Concordance between suboptimal antibiotic and opioid prescribing: Can we identify common targets for antibiotic and opioid stewardship?

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Abstract

Background

Antimicrobial resistance and opioid misuse both present major public health challenges. Identifying high prescribers of both of these agents can help to provide a common target for intervention. We sought to determine the correlation between suboptimal antibiotic and opioid prescribers and identify predictors of concordant high prescribers in the primary care setting.

Methods

We performed a 1-year cross-sectional study of primary care physicians in Ontario, Canada. We defined high prescribers as the top quartile of antibiotic or opioid prescribers using three antibiotic and three opioid prescribing metrics. We tabulated agreement between prescribing categories using the kappa statistic. We built a multivariable logistic regression model to identify predictors of both high antibiotic and opioid initiation.

Results

We included 9,469 physicians. We observed minimal overlap between high antibiotic initiation and opioid initiation (6% of prescribers) with kappa=0.00 (95% CI -0.02 to 0.02). After adjustment for patient population, key predictors of being a high prescriber in both categories include older patient population (aOR 1.42, 95%CI 1.24 to 1.62), physician male gender (aOR 1.46, 95%CI 1.14 to 1.86), and late career stage (aOR 1.76, 95%CI 1.26 to 2.46).

Interpretation

Among primary care physicians, there was a lack of association between high antibiotic prescribing and high opioid prescribing. While there is overlap in the behavioural science underlying suboptimal prescribing, our findings suggest separate tailored approaches to antibiotic and opioid stewardship strategies are needed.

Introduction

Rising antimicrobial resistance (AMR) is an urgent public health threat. Most antibiotics prescribed in humans are in the outpatient setting, acting as an important driver for antibiotic resistance in the community (1). In the US alone, antibiotic resistant infections claim 23,000 lives annually (2). At the same time another drug-related public health crisis looms. The epidemic of opioid overuse is rapidly evolving, and in the United States, prescription opioids are associated with 17,000 overdose-related deaths annually (3). While the use of non-prescribed opioid related deaths is increasing, prescription opioids still account for at least 25% of opioid-related deaths (4).

Despite their obvious differences, these two public health threats have notable commonalities. In North America, both antibiotic and opioid overuse are largely iatrogenic in origin due to over-prescribing behaviour (5). There is wide variability in prescribing practices for both of these drug classes, which is not fully explained by differences in practice settings and patient populations (6–8). Additionally, patients of high prescribers of both antibiotics and opioids are more likely to experience harm (6,8) providing an impetus for urgent intervention.

Understanding overlap in over-prescribing can help identify unique prescriber populations where antibiotic and opioid stewardship can be focused and support aligned efforts to improve the use of these agents and reduce their harm. Our objective was to evaluate the correlation between suboptimal opioid and antibiotic prescribers as well as to identify predictors of concordant high prescribers in the primary care setting.

Methods

Study Design and Setting

We performed a 1 year cross-sectional study evaluating primary care physician prescribers of opioids and antibiotics during the period of March 1, 2017 to February 28, 2018. We conducted this study at ICES (formerly the Institute for Clinical Evaluative Sciences) in Ontario, Canada's most populous province. ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. ICES is considered a prescribed entity under Ontario's *Personal Health Information Protection Act*, which securely collects, stores, and analyzes personal health information for the 14 million residents of the province.

Eligible Population

Eligible physicians included all primary care physicians in Ontario. We excluded physicians with less than 500 patient visits per year, physicians prescribing the lowest 5% of antibiotic prescriptions, the lowest 5% of opioid prescribers to ensure that only active prescribers were included in the cohort. We also excluded physicians with a focus or specialty of pain (20 or more billings for pain management) or palliative care (25% or more of all billings were for a palliative care indication) to ensure high opioid prescribers were not categorized as such due to their unique practice setting and patient population.

