

Using EHRs to characterize prescription patterns:

Focus on antidepressants in non-psychiatric outpatient settings

Joseph J. Deferio, MPH; Tomer T. Levin, MBBS; Judith Cukor, PhD; Samprit Banerjee, PhD;
Rozan Abdulrahman, MPH; Amit Sheth, PhD; Neel Mehta, MD; Jyotishman Pathak, PhD

Joseph Deferio, M.P.H.
Division of Health Informatics
Department of Healthcare Policy and Research
Weill Cornell Medicine
New York, NY



- Treatment for depression is increasingly occurring in the primary care setting¹⁻⁴
- Nearly 12% of the US population is taking antidepressants⁵⁻⁶
 - Estimated that 30% are for ‘off-label’ indications⁷⁻⁹
- Much is still unknown about antidepressant prescription patterns in outpatient settings
- Electronic Health Records (EHRs) provide a platform to study prescription patterns
 - Longitudinal data collection
 - Multiple care settings
 - Structured and Unstructured data

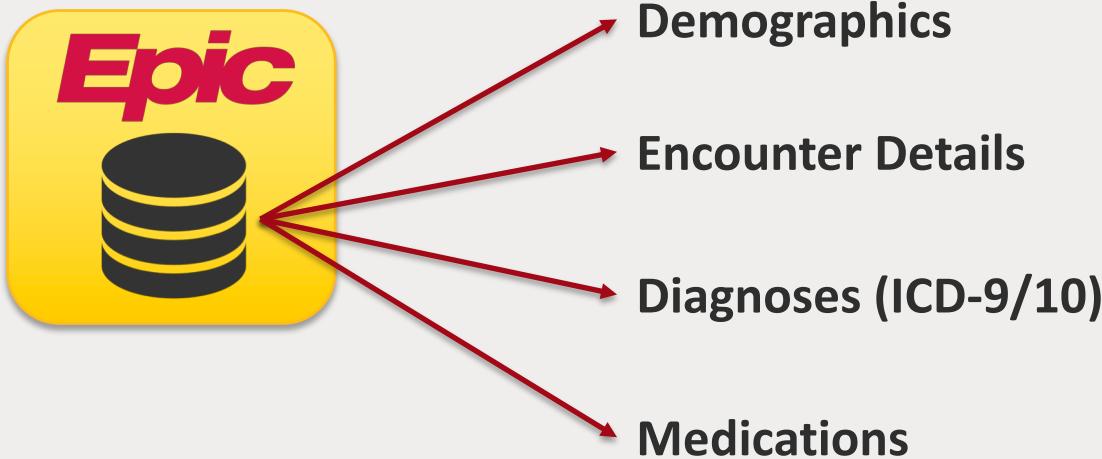


OBJECTIVE:

To characterize non-psychiatric prescription patterns of antidepressants according to drug labels and evidence assessments (on-label, evidence-based, off-label) using structured outpatient EHR data



We employed a retrospective study design using outpatient EHR data:

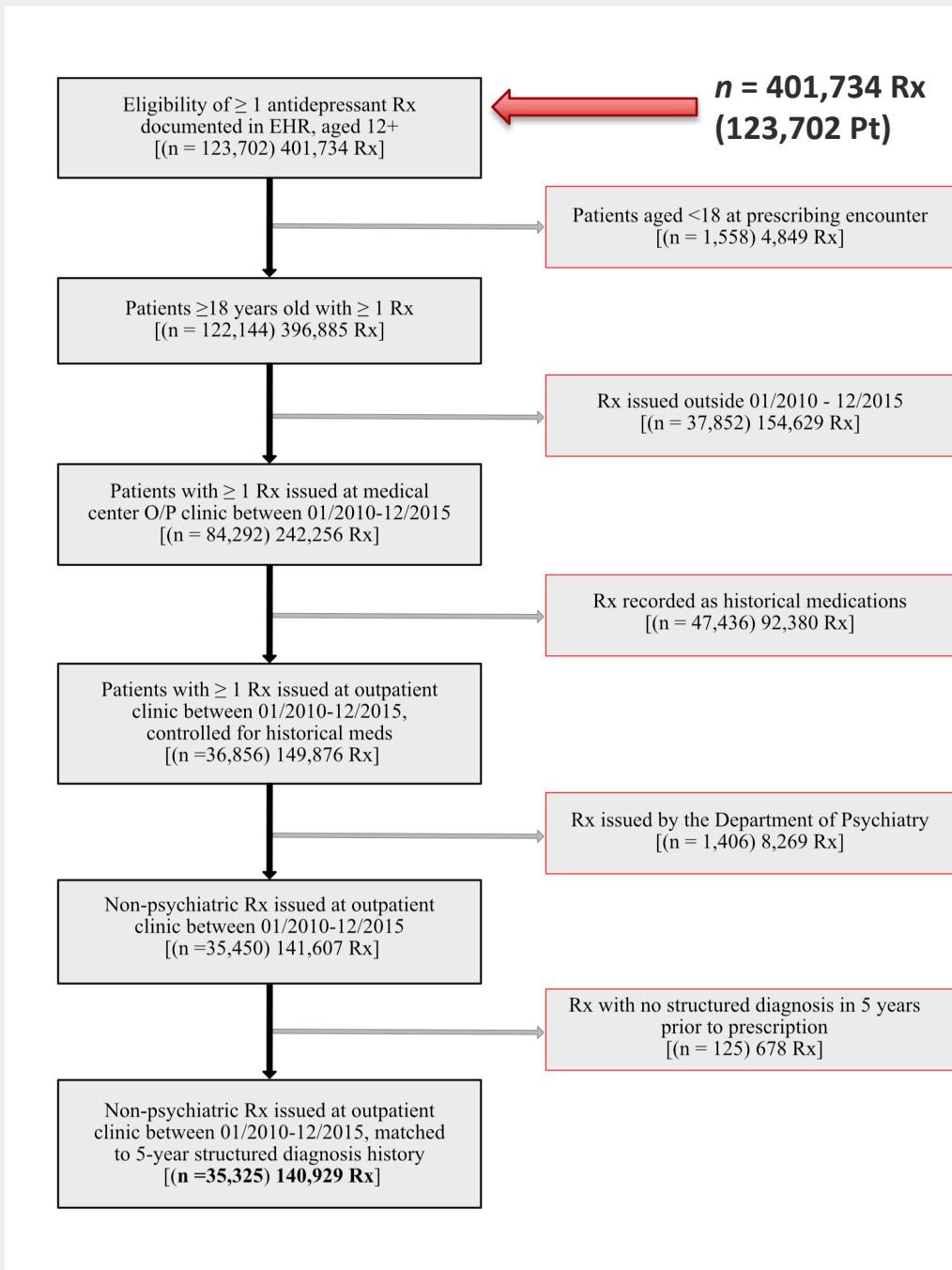


Antidepressants were identified using National Drug Codes (NDC) provided by the National Committee for Quality Assurance (NCQA)

