

The Association of EHR Drug Safety Alerts and Co-prescribing of Opioids and Benzodiazepines



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BACKGROUND

Concurrent opioid and benzodiazepine use is associated with an increased risk of overdose, compared with opioid users who do not use benzodiazepines.^{1,2} Reflecting this safety concern, the Center for Disease Control and Prevention's 2016 chronic pain guideline recommended against co-prescribing opioids and benzodiazepines.³ Nevertheless, clinicians frequently co-prescribe these medications. A recent estimate finds that 17% of opioid users concurrently use a benzodiazepine.¹

OBJECTIVE

To determine the percentage of visits resulting in an opioid prescription for a patient with an active benzodiazepine prescription, and vice versa, before and after the implementation of an electronic health record (EHR) alert notifying clinicians at the time of prescribing of the dangers of concurrent opioid and benzodiazepine use.

METHODS AND FINDINGS

We conducted a retrospective analysis using EHR data from all office and outpatient clinic visits occurring between April 2017 and April 2018 at Fairview Health Systems, a large integrated delivery system in the greater Minneapolis-St. Paul metropolitan area. On October 11, 2017, Fairview initiated an EHR alert designed to deter concurrent prescribing of opioids and benzodiazepines in office settings. Upon initiation of an opioid order, the alert notified clinicians of overlap with an active benzodiazepine prescription, and vice versa; warned of the safety risk, and recommended ordering Naloxone. The clinician could easily dismiss the alert without changing or justifying the prescription order.

We created two analytic samples of office visits with patients at risk for co-prescribing: those with an active opioid prescription at the time of visit (observed in the patient's

medication history) and those with an active benzodiazepine prescription. Our outcome of interest was an indicator for benzodiazepine prescribing and opioid prescribing in the visit, respectively. We used interrupted time series linear regression models to estimate the probability of co-prescribing in each sample before and after the intervention began. We assessed changes in the probability of co-prescribing, testing for a change in level at the time of the intervention and a change in trend. Regression models controlled for patient characteristics (age, sex, race/ethnicity, history of chronic pain, history of substance use disorder) and clinician characteristics (clinician type and department). Analyses were conducted using SAS 9.4 and Stata 13.1. The study was approved by the University of Minnesota IRB.

We identified 211,323 office visits for patients with a current opioid prescription and 85,817 office visits for patients with a current benzodiazepine prescription. The characteristics of the samples are described in the Table 1. Figure 1 shows the unadjusted trends in prescribing, along with the results of the regression models. We observed no significant change in the level of benzodiazepine prescribing immediately following the intervention ($p = 0.56$), and the adjusted trend in benzodiazepine prescribing decreased after the intervention ($p = 0.02$). There was no statistically significant change in the level of opioid prescribing ($p = 0.24$) or in the trend in opioid prescribing after the intervention ($p = 0.80$).

DISCUSSION

We find that the introduction of an EHR alert designed to deter co-prescribing of opioids and benzodiazepines in an outpatient setting had little to no effect on the co-prescribing decisions of clinicians within a large integrated delivery system. This result may reflect that clinicians considered co-prescribing clinically appropriate and beneficial, even after receiving safety information. However, other research finds that physicians frequently override clinical decision support alerts related to opioids, suggesting that clinicians may suffer from EHR alert fatigue.⁴

One advantage of using EHR data is the ability to observe medication orders along with detailed diagnosis information recorded during the associated visit. However, our analysis has limitations. Our ability to identify concurrent opioid and