Data Sources

Antibiotic prescribing was identified using Xponent™, a database owned by IQVIA. This database includes dispensed outpatient medications aggregated at the physician level. We included oral antibiotics in the World Health Organization Anatomical Therapeutic Chemical Classification J01. (9) A list of included antibiotic classes is shown in Appendix 1. Only new antibiotic prescriptions were included. Xponent™ captures 61% of medications dispensed from community pharmacies in the province, and a patented, internally-validated geospatial projection algorithm extrapolates these data to estimate 100% of prescribing by physicians (10). We previously undertook a validation analysis in patients ≥65 years of age which revealed that this database has reasonable performance at identifying high antibiotic prescribing physicians when compared with the Ontario Drug Benefit (ODB) database, the province's highly accurate outpatient drug dispensing database (11).

Opioid prescribing was identified using the province's Narcotics Monitoring System (NMS) which collects patient-level dispensing data for all controlled drugs (including opioids) from all outpatient pharmacies in Ontario, regardless of payer (12). All opioids or opioid-containing combination products within NMS were captured regardless of indication with the exception of opioids primarily used for managing opioid use disorder (methadone and buprenorphine/naloxone). A list of included opioids is shown in Appendix 2.

Both Xponent™ and NMS include unique identifiers for each physician, allowing data to be linked with ICES databases. Ontario has a universal healthcare system which provides publicly funded access to healthcare to all citizens, permanent residents, and certain refugees. Population-wide ICES databases included the Registered Persons Database (RPDB) which contains demographic information such as date of birth, date of death, and sex; the Ontario Health Insurance Plan (OHIP) database which contains all physician billing information; ICES Physician Database (IPDB), which contains demographic information on all licensed Ontario physicians; and the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD), containing hospital visit-related information.

Exposures and Covariates

Our main exposures of interest included practice and physician level factors that may be associated with suboptimal prescribing practices. Practice-level covariates included aggregate patient age, sex, neighborhood income quintile, comorbidities (i.e., acute myocardial infarction, congestive heart failure, chronic obstructive pulmonary disease, diabetes, hypertension, asthma, mental health diagnosis in previous year), and previous healthcare utilization. Physician-level covariates included gender, years since medical graduation (early career: <11 years, mid-career: 11-24 years, late career: >24 years), country of medical school, and patient visits.

Outcomes: Suboptimal Antibiotic and Opioid Prescribing Indicators

The main primary and secondary outcomes were measured at the prescriber level, as six separate metrics. Physicians ranked in the top quartile of any of these metrics were considered “high prescribers” for that particular metric.

Primary Outcomes

128 *Antibiotic Initiation* was defined as a physician's antibiotic prescription volume (number of prescriptions) divided by their patient visits to determine their antibiotic initiation rate. *Opioid Initiation* was estimated as the volume of opioid prescriptions initiated by a prescriber. It was calculated by dividing the number of patients with one or more opioid prescription written by that physician by the number of patients seen by that physician during the study period.

Secondary Outcomes

Antibiotic Selection was defined as the proportion of all antibiotics prescribed that were broad-spectrum. Broad-spectrum antibiotic classes included penicillin with beta lactamase inhibitor, fluoroquinolones, macrolides, 2^{nd} and 3^{rd} generation cephalosporins, and clindamycin. This definition is based on previous studies on broad spectrum prescribing and identified risk of community-acquired *C. difficile* infection (13,14).

Opioid Selection was defined as the proportion of a physician's patients prescribed an opioid who received a prescription for one or more high-dose opioids. High dose opioids were defined as any prescription with a dispensed daily dose greater than 90 morphine milligram equivalents (MME). The Canadian Guideline for Opioids for Chronic Non-Cancer Pain and United States Centers for Disease Control Guideline for Prescribing Opioids for Chronic Pain recommend avoiding increasing doses beyond 90 MME or carefully justifying any decisions to titrate to this dose (15,16).

Antibiotic Duration was defined as the proportion of all antibiotic prescriptions that were prescribed for a duration of longer than 8 days. This threshold was selected as most uncomplicated infections managed in primary care settings require duration of antibiotic therapy of 7 days or less (17). A previous analysis by our team found wide inter-physician variability in long duration antibiotic prescribing in the community setting (18).

Opioid Duration was defined as the proportion of a physician's patients prescribed an opioid with one or more opioid prescriptions with a dispensed duration longer than 28 days. Guidelines recommend limiting initial opioid treatment for acute pain to no longer than 7 days (15). The probability of continuing on a long-term opioid (1 year or longer) increases significantly when the first prescription supply exceeds 10 or 30 days (19). A conservative estimate of 28 days was selected to identify prescribers who select longer courses of opioid therapy.