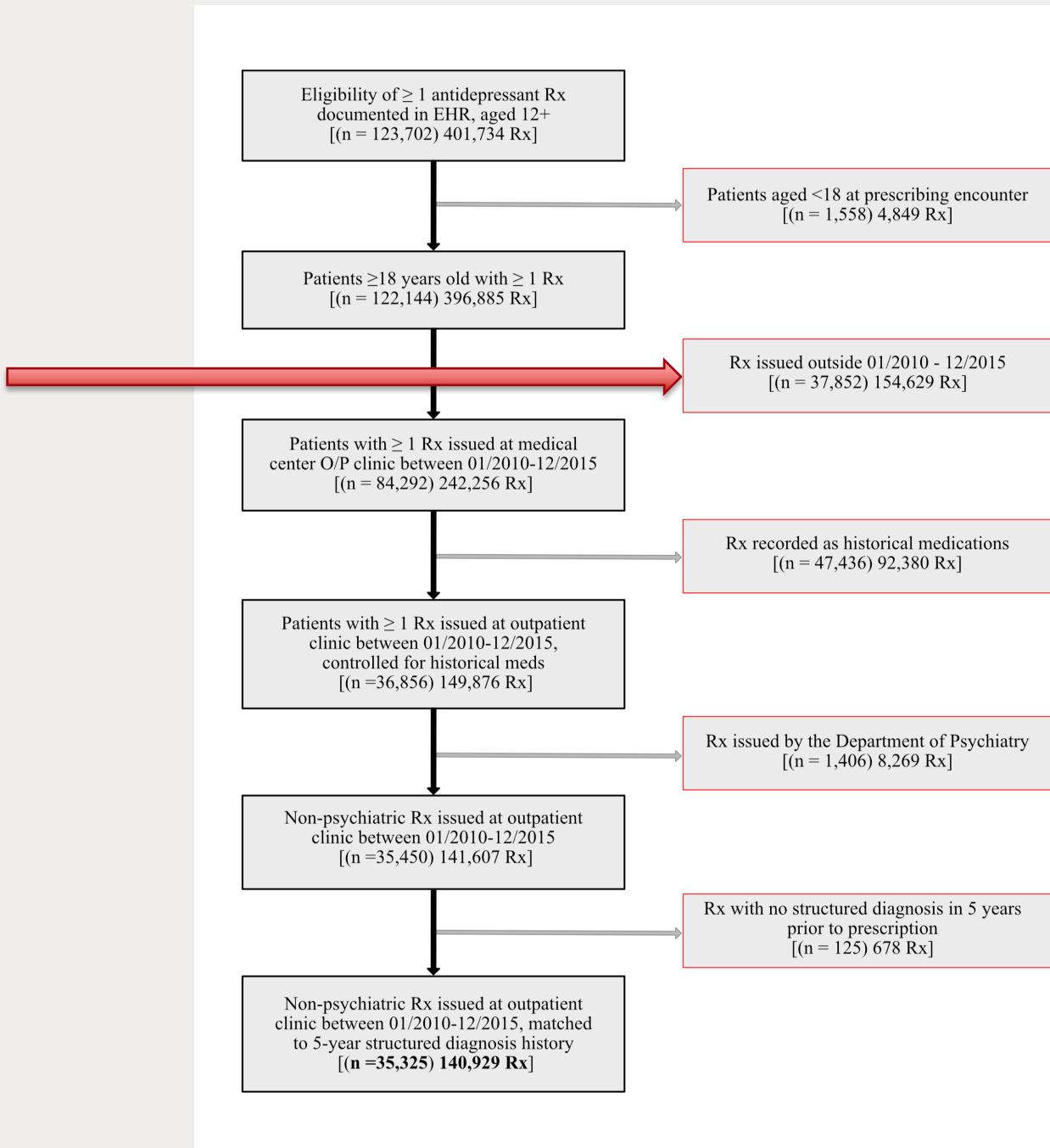


Study Inclusion CONSORT Diagram

- Patient aged ≥ 18 years
- Antidepressant prescription ≥ 1
- Outpatient setting
- Structured diagnosis history