Table 1 Sample Characteristics

	Appointments with current opioid				Appointments with current benzodiazepine									
	(Total N = 211,323)				(Total N = 85,817)									
	Total		Did not receive benzodiazepine (N = 206,127)	Received benzodiazepine (N = 5196)	P value*	Total		Did not receive opioid (N = 77,408)	Received opioid (N = 8409)	P value*				
Patient age in years, mean (SD)	55	(17.58)	55.36	(17.63)	52.29	(14.74)	0.00	53	(17.12)	53.50	(17.41)	52.54	(14.31)	0.00
Female, no. (%)	124,901	(59)	121,362	(59)	3533	(68)	0.00	58,093	(68)	52,327	(68)	5766	(69)	0.07
Race/ethnicity:														
White	185,810	(88)	181,122	(88)	4688	(90)	0.00	79,825	(93)	72,250	(93)	7575	(90)	0.00
Black	15,963	(8)	15,629	(8)	334	(6)	0.00	3345	(4)	2794	(4)	551	(7)	0.00
Asian	4266	(2)	4224	(2)	42	(1)	0.00	1056	(1)	981	(1)	75	(1)	0.00
Hispanic or Latino	3058	(1)	3010	(1)	48	(1)	0.00	879	(1)	789	(1)	90	(1)	0.66
Other	2226	(1)	2142	(1)	84	(2)	0.00	712	(1)	594	(1)	118	(1)	0.00
History of substance use disorder**	34,559	(16)	33,276	(16)	1283	(25)	0.00	12,289	(14)	9914	(12)	2375	(28)	0.00
History of pain diagnoses	121,888	(58)	117,987	(57)	3901	(75)	0.00	42,449	(49)	35,481	(46)	6968	(83)	0.00
Clinician type														
Physician	158,560	(75)	154,923	(75)	3637	(70)	0.00	61,434	(72)	55,346	(72)	6088	(72)	0.08
Nurse practitioner	26,896	(13)	26,081	(13)	815	(16)	0.00	12,670	(15)	11,459	(15)	1211	(14)	0.32
Physician assistant	25,867	(12)	25,123	(12)	744	(14)	0.00	11,713	(14)	10,603	(14)	1110	(14)	0.21
Department type														
Family or internal medicine	112,840	(53)	102,974	(50)	4377	(84)	0.00	52,689	(61)	46,136	(60)	6553	(78)	0.00
Surgical	26,300	(12)	26,201	(13)	99	(2)	0.00	5076	(6)	4774	(6)	302	(4)	0.00
Other/specialty	72,183	(34)	76,952	(37)	720	(14)	0.00	28,052	(33)	26,498	(34)	1554	(18)	0.00

*P values come from two-sided t tests for a difference in means

**Patients are considered to have a history of substance use disorder/pain if any ICD-10 diagnoses for substance use disorder/pain appear in their EHR records in the past 6 months

benzodiazepine use relies on the start and end date of medications prescribed by Fairview providers. We cannot observe

whether the patient fills a prescription, takes the medication as indicated, or receives a prescription from an outside clinician.

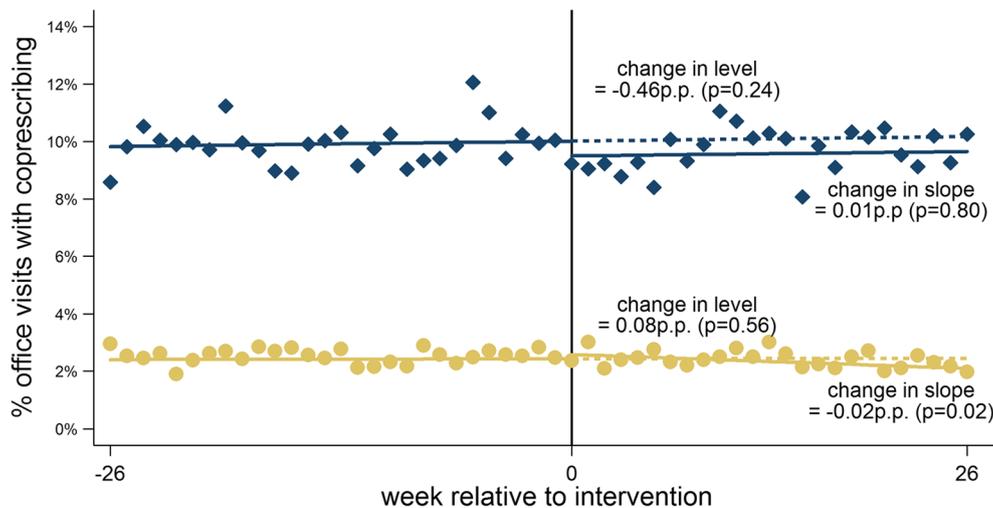


Fig. 1 Interrupted time series regression results: opioid and benzodiazepine co-prescribing by week ◆ opioids, observed, — opioids, adjusted time trend, - - opioids, extension of pre-trend, ● benzodiazepines, observed, — benzodiazepines, adjusted time trend, - - benzodiazepines, extension of pre-trend.

As EHRs become increasingly widespread in clinical practices, clinical decision support tools within the EHR are increasingly deployed to steer providers toward higher quality care. Recent efforts to curb potential over-prescribing of controlled substances have used the EHR to deliver clinical decision support at the time of prescribing.⁵ EHR-based interventions that go beyond provision of safety information—whether by setting a small default prescription quantity or by requiring that a clinician justify a particular prescribing decision—may prove more successful in encouraging appropriate prescribing.

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Compliance with Ethical Standards:

The study was approved by the University of Minnesota IRB.

Conflict of Interest: Ms. Smith reports no conflict of interest. Dr. Golberstein reports no conflict of interest. Ms. Anderson reports no conflict of interest. Dr. Christiaansen reports no conflict of interest. Dr. Paterson reports no conflict of interest. Dr. Short reports no conflict of interest. Dr. Neprash reports receiving consulting compensation from athenahealth, Inc.

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