Statistical Analysis

Physicians in the bottom 75% (non-high prescriber) and top 25% (high prescriber) of antibiotic and opioid initiation categories were compared descriptively in terms of their individual and practice characteristics. A kappa statistic with 95% confidence intervals was calculated to determine the agreement between high antibiotic and high opioid initiation (primary analysis) and high prescribing in at least two categories of antibiotic and opioid categories (e.g., initiation, selection, and duration). Kappa values were categorized in terms of their extent of agreement between categories: 0 to 0.20 (none to slight); 0.21 to 0.40 (fair); 0.41 to 0.60 (moderate); 0.61 to 0.80 (substantial); 0.81 to 1.00 (almost perfect) (20).

We built a mixed-effects logistic regression model with the binary outcome of high opioid *and* high antibiotic initiating physicians compared to all other physicians, with random intercepts for each physician. First, a null model was prepared with only the physician random intercept, then we added the physician and practice characteristics listed above to identify independent predictors associated with high initiation of both antibiotics and opioids.

Ethics

This project has Ethics Research Board approval from Public Health Ontario

Results

During the study period, there were 13,091 potentially eligible family or general practice physicians, of which we included 9,994. (Figure 1) The median number of daily patient visits per physician was 18 (IQR 14-25). Ninety one (91%) of practices were in an urban setting. Antibiotic and opioid prescribing indices varied across physicians. Antibiotics were initiated in a median of 8.9% of visits (IQR 6.0 to 13.1%); the median proportion of patients with an opioid initiated during the study period was 5.7% (IQR 3.4 to 9.1%); broad spectrum antibiotics were selected in 40% of antibiotic prescriptions (IQR 31 to 51%); high dose opioids were selected in 6.1% of prescriptions (IQR 2.0% to 10.9%); proportion of prolonged duration antibiotic prescriptions was 32% (IQR 21 to 46%); and the proportion of prolonged duration opioid prescriptions was 27% (IQR 11 to 41%).

High Antibiotic Prescribers

High antibiotic initiators tended to work in busier practices with a greater proportion of patient visits per day, were more likely to be male and had a greater proportion of visits that were emergency room visits when compared to non-high prescribers of antibiotics. (Table 1).

There was negligible to weak association between the different antibiotic prescribing indices: antibiotic initiation-antibiotic selection (kappa 0.05, 95%CI 0.03 to 0.07); antibiotic initiation-antibiotic duration (kappa 0.06, 95% CI 0.04 to 0.08); and antibiotic selection-antibiotic duration (kappa 0.06, 95% CI 0.04 to 0.08). (Figure 2)

High Opioid Prescribers

High opioid initiators were more likely to be male, are in late career, have more nursing home patient visits, have a greater proportion of patients aged 65 or older, and a greater number of patient visits when compared to non-high prescribers of opioids. (Table 1)

There was slight agreement between the different opioid prescribing indices: opioid initiation-opioid selection (kappa 0.16, 95% CI 0.14 to 0.18); opioid initiation-opioid duration (kappa 0.15, 95% CI 0.13 to 0.17); and opioid selection-opioid duration (kappa 0.18, 95% CI 0.16 to 0.20). (Figure 2)

High Prescribers of Both Antibiotics and Opioids

The kappa coefficient between high antibiotic and high opioid initiators was 0.00 (95% CI -0.02 to 0.02) indicating there is a lack of agreement between these 2 groups and the overlap in the groups is no greater than that due to chance alone. Among all physicians, a small subset, 573

(6.2%) were both high antibiotic *and* high opioid initiators (antibiotic initiation-opioid initiation). (Figure 3)

There was low agreement between the other antibiotic and opioid prescribing indices. The highest agreement, albeit slight, was between antibiotic selection-opioid initiation (kappa 0.18, 95% CI 0.16 to 0.20) and antibiotic selection-opioid duration (kappa 0.12, 95% CI 0.10 to 0.14). The lowest agreement was between antibiotic duration-opioid selection (kappa 0.03, 95% CI 0.01 to 0.05), antibiotic selection-opioid selection (kappa –0.02, 95% CI -0.04 to 0.00) and antibiotic initiation-opioid initiation (as above). (Figure 3)