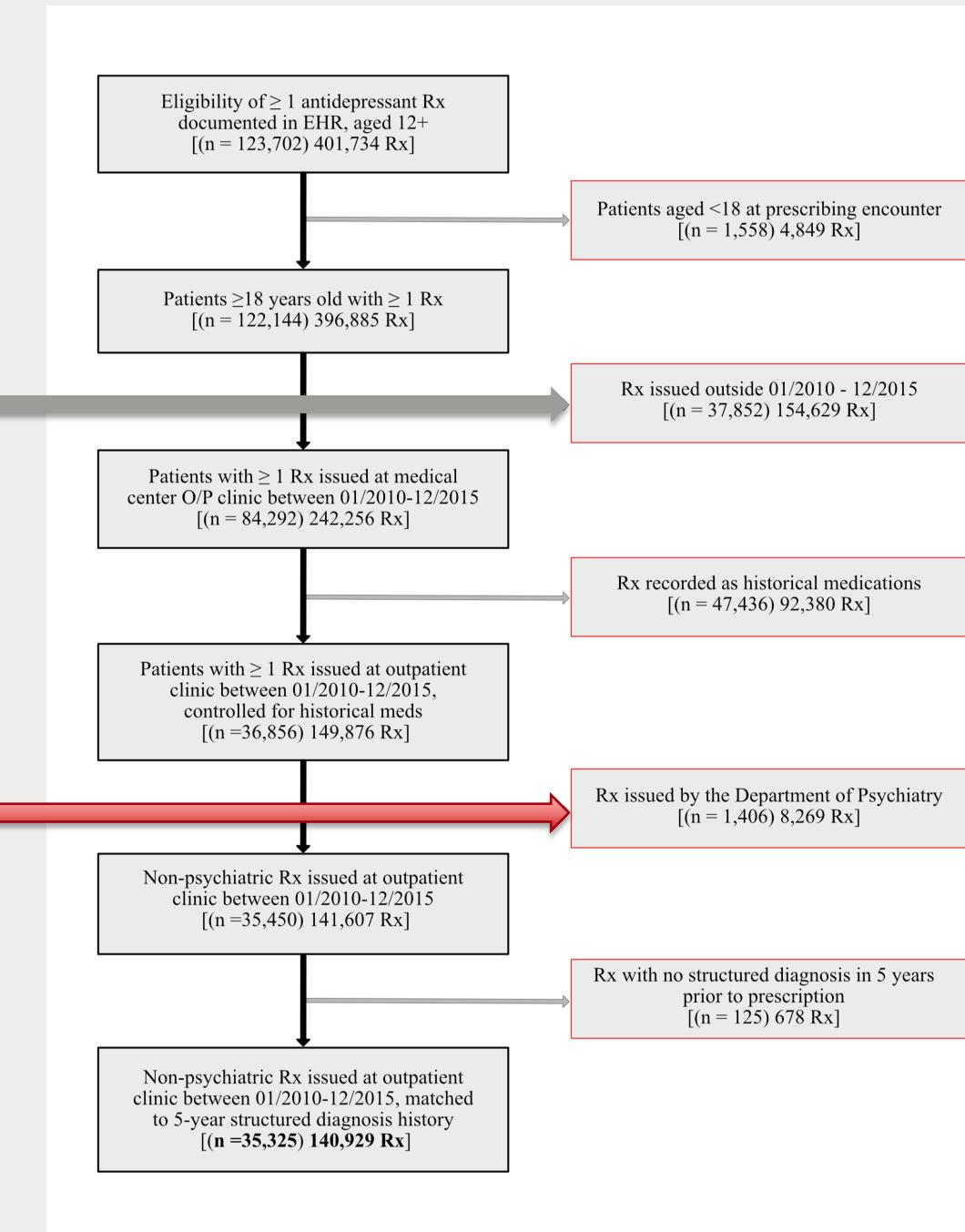


Rx limited to 5 full years, 2010-2015



Rx limited to 5 full years, 2010-2015

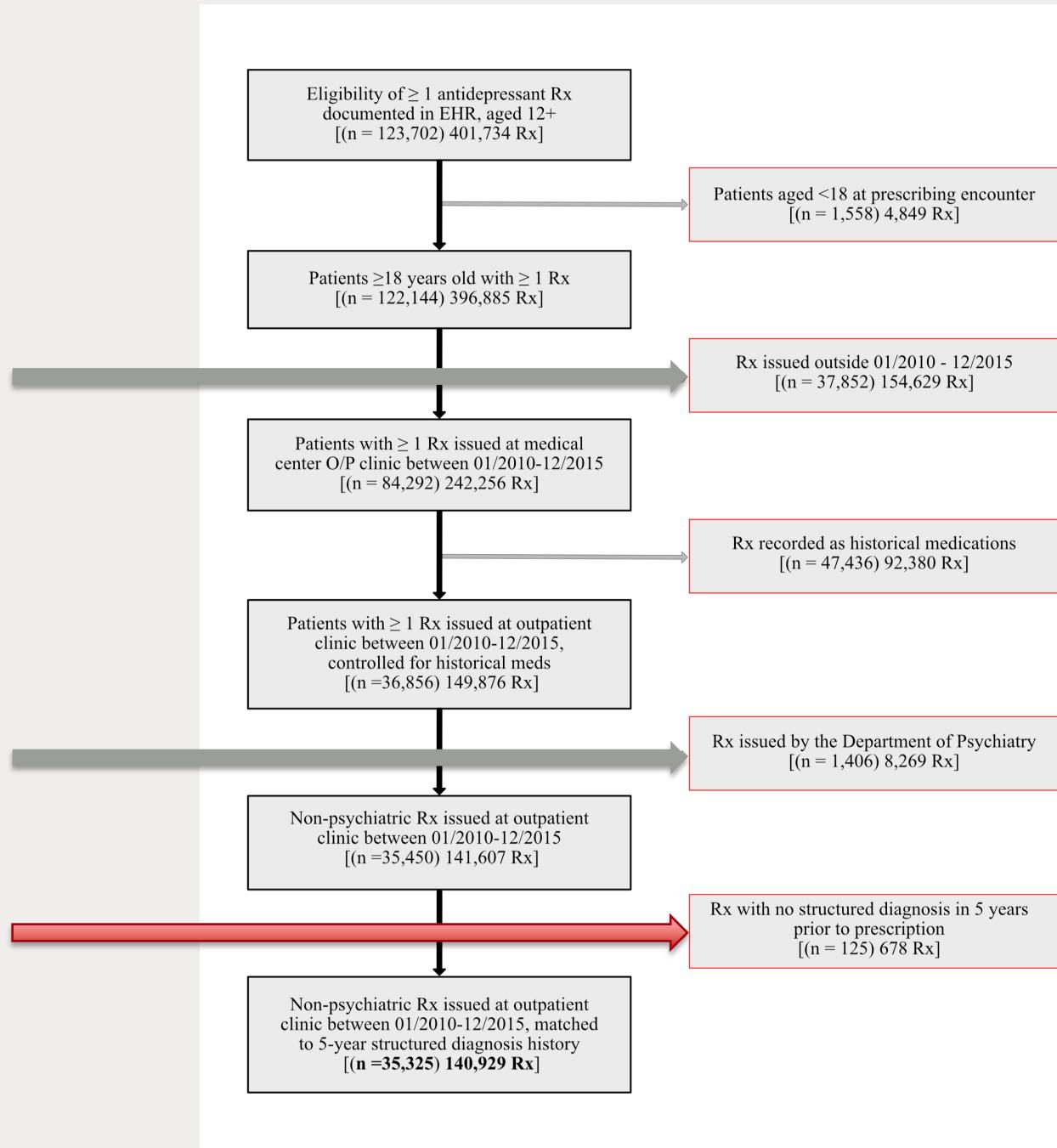
Rx by Psychology Dept., removed



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Rx by Psychology Dept., removed

