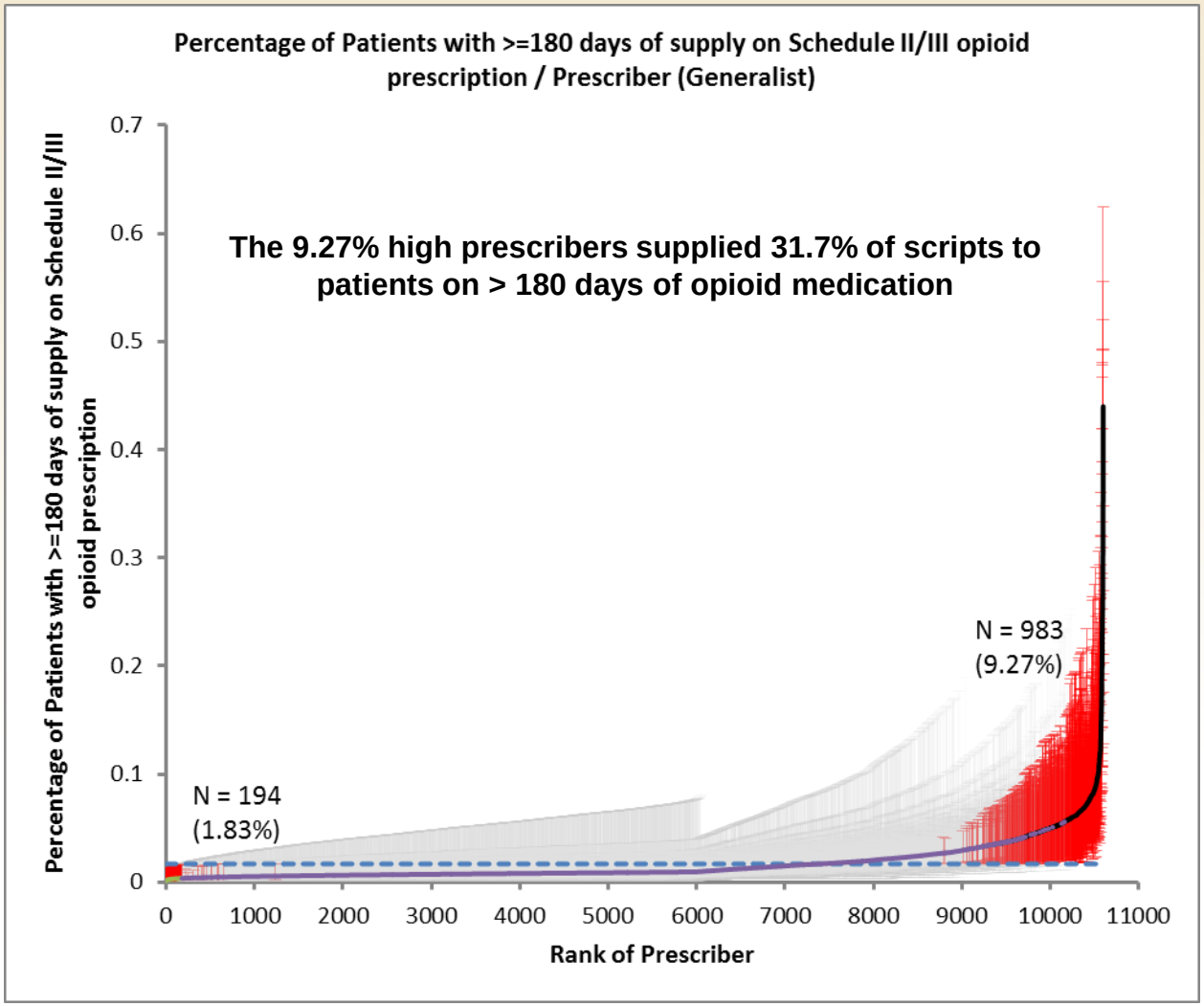

Percentage of Patients with Schedule II/III Opioid Prescription / Prescriber (Generalist)
ICC >0.20 (we're still working on it)
Rate of Patients with Schedule II/III Prescription
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
N = 1,639
(15.46%)
N = 1,654
(15.61%)
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000
11000
Rank of Prescriber


Percentage of Patients with Schedule II/III Opioid Prescription / Prescriber (Emergency Medicine)
Rate of Patients with Schedule II/III prescription
0.8
0.6
0.4
0.2
0
N =109
(9.24%)
N = 99
(8.39%)
0
200
400
600
800
1000
1200
Rank of Prescriber

	% of any Schedule II/III opioid use	ICC
All physicians	11.52%	0.3905
Generalist	9.99%	0.2338
Emergency	24.30%	0.1071
Orthopaedic	43.92%	0.1128

	Prescriptions prescribed by prescribers in high group	% of prescribers in high group
All physicians	33.82%	16.19%
Generalist	41.99%	15.61%
Emergency	14.93%	9.24%
Orthopaedic	15.61%	11.60%


Percentage of Patients with >=90 days of supply on Schedule II/III opioid prescription / Prescriber (Generalist)
The 11.28% high prescribers supplied 36.7% of all opioid scripts for patients getting > 90 days of opioids
Rate of Patients with >=90 days of supply on Schedule II/III opioid prescription
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
N = 522
(4.92%)
N = 1,196
(11.28%)
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000
11000
Rank of Prescriber


Percentage of Patients with >=180 days of supply on Schedule II/III opioid prescription / Prescriber (Generalist)
The 9.27% high prescribers supplied 31.7% of scripts to patients on > 180 days of opioid medication
Percentage of Patients with >=180 days of supply on Schedule II/III opioid prescription
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
N = 983
(9.27%)
N = 194
(1.83%)
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000
11000
Rank of Prescriber

Conclusion

Part D Medicare data are fun.