Predictors of Combined High Opioid and Antibiotic Initiation

In the multivariable analysis, predictors of physicians who ranked as both high antibiotic and high opioid prescribers included proportion of adult patients aged 65 or older (aOR 1.42, 95%CI 1.24 to 1.62, per 10% increase), proportion of patients with ER visits within the previous two years (aOR 1.24 95%CI 1.10 to 1.39, per 10% increase), physician male gender (aOR 1.46, 95%CI 1.14 to 1.86), mid-career compared to early career (aOR 1.41, 95%CI 1.01 to 1.99), late career compared to early career (aOR 1.76, 95%CI 1.26 to 2.46), proportion of all visits that were nursing home visits (aOR 1.08, 95%CI 1.01 to 1.15, per 10% increase). Variables associated with not ranking as a high prescriber of both antibiotics and opioids include a higher number of daily visits (compared to less than 10 visits/day, 10-20 visits/ day (aOR 0.59, 95%CI 0.44-0.78, >20 visits per day (aOR 0.61 95%CI 0.45-0.83)), rural practice (aOR 0.56, 95% CI 0.40 to 0.78) and high income quintile of patient population (aOR 0.70, 95%CI 0.54-0.90). (Table 2)

Interpretation

Our study of over 9,000 primary care physicians indicates that there is a lack of correlation between being a high antibiotic prescriber and being a high opioid prescriber when considering various categories of suboptimal prescribing (initiation, selection and duration). This finding indicates that suboptimal antibiotic and opioid prescribers tend to be different, with minimal overlap, suggesting key differences in patient populations and drivers for antibiotic and opioid overuse. Although we did not observe a significant overlap beyond what would be expected by chance in physicians who are both high antibiotic and high opioid prescribers, we did find a small subset of high prescribers of both antibiotics and opioids that have unique characteristics when compared to other physicians. Most notably, these physicians were more likely to be male and be practicing in a later stage of career.

Other studies have found associations between antibiotic and prescribing of other medications. Quinn *et al*. conducted a population-based cohort study of nursing home physicians, also in the province of Ontario, Canada (21). The authors found that compared to average intensity antibiotic prescribers, high intensity antibiotic prescribers were more likely to prescribe proton-pump inhibitors (OR 1.38, 95% CI 1.27 to 1.51), benzodiazepines (OR 1.21, 95% CI 1.11 to 1.32), and opioids (OR 1.28, 95% CI 1.17 to 1.39). The authors defined high prescribers as those that prescribe above the upper 2 standard-deviation limit based on proportions of their patients receiving a prescription for one of these medications. This equated to 17% of physicians being classified as high antibiotic prescribers whereas in our study we defined a high prescriber as being in the top 25%. These differences in definitions, methodology, as well as the more narrow and defined population of long-term care prescribers, may account for the differences in findings compared to our study. Similarly, a study by Li *et al*. evaluating primary care practices in the UK found that antibiotic prescribing was associated with prescribing of other medications, which persisted after adjustment for practice and patient characteristics (22). Prescribing was defined by the number of prescriptions for a given medication divided by the practice size. However, the authors didn't specifically explore the association between antibiotic and opioid prescribing. The authors conclude that the propensity to prescribe antibiotics is linked to the propensity to prescribe medications in general, suggesting that antimicrobial stewardship interventions should address broader prescribing behaviours beyond knowledge of appropriate antibiotic use.

Our study also differs from previous analyses in that we have evaluated three different decision points of antibiotic and opioid prescribing: initiation, selection of the regimen, and treatment duration. Daneman *et al*. evaluated antibiotic prescribers in nursing homes and found that prescribing behaviour differs substantially across these three domains of prescribing (23). Although prescribing tendencies remain consistent over time for each individual prescriber, similar to our findings, there was weak to no correlation between the different tendencies of initiation, selection, and duration of antibiotics prescribed by primary care physicians in a long-term care setting. This suggests that strategies to optimize prescribing should be tailored to the specific prescribing behaviour of interest.