Rx with no diagnosis data, removed

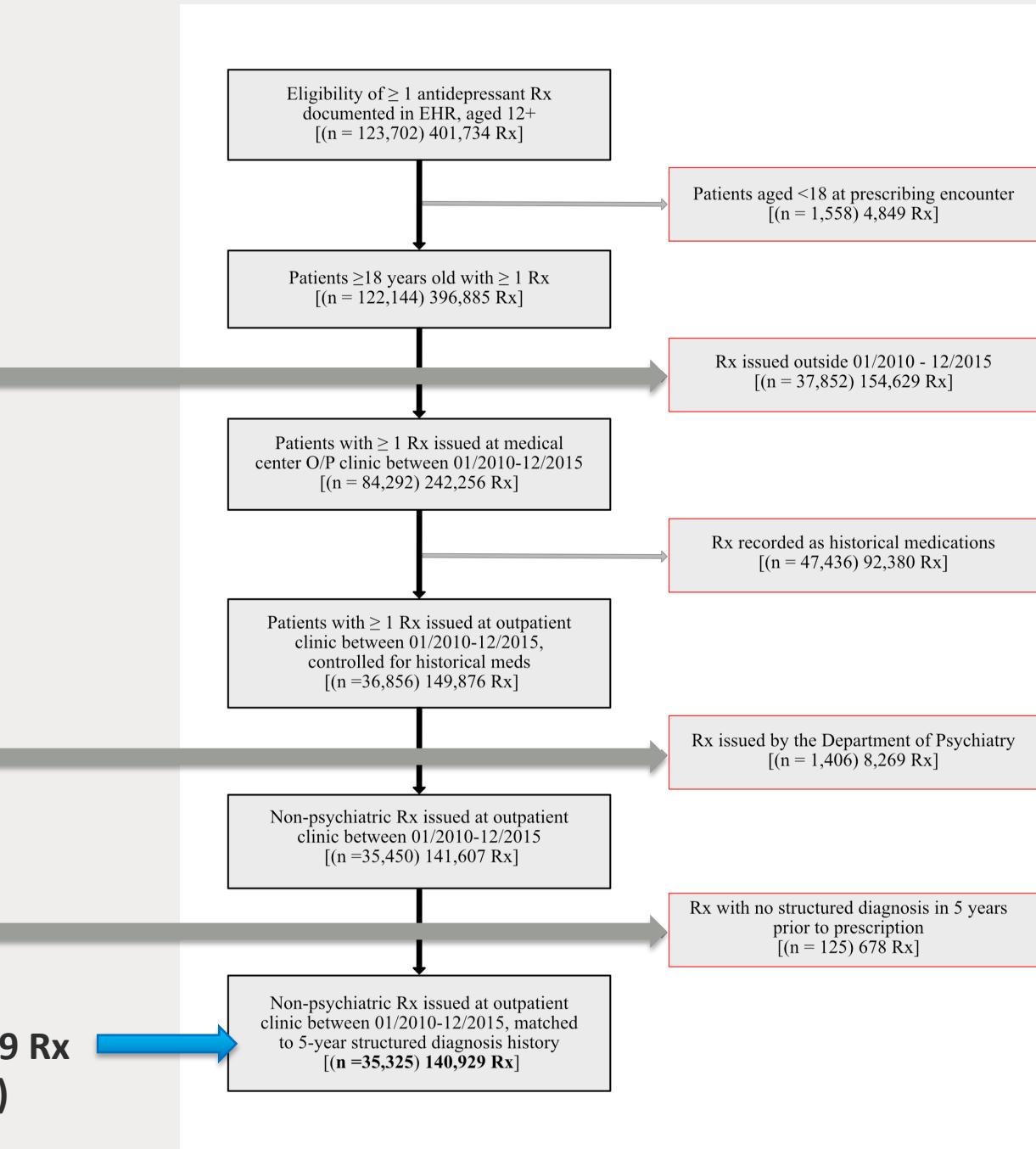


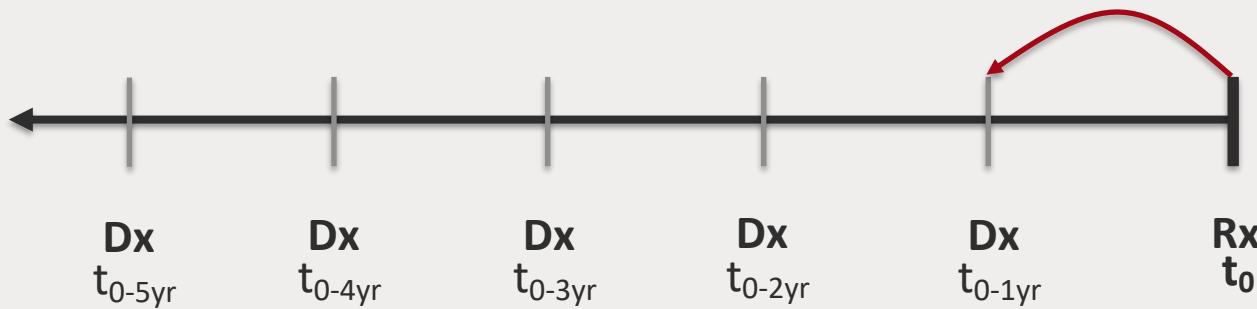
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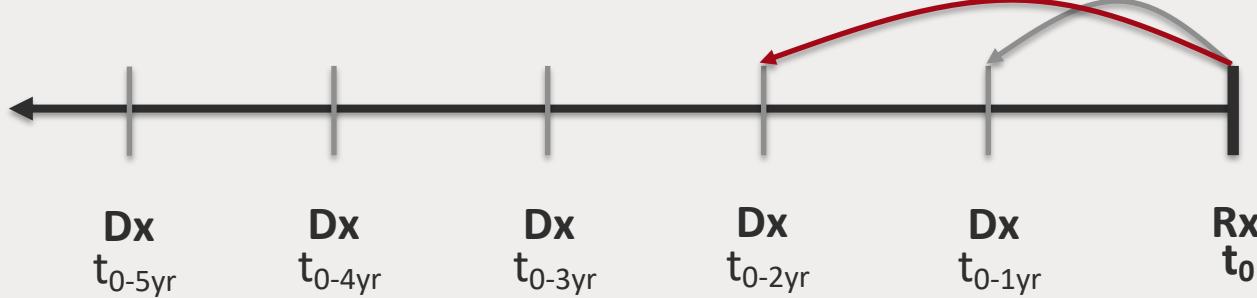
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**$n = 140,929 \text{ Rx}$
(35,325 Pt)**

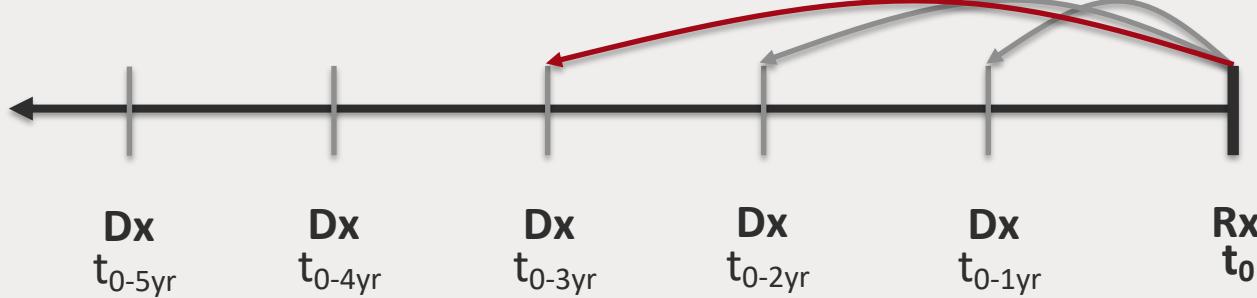




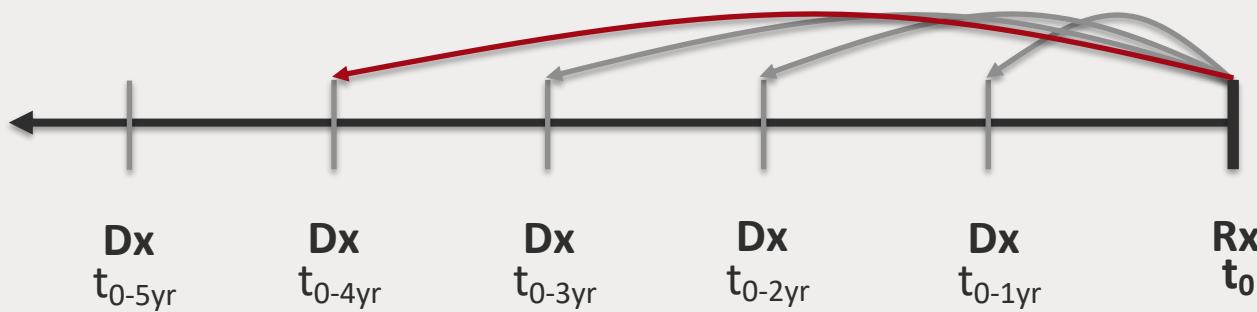
Antidepressant Rx were matched to all of the corresponding patient's diagnoses up to 5 years prior to the prescription date (t_0) to create **medication-diagnosis pairs**



