Supplementary Online Content

Seamans MJ, Carey TS, Westreich DJ, et al. Association of household opioid availability and prescription opioid initiation among household members. *JAMA Intern Med*. Published online December 11, 2017. doi:10.1001/jamainternmed.2017.7280

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. List of Diagnostic Codes Used for Defining Inclusion and Exclusion Criteria, Covariates, and Outcome.

Inclusion Criteria	***Outpatient pharmacy dispensing claim for these analgesics (transdermal or oral formulations only)***
Opioids	Hydrocodone, codeine, oxycodone, propoxyphene, tramadol, fentanyl, morphine, hydromorphone, and dhcodeine
NSAIDs	Diclofenac Potassium, Diclofenac Sodium, Diclofenac Sodium/Misoprostol, Esomeprazole Magnesium/Naproxen, Etodolac, Famotidine/Ibuprofen, Fenoprofen Calcium, Flurbiprofen, Ibuprofen (excluding intravenous), Ibuprofen Lysine, Indomethacin and Indomethacin Sodium (excluding rectal suppositories), Ketoprofen, Ketorolac Tromethamine (excluding injection, intramuscular, and nasal routes), Lansoprazole/Naproxen, Meclofenamate Sodium, Mefenamic Acid, Meloxicam, Nabumetone, Naproxen, Naproxen Sodium, Naproxen Sodium/Sumatriptan Succinate, Oxaprozin, Piroxicam, Sulindac, Tolmetin Sodium
Exclusion Criteria	***Any visit with any one of these codes***
Malignancy	ICD-9 Codes: 140.x-195.x, 196.x-198.x, 199.x, 234.x, 235.x-238.x, 239.x
Hospice care	HCPCS code G0065, G0182, G0337, Q5001, Q5002, Q5003, Q5004, Q5005, Q5006, Q5007, Q5008, Q5009, Q5010, S0255, S0271, S9126, T2042, T2043, T2044, T2045, T2046 or ICD-9 code V667
Covariates	
Chronic back pain	ICD-9: 724.xx
Back and neck pain	ICD-9: 721.xx, 722.xx, 723.xx, 724.xx, 737.1, 737.2, 738.2, 728.4, 738.5, 739.1, 739.2, 739.3, 739.4, 756.1, 846.0, 846.1, 846.2, 846.3, 846.8, 846.9, 847.0, 847.1, 847.2, 847.3, 847.9
Back disorder	ICD-9: 721.xx, 722.xx, 723.xx, 724.xx, 737.xx
Migraine	ICD-9: 346.xx
Headache	ICD-9: 784.0x
Fibromyalgia	ICD-9: 729.1x
Fracture	ICD-9: 800.xx-829.xx, 733.1x
Use of benzodiazepine	At least one prescription for alprazolam, amitriptyline hydrochloride/chlordiazepoxide, chlordiazepoxide, chlordiazepoxide hydrochloride/methscopolamine nitrate, clonazepam, clorazepate, diazepam, flurazepam, lorazepam, oxazepam, temazepam, or triazolam
Use of selective serotonin reuptake inhibitor	At least one prescription for citalopram, fluoxetine, fluvoxamine, mirtazapine, nefazodone, paroxetine, sertraline, or venlafaxine

Use of ADHD medication	At least one prescription for amphetamine, dextroamphetamine, lisdexamfetamine dimesylate, or methamphetamine hydrochloride
Use of sleep medications	At least one prescription for eszopiclone, ramelteon, trazodone, zaleplon, or zolpidem
Use of muscle relaxants	At least one prescription for aspirin/carisoprodol/codeine phosphate, carisoprodol, cyclobenzaprine, metaxalone, methocarbamol, aspirin/methocarbamol, or aspirin/carisoprodol
Use of statins	At least one prescription for atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, or simvastatin
Use of antibiotics	At least one prescription for tetracyclines, amphenicols, penicillin, beta lactamase inhibitors, macrolides, lincosamides, streptogramins, streptomycins, aminoglycosides, fluoroquinolones, or glycopeptides

eTable 2. Bias analysis examining risk difference of opioid initiation by household opioid availability assuming different distributions of an unmeasured binary confounder.