While high prescribing of antibiotics did not predict high prescribing of opioids, a small subset of clinicians are high prescribers in both categories. These findings echo recent cohort studies indicating that male physicians were more likely to prescribe an antibiotic for a viral indication (24) and that those physicians who have been in late career were more likely to prescribe unnecessary or prolonged antibiotic courses (24,25).

Behavioural, emotional and sociological drivers are associated with overuse of both antibiotics and opioids. Beliefs about consequences centered around fear of under-treatment have been reported with both of these agents. Additionally the social influence of patient pressures or perceived desire for these agents may play a role in prescribing them unnecessarily (26,27). Despite these similarities, there are clear differences in the drivers of antibiotic and opioid misuse. Antibiotics, typically prescribed acutely often have a perceived benefit that outweighs their harms, especially as the harms of antibiotics are less visible to the prescriber and may be more distant or dealt with by another provider (e.g., antimicrobial resistance or *C. difficile* infection). On the other hand opioids are typically problematic when used chronically, hence inter-disciplinary and continuity of care issues arise in terms of starting and stopping the medication. Additionally the harms of opioid overuse (e.g., addiction, diversion) may be more visible and tangible to the prescriber as the initial prescriber may need to re-assess, titrate, taper or discontinue the medication. Despite their important role as public health threats, these stark differences in drivers of misuse mean that the physicians over-prescribing antibiotics and opioids are mostly distinct. There is much overlap in the behavioural science behind over-prescribing, but public health efforts should be tailored to the specific drug class, and prescribing behaviour, of interest. These findings may be useful for public health professionals, family physicians, opioid and antibiotic stewards seeking to develop strategies and identify efficiencies in addressing high prescribing practices.

Limitations

Limitations to this work include the potential for unmeasured confounders. Since high-opioid and high-antibiotic prescribers tend to work in different practice settings these differences may contribute to less overlap than would otherwise be expected. Canadian opioid prescribing guidelines for chronic non-cancer pain (16) were released in 2017 during this study period and may have shifted practice patterns towards reduced opioid use, particularly for those who were previously high prescribers. This could have potentially masked any overlap that may have previously existed between high opioid and antibiotic prescribers. In fact, abrupt discontinuation of opioids represents inappropriate prescribing as this can lead to withdrawal symptoms. It is also important to note that although six separate metrics of antibiotic and opioid prescribing were selected as proxy measures of appropriateness, this does not equate to a definitive assessment of appropriateness. This is significant since opioid and antibiotic stewardship efforts aim to optimize the appropriate use of these medications rather than indiscriminately reduce their use. An additional limitation is that there is no standard definition of "high-prescriber". We chose to use top quartile in our study as this has been previously measured and validated against other standard metrics of antibiotic use (11).

Conclusion

Among primary care physicians, there was minimal overlap between those who are high antibiotic prescribers and high opioid prescribers. Although these physicians tend to be different, predictors of a small subset of both high antibiotic and high opioid prescribers include practices with an older patient population, late career physicians and male gender. Antibiotic and opioid stewardship strategies to address these public health crises require tailored approaches.

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Table 1. Characteristics of High and Low Antibiotic and Opioid Initiators