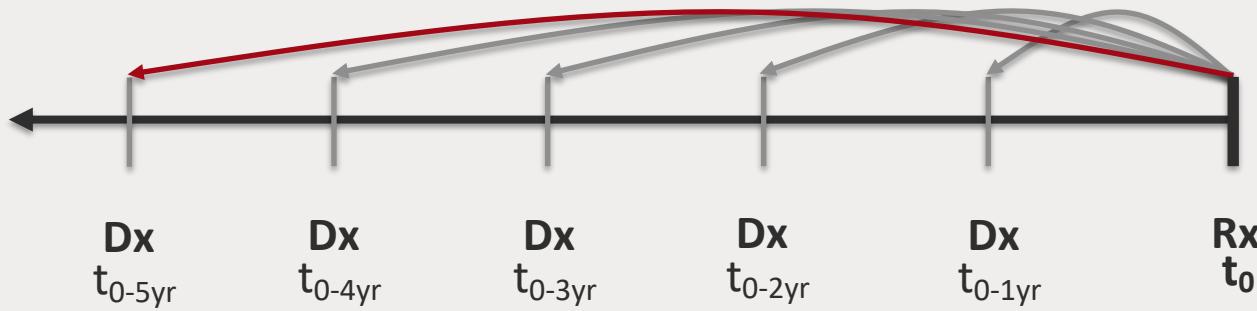
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Antidepressant Prescription Classification

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All Drug Disease Toxicology

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Escitalopram
Dosing Escitalopram
Adverse Effects Escitalopram
Indications Escitalopram
Interactions Escitalopram

Escitalopram Oral Solution USP 40
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Center for Medicare Advocacy. Cma report: Medicare coverage for off-label drug use: Center for Medicare Advocacy; 2010 [Available from: <http://www.medicareadvocacy.org/cma-report-medicare-coverage-for-off-label-drug-use/>]

Quick Answers

In-Depth

Dosing/Administration

Adult Dosing

Pediatric Dosing

FDA Uses

Non-FDA Uses

Dose Adjustments

Administration

Comparative Efficacy

Place In Therapy

FDA Uses: **on-label**

Non-FDA uses: **evidence-based***

All other uses: **off-label**

*Evidence-based indications were only accepted if they met a minimum threshold based on class of recommendation (I, IIa, IIb) and strength of evidence category (A or B)



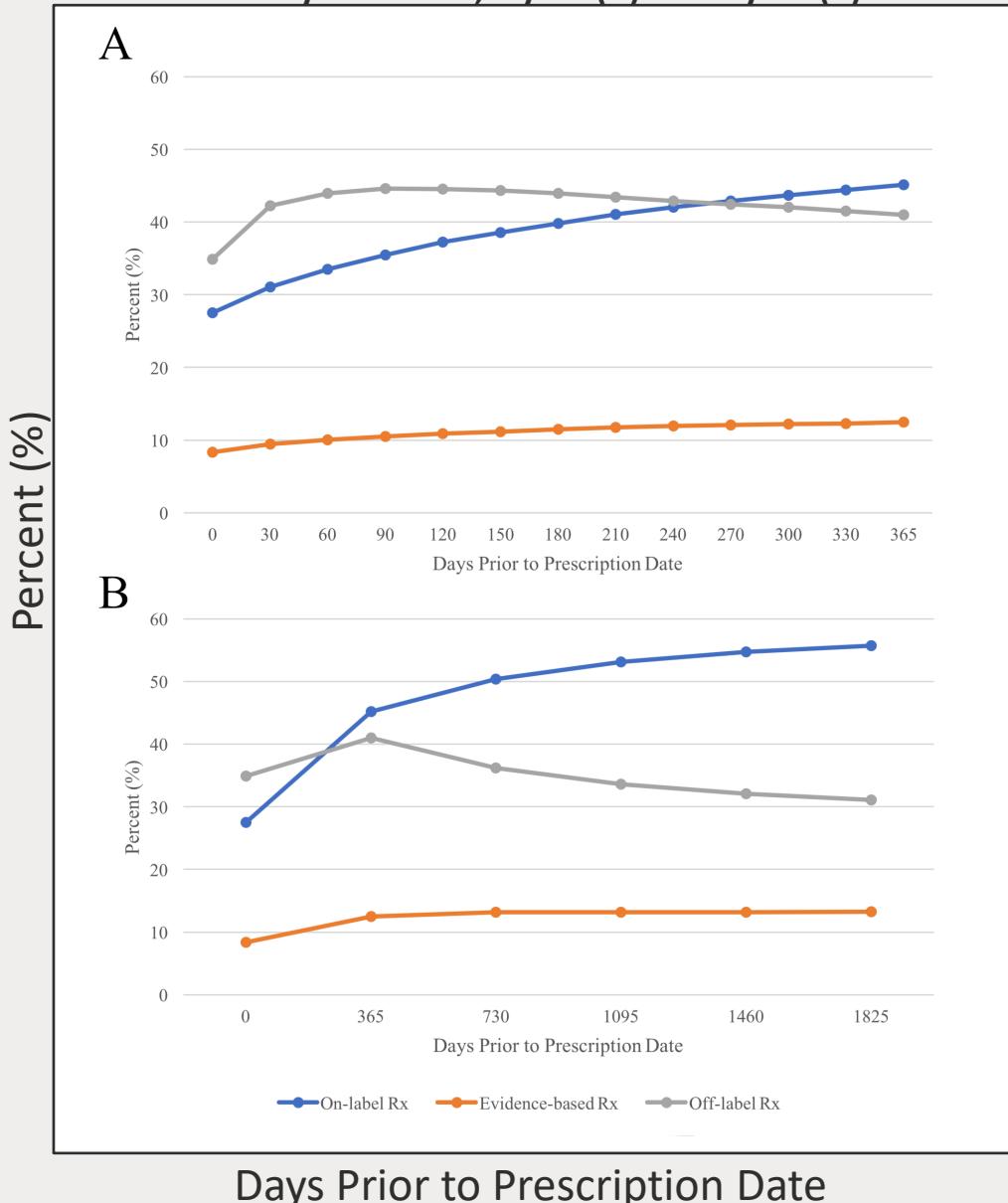
Results of prescription classification across the different 'look-back' windows