Variables	Antibiotic Initiators Lowest 75% N = 7496	Antibiotic Initiators Highest 25% N = 2498	Opioid Initiators Lowest 75% N = 7496	Opioid Initiators Highest 25% N = 2498
Physician characteristics, n (%)				
Median daily patient visits				
<10	528 (7.04)	194 (7.77)	494 (6.59)	228 (9.13)
10-20	3746 (49.97)	1068 (42.75)	3814 (50.88)	1000 (40.03)
>20	3222 (42.98)	1236 (49.48)	3188 (42.53)	1270 (50.84)
Age (median, IQR)	53 (44-61)	53 (44-61)	51 (42-59)	58 (49-66)
Gender				
F	3533 (47.13)	933 (37.35)	3784 (50.48)	682 (27.3)
M	3963 (52.87)	1565 (62.65)	3712 (49.52)	1816 (72.7)
Years since medical graduation				
<11y	1644 (21.93)	482 (19.3)	1830 (24.41)	296 (11.85)
11-24y	2173 (28.99)	767 (30.7)	2410 (32.15)	530 (21.22)
>24y	3679 (49.08)	1249 (50)	3256 (43.44)	1672 (66.93)
Country of medical school				
Canada/U.S.	4661 (62.18)	1527 (61.13)	4525 (60.37)	1663 (66.57)
Other	1703 (22.72)	620 (24.82)	1657 (22.11)	666 (26.66)
Unknown	1132 (15.1)	351 (14.05)	1314 (17.53)	169 (6.77)
Rurality				
Urban	6791 (90.59)	2296 (91.91)	6891 (91.93)	2196 (87.91)
Rural	705 (9.41)	202 (8.09)	605 (8.07)	302 (12.09)
Emergency visits (mean proportion, SD)	8.35 (22.56)	20.9 (35.13)	14.03 (29.34)	3.85 (14.78)
Long-term care visits (mean proportion, SD)	2.44 (8.95)	1.59 (8.74)	1.03 (4.78)	5.81 (15.22)
Roster size (median, IQR)	1101 (751.5-1540)	1080 (616-1561)	1026 (683-1448)	1303 (893-1729)
Practice characteristics, n (%)				
Age group (mean proportion, SD)				
<18	15.55 (7.08)	17.73 (6.95)	17.1 (7.06)	13.06 (6.37)
18-64	60.48 (9.97)	61.29 (9.61)	62 (8.98)	56.72 (11.33)
65+	23.98 (12.38)	20.98 (11.45)	20.9 (10.25)	30.21 (14.73)
Female (mean proportion, SD)	57.07 (9.09)	56.07 (6.86)	57.71 (8.54)	54.15 (8.2)
Neighbourhood income quintile of patient population**				
Low (quintile 1-3)	6141 (81.92)	2050 (82.07)	5942 (79.27)	2249 (90.03)
High (quintile 4-5)	1355 (18.08)	448 (17.93)	1554 (20.73)	249 (9.97)
Comorbidities in the previous 2 years (mean proportion, SD)				
AMI	0.52 (0.5)	0.51 (0.44)	0.47 (0.45)	0.66 (0.56)
CHF	0.88 (0.94)	0.8 (0.74)	0.78 (0.81)	1.09 (1.1)
COPD	1.16 (0.82)	1.14 (0.7)	1.07 (0.73)	1.43 (0.91)
Diabetes	1.55 (0.79)	1.42 (0.6)	1.45 (0.71)	1.72 (0.83)
Hypertension	2.26 (0.88)	2.09 (0.78)	2.15 (0.8)	2.42 (1)
Asthma	0.94 (0.48)	1.07 (0.46)	1.01 (0.46)	0.84 (0.52)
Psychiatric	20.62 (7.82)	20.75 (6.22)	20.59 (6.89)	20.84 (8.92)
Healthcare utilization in the previous 2 years (mean proportion, SD)				
Hospitalization	14.65 (6.28)	14.99 (5.99)	14.44 (5.75)	15.62 (7.34)
ED visits	41.94 (12.17)	46.09 (13.69)	42.69 (12.75)	43.82 (12.49)

421 **Table 2. Predictors of Physicians Who Are Both High Antibiotic and High Opioid Prescribers**

Variables		Model	
		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Practice characteristics			
Age group proportion (per 10%)			
	<18	0.71 (0.63-0.8)	1.25 (1.03-1.53)
	65+	1.31 (1.24-1.38)	1.42 (1.24-1.62)
Female proportion (per 10%)		0.74 (0.67-0.81)	0.85 (0.74-0.97)
Mean Neighbourhood income quintile of patient population			
	High	0.62 (0.49-0.79)	0.7 (0.54-0.90)
	Low	reference	Reference
Comorbidities proportion in the previous 2 years			
	AMI	1.37 (1.20-1.56)	1.12 (0.86-1.47)
	CHF	1.13 (1.05-1.22)	0.68 (0.55-0.83)
	COPD	1.22 (1.12-1.33)	1.03 (0.9-1.17)
	Diabetes	1.1 (1-1.21)	0.95 (0.83-1.08)
	Hypertension	1.09 (1-1.19)	1.03 (0.92-1.14)
	Asthma	0.62 (0.51-0.75)	0.85 (0.69-1.05)
	Psychiatric	1 (0.99-1.01)	1 (0.99-1.01)
Healthcare utilization proportion in the previous 2 years (per 10%)			
	Hospitalization	1.22 (1.09-1.37)	0.95 (0.69-1.32)
	ED visits	1.11 (1.05-1.19)	1.24 (1.1-1.39)
Physician characteristics			
Gender			
	M	2.12 (1.77-2.53)	1.46 (1.14-1.86)
	F	reference	reference
Years since medical graduation			
	11-24y	1.76 (1.31-2.37)	1.41 (1.01-1.99)
	>24y	2.79 (2.13-3.64)	1.76 (1.26-2.46)
	<11y	reference	reference
Country of medical school			
	Other	0.89 (0.73-1.08)	0.96 (0.78-1.18)
	Unknown	0.34 (0.24-0.48)	0.6 (0.4-0.9)
	Canada/U.S.	reference	reference
Median daily patient visits			
	10-20	0.38 (0.26-0.55)	0.59 (0.44-0.78)
	20+	1.13 (0.93-1.37)	0.61 (0.45-0.83)
	0-9	reference	reference
Rurality			
	Rural	0.98 (0.73-1.3)	0.56 (0.4-0.78)
	Urban	reference	reference
Proportion Emergency visits (per 10%)		0.96 (0.93-0.99)	0.94 (0.9-0.98)
Proportion Long-term care visits (per 10%)		1.14 (1.06-1.22)	1.08 (1.01-1.15)

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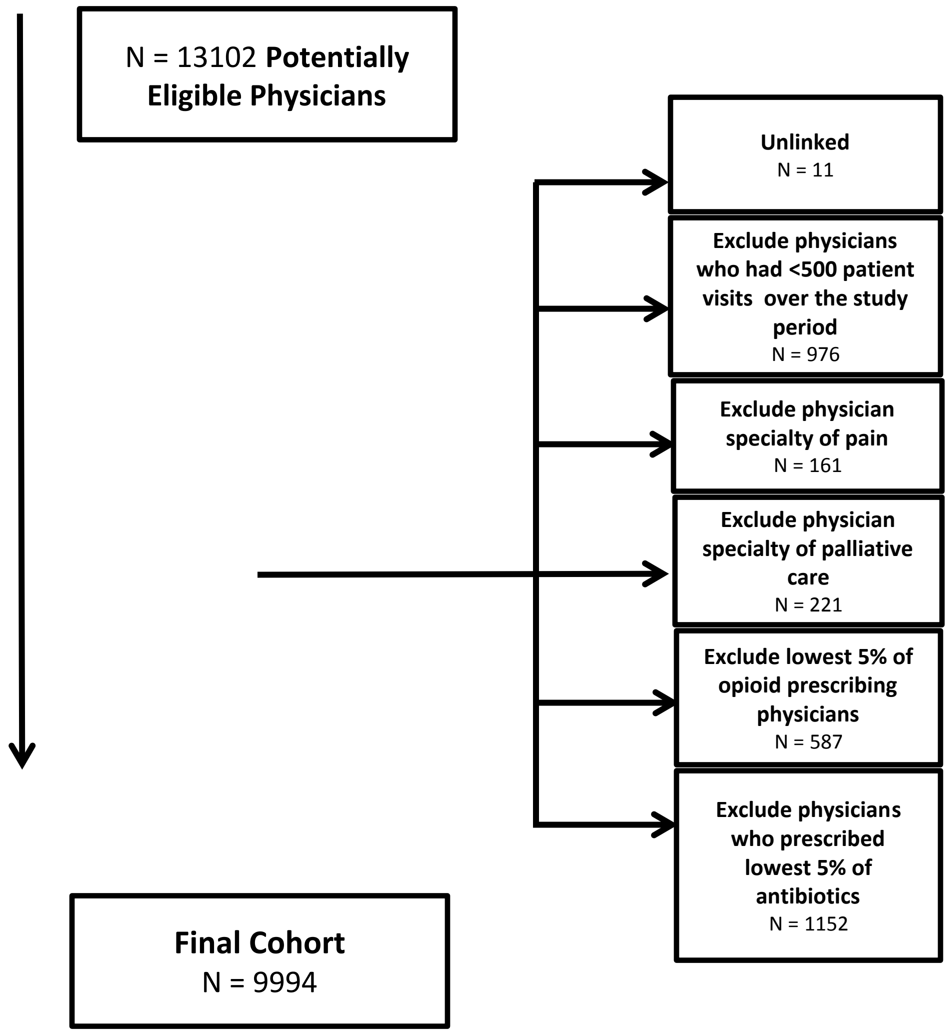
Figure 1. Flow Diagram of Study Exclusions