Blue = on-label

Gray = off-label

Orange = Evidence-based

Prescription Classification adjusted by No. of days of Medical History Examined, 1 year (A) and 5 year (B)

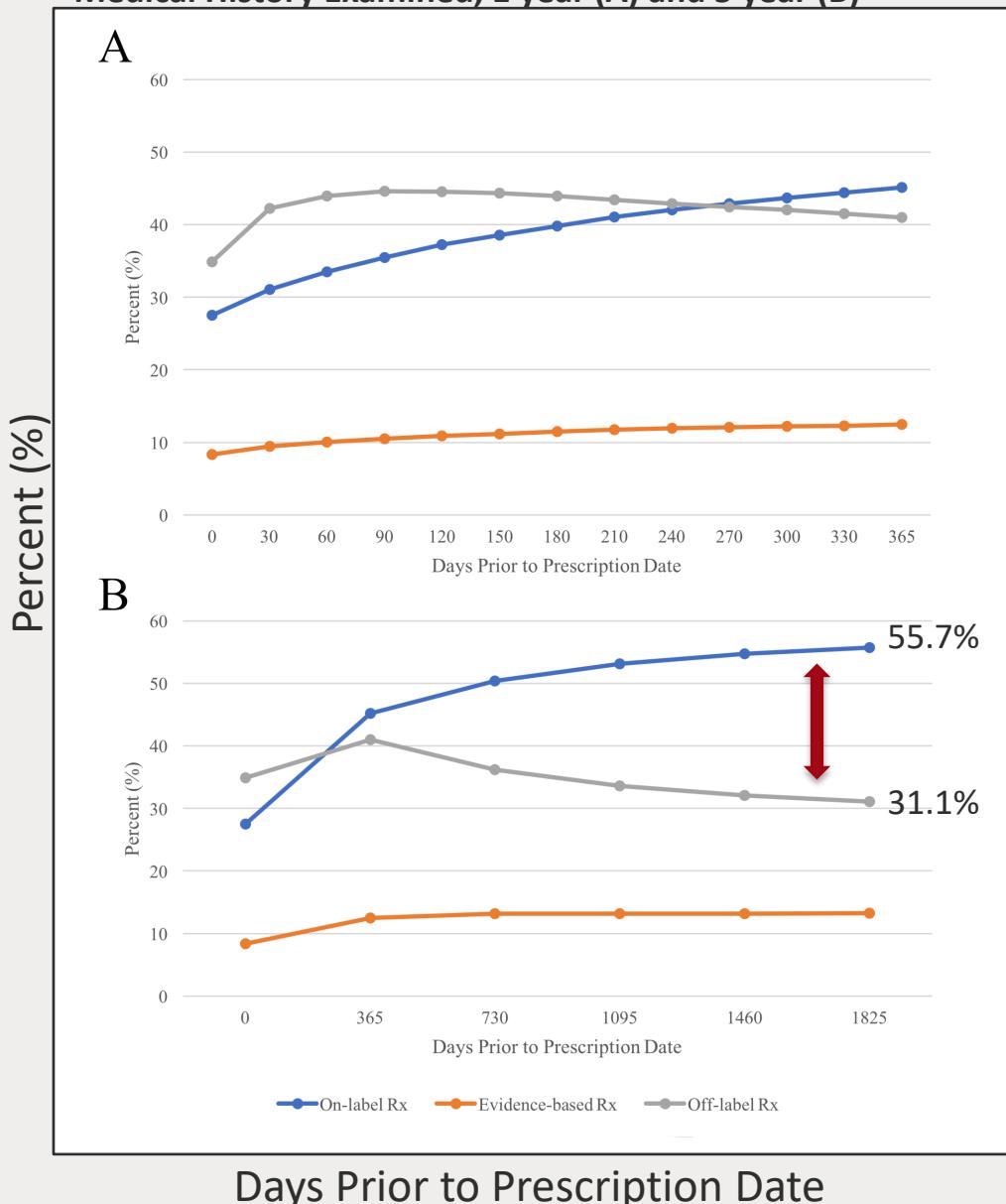


As look-back window increased ($L \rightarrow R$):

\uparrow No. of **on-label** prescriptions

\downarrow No. of **off-label** prescriptions

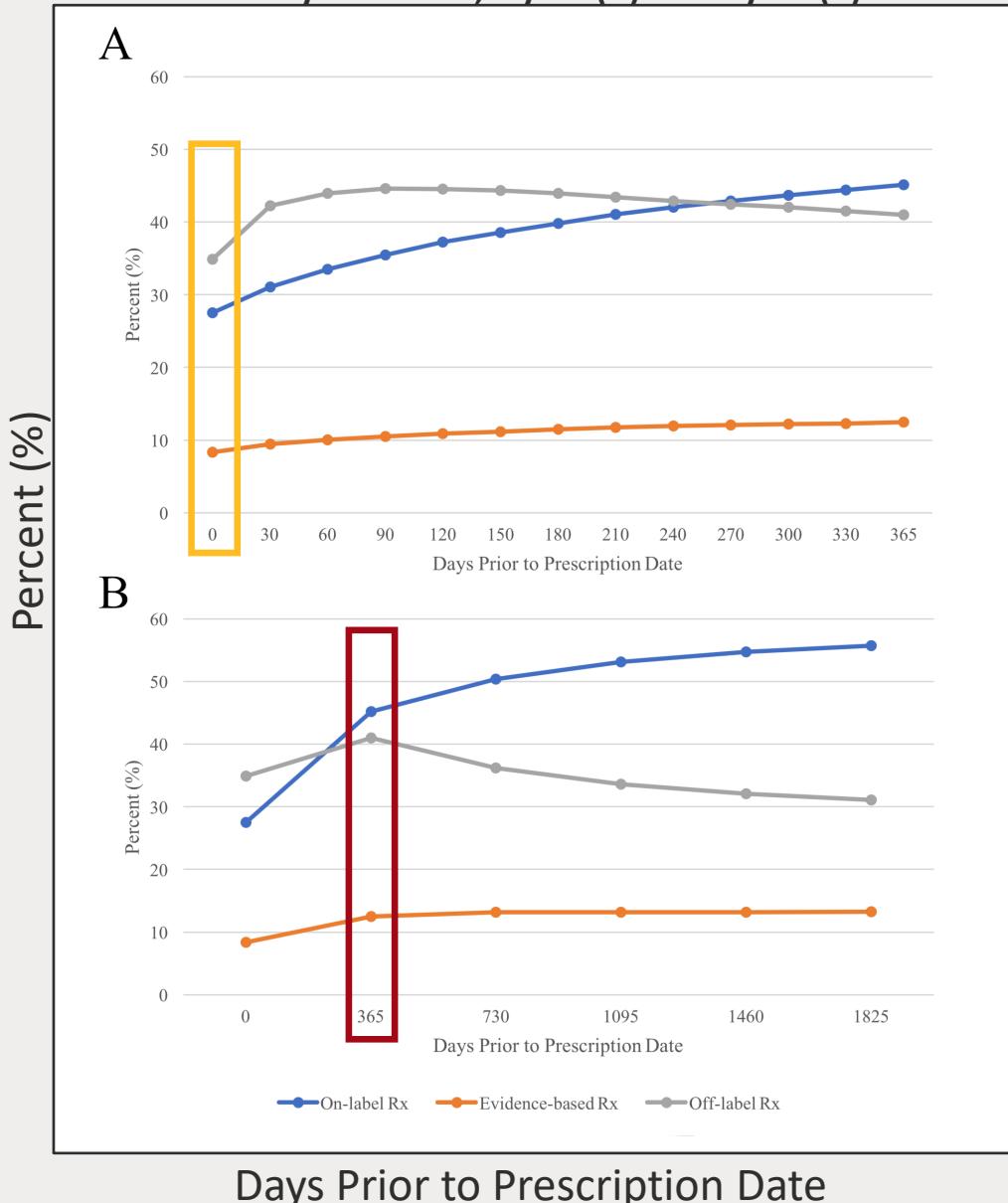
Prescription Classification adjusted by No. of days of Medical History Examined, 1 year (A) and 5 year (B)



70.7%: the number of antidepressant prescriptions that had a structured diagnosis code on the day of prescription

98.6%: the number of antidepressant prescriptions matched to a structured diagnosis using a 1 year look-back window

Prescription Classification adjusted by No. of days of Medical History Examined, 1 year (A) and 5 year (B)



Validation of Prescription Classification

1. Randomly selected 1% of unique patient charts for those that received a prescription for an off-label use
2. Compared diagnoses in EHR to those that were listed in our dataset
3. Reviewed clinical notes to determine physician-documented indication
4. Repeated steps 1-3 for on-label prescriptions



Table 2 Treatment Indications and Prescribing Patterns for Antidepressant Medications, 2010-2015

Prescription Diagnoses ^a	No. of Prescriptions (%) ^b	No. of On-label Rx (%) ^c	No. of Rx where evidence favors efficacy (%) ^d	No. of Rx for Off-label Uses (%)
	<i>n</i> = 140 929 (100)	<i>n</i> = 78 468 (55.7)	<i>n</i> = 18 613 (13.2)	<i>n</i> = 43 848 (31.1)
Depressive disorders	67 233 (47.7)	65 475 (97.4)	1758 (2.6)	0 (0)
Pain	48 680 (34.5)	33 591 (69.0)	7233 (14.9)	7856 (16.1)
Anxiety disorders	32 890 (23.3)	23 490 (71.4)	5049 (15.4)	4351 (13.2)
Symptoms	23 240 (16.5)	16 968 (73.0)	3506 (15.1)	2766 (11.9)
Digestive system disorders	21 596 (15.3)	16 051 (74.3)	2855 (13.2)	2690 (12.5)
Insomnia	18 377 (13.0)	12 610 (68.6)	4609 (25.1)	1158 (6.3)
Weight problems	16 612 (11.8)	12 342 (74.3)	1565 (9.4)	2705 (16.3)
Headache / Migraine	15 109 (10.7)	8043 (53.2)	3354 (22.2)	3712 (24.6)
Urinary system disorders	14 604 (10.4)	11 248 (77.0)	1876 (12.8)	1480 (10.1)
Dermatological conditions	11 471 (8.1)	8404 (73.3)	1932 (16.8)	1135 (9.9)
Sleep disorders	10 456 (7.4)	7797 (74.6)	1301 (12.4)	1358 (13.0)
Nicotine dependence	8593 (6.1)	7504 (87.3)	791 (9.2)	298 (3.5)
Fibromyalgia	7702 (5.5)	4655 (60.4)	1716 (22.3)	1331 (17.3)

34.5% of prescriptions had some history of pain

23.3% of prescriptions had a history of anxiety



Table 3 Prescribing Trends of Antidepressant Prescriptions for Off-label Uses by Top 8 Department Specialties and Diagnosis Classes, 2010-2015

Specialty No. of Off-label Rx (%) ^a	Prominent Diagnosis Class	No. of Off-label Rx with Dx Class (%)^b	Prominent Diagnoses^c	Drug Class (%)^c
Internal Medicine <i>n = 20834 (26.7)</i>	Hypertension	3296 (15.8)	Hypertension, Essential hypertension, Benign hypertension, Elevated BP, Hypertensive retinopathy	SSRI (60), Phenyl, Misc, Tricyclic
	Pain	3231 (15.5)	Back pain, Knee pain, Chest pain, Neck pain, Osteoarthritis, Rheumatoid arthritis, Shoulder pain, Abdominal pain, Neuropathic pain, Chronic pain, Limb pain, Sciatica, Arthralgia, Cervicalgia, etc.	SSRI (57), Phenyl, Tricyclic, Misc
	Hyperlipidemia	3002 (14.4)	Hyperlipidemia, Hypercholesterolemia, Mixed hyperlipidemia, Familial hyperlipidemia, Other and unspecified hyperlipidemia, etc.	SSRI (64), Phenyl, Misc, SNRI
	Anxiety	2962 (14.2)	Anxiety, Generalized anxiety disorder, Chronic anxiety, adjustment disorder, etc.	SSRI (80), Misc, SNRI
	Diabetes	1792 (8.6)	DM, T2DM, T2 or unspecified DM, Diabetes uncomplicated adult-type II, T2DM controlled, etc.	SSRI (55), Phenyl, Tricyclic, Misc, SNRI
	Symptoms	1749 (8.4)	Fatigue, Cough, Other malaise and fatigue, Memory loss, Shortness of breath, Dizziness, etc.	SSRI (70), Phenyl, SNRI, Misc
	Digestive Disorder	1150 (5.5)	Diarrhea, Constipation, IBS, Dysphagia, Abdominal bloating, Chronic constipation, Nausea, Rectal bleeding, Gastritis, Vomiting, Crohn's Disease, etc.	SSRI (62), Phenyl, Tricyclic, Misc
	Cardiac Conditions	923 (4.4)	Coronary artery disease, Atrial fibrillation, Coronary atherosclerosis, CHF, Mitral valve disorders, Chronic ischemic heart disease, Aortic valve disorders, Chronic diastolic heart failure, etc.	SSRI (54), Phenyl, Tricyclic, Misc
Neurology <i>n = 8158 (42.3)</i>	Headache / Migraine	2787 (34.2)	Headache, Chronic migraine w/o aura, Migraine w/o aura, Migraine, Chronic daily headache, Tension headache, Migraine w/ aura, Daily persistent headaches, etc.	Tricyclic (76), SNRI, SSRI
	Cerebral Degeneration	1459 (17.9)	Multiple Sclerosis, Alzheimer's, Dementia, Other degenerative diseases of basal ganglia, Frontotemporal lobar degeneration, etc.	SSRI (56), SNRI, Tricyclic, Misc, Phenyl
	Pain	1193 (14.6)	Cervical radiculopathy, Lumbar radiculopathy, Neck pain, Cervicalgia, Neuropathic pain, Neuralgias, Back pain, Brachial neuritis or radiculitis, Diabetic neuropathy, etc.	Tricyclic (55), SNRI, SSRI
	Sleep Disorders	524 (6.4)	Sleep disturbance unspecified, OSA, Hypersomnia, RLS/PLM, Narcolepsy, Sleep apnea, Delayed sleep phase syndrome, REM sleep behavior disorder, etc.	SSRI (25), Tricyclic, Phenyl, Tetracyclic, SNRI
	Parkinson's Disease	505 (6.2)	Parkinson's disease (paralysis agitans), Secondary parkinsonism	SSRI (48), Tetracyclic, SNRI, Tricyclic