Figure 2. Concordance between suboptimal antibiotic and opioid prescribing metrics (within class) kappa (95% CI)

Figure 3. **Concordance between suboptimal antibiotic and opioid prescribing metrics (cross opioid-antibiotic class)** kappa (95% CI)


N = 13102 Potentially Eligible Physicians
Unlinked N = 11
Exclude physicians who had <500 patient visits over the study period N = 976
Exclude physician specialty of pain N = 161
Exclude physician specialty of palliative care N = 221
Exclude lowest 5% of opioid prescribing physicians N = 587
Exclude physicians who prescribed lowest 5% of antibiotics N = 1152
Final Cohort N = 9994

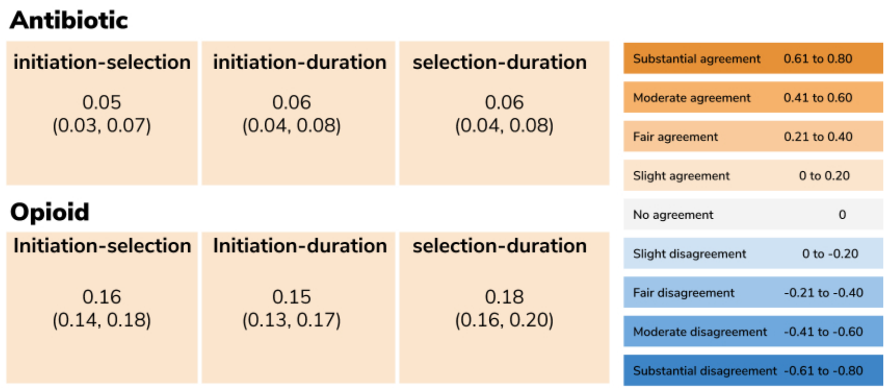


Figure 2. Concordance between suboptimal antibiotic and opioid prescribing metrics (within class) kappa (95% CI)

338x190mm (72 x 72 DPI)

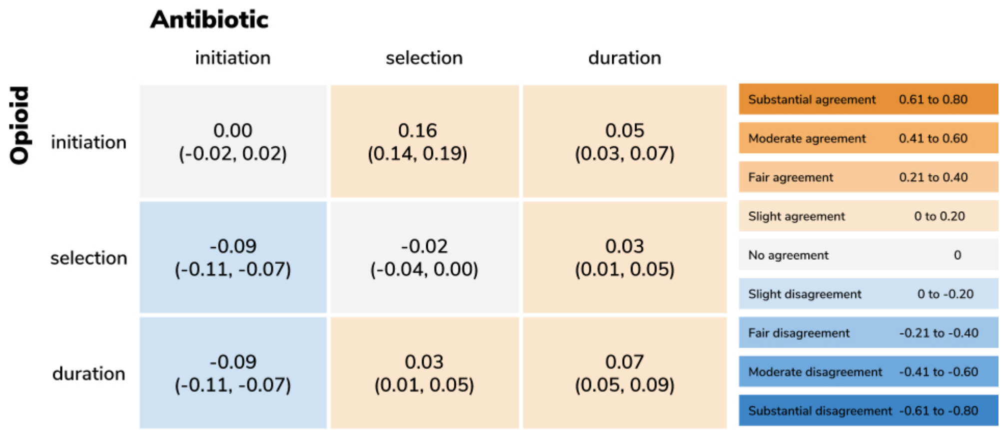


Figure 3. Concordance between suboptimal antibiotic and opioid prescribing metrics (cross opioid-antibiotic class) kappa (95% CI)

338x190mm (72 x 72 DPI)