Off-label use prescriptions were then broken down by prescribing department



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Pain Medicine / Management: 53% off-label

- disc disorders, lumbar radiculopathy, low back pain, neck pain, neuropathic pain, etc.
- **97% of prescriptions were for tricyclic antidepressants (TCAs)**
- the **American College of Physicians** recommends TCAs for the treatment of low back pain (ex. Nortriptyline and Duloxetine)¹²



Results from the Sensitivity Analysis

Table 4 Sample of Results from Chart Review of EHR-Documented Prescriptions for Off-label Uses ($n = 270$)

Specialty	Prescription	Encounter Diagnosis	Prescription Diagnosis	Indication for Rx in Clinical Text	Excerpt from Clinical Text
Internal Medicine	Trazodone HCl 50mg	Hypercholesterolemia, HTN, Spina bifida, T2DM, Peripheral edema		Rx admin for insomnia	<i>"Insomnia - c/w trazodone at night"</i>
	Paroxetine 20mg	Hypertension, Smoking	Hypertension	Rx admin to treat depression	<i>"Depression: stable:continue Paxil and trazodone for sleep"</i>
Neurology	Bupropion 75mg	Headache, Vertigo	Headache	Rx admin to treat depression and/or migraines	<i>"history of migraines and depression, both well controlled on bupropion and amitriptyline"</i>
	Escitalopram Oxalate 5mg	Parkinson's disease, Localization-related epilepsy and epileptic syndromes, Memory loss	Parkinson's disease, Localization-related epilepsy and epileptic syndromes, Memory loss	Rx admin to treat depression	<i>"Will try an antidepressant to see if it helps to improve interest in activities. The history is suggestive of depression"</i>
Infectious Disease	Nortriptyline HCl 25mg	HIV, Systolic Murmur	HIV	Rx admin for chronic foot pain (not neuropathic)	<i>"foot pain - chronic, not neuropathy apparently, will give trial of nortrip in case"</i>
	Mirtazapine 7.5mg	HIV, Insomnia, PPD Screen	Insomnia	Rx admin for OCD / insomnia, past Rx also assoc. with HIV, OCD	<i>"still not entirely clear how pt is taking mirtazapine or how frequently. Advised that pt try to take it every night, which may reduce overall anxiety"</i>
Pain Medicine / Management	Nortriptyline HCl 25mg	Lumbar radiculopathy, Disc disorder of lumbar region, Sacroiliitis, Spondylolisthesis grade 1, Spinal stenosis		Rx admin to treat neuropathic pain, Pt listed as being depressed 4mo prior	<i>"Back pain improved with addition of nortriptyline"</i>
	Nortriptyline HCl 10mg	Low back pain, Disc disorder of lumbar region, Lumbar radiculopathy, Knee pain, Myofascial muscle pain, Foraminal stenosis of lumbar region		Rx admin to treat neuropathic pain	<i>"Has been taking increased dose of nortriptyline since last visit and notes much less pain radiating to leg"</i>



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69% of 270 randomly sampled off-label prescriptions did not have a structured diagnosis linked with the medication.

Specialty	Prescription	Encounter Diagnoses	Prescription Diagnosis	Indication for Rx in Clinical Text
Oncology	Citalopram HBr 20mg	Breast cancer	n/a	Rx admin to treat depressed mood
Gastroenterology & Hepatology	Citalopram HBr 20mg	Insect bite, Hepatitis C	n/a	Rx admin to treat depression/anxiety assoc. with PEG-Intron medication (Hep C)
Endocrinology	Bupropion HCl ER 100mg	Abnormal weight gain, Essential hypertension, sleep disorder, proteinuria	Abnormal weight gain	Rx admin for smoking cessation and excessive eating and mood



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However, **39% of the random sample of off-label prescriptions included a physician-documented history of depression or cited depression as the indication in free-text clinical notes**

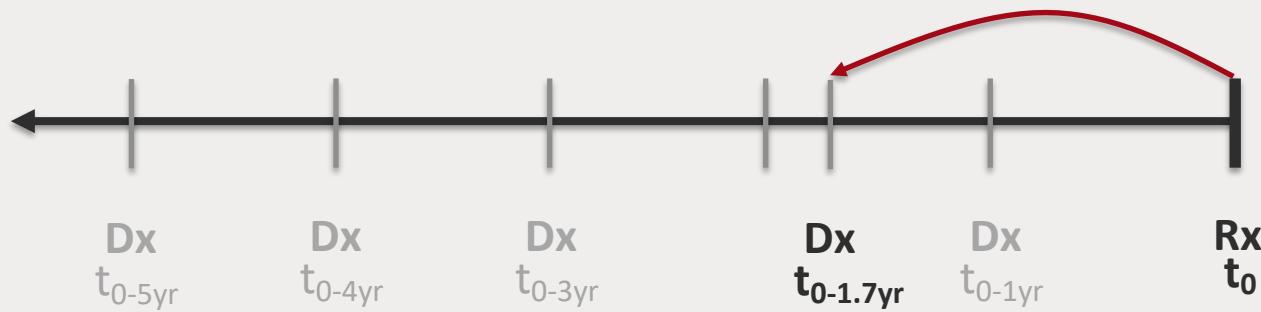
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How well did our methodology actually characterize prescriptions?



According to our sensitivity analysis, we **accurately** captured the physician-documented indication in **83% of the on-label prescriptions.**



On average, the earliest diagnosis that could be considered on-label was made 1.74 years prior to the Rx date (t₀)



What does this all mean?



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Computerized Provider Order Entry (CPOE) system**



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Using a look-back window could help to "fill in the blanks" where linked diagnoses are missing



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**Despite being off-label, there are a number of antidepressants
that are widely used by clinicians to effectively treat pain**



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Computerized Provider Order Entry (CPOE) system

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**Analysis of structured data and NLP on unstructured clinical
text can help to further validate findings.**