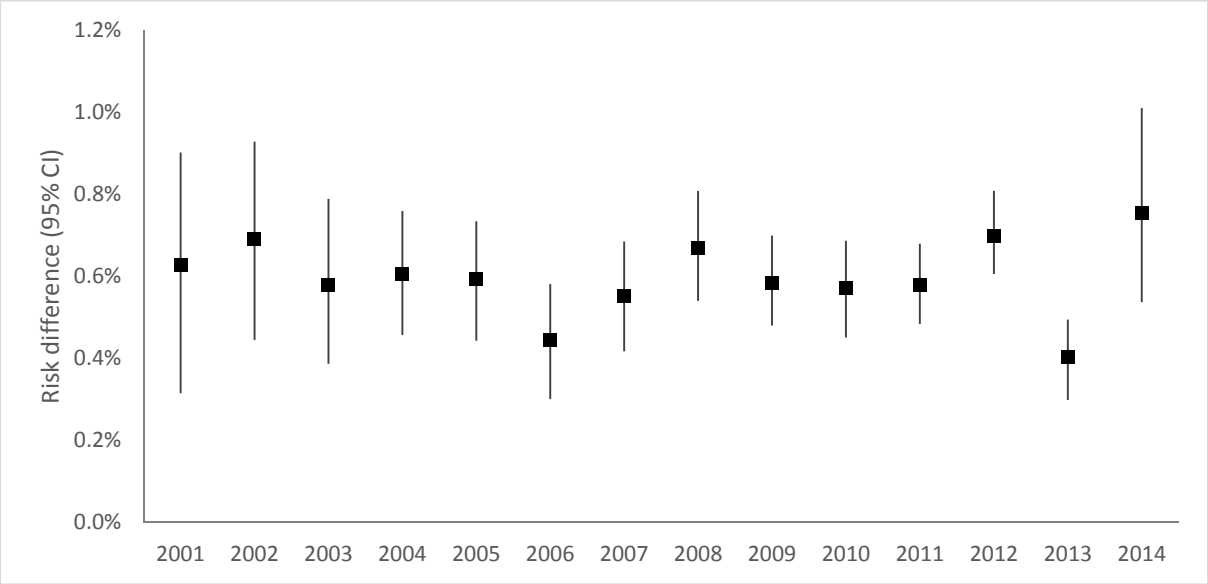
PD of unmeasured confounder across household exposure	RD of unmeasured confounder-opioid initiation relationship			
	0.6	**0.7**	**0.8**	**0.9**
0.1	0.65 (0.62, 0.68)	0.64 (0.61, 0.67)	0.63 (0.60, 0.66)	0.62 (0.59, 0.65)
0.2	0.59 (0.56, 0.62)	0.57 (0.54, 0.60)	0.55 (0.52, 0.58)	0.53 (0.50, 0.56)
0.3	0.53 (0.50, 0.56)	0.50 (0.47, 0.53)	0.47 (0.44, 0.50)	0.44 (0.41, 0.47)
0.4	0.47 (0.44, 0.50)	0.43 (0.40, 0.46)	0.39 (0.36, 0.42)	0.35 (0.32, 0.38)
0.5	0.41 (0.38, 0.44)	0.36 (0.33, 0.39)	0.31 (0.28, 0.34)	0.26 (0.23, 0.29)
0.6	0.35 (0.32, 0.38)	0.29 (0.26, 0.32)	0.23 (0.20, 0.26)	0.17 (0.14, 0.20)
0.7	0.29 (0.26, 0.32)	0.22 (0.19, 0.25)	0.15 (0.12, 0.18)	0.08 (0.05, 0.11)
0.8	0.23 (0.20, 0.26)	0.15 (0.12, 0.18)	0.07 (0.04, 0.10)	-0.01 (-0.04, 0.02)
0.9	0.17 (0.14, 0.20)	0.08 (0.05, 0.11)	-0.01 (-0.04, 0.02)	-0.10 (-0.13, -0.07)

Prevalence difference (PD) per 100 enrollees of unmeasured confounder across levels of household opioid availability. Risk difference (RD) per 100 enrollees estimating the association between an unmeasured confounder and opioid initiation within all inverse probability weighted strata. Observed inverse probability weighted risk difference of 0.71 per 100 enrollees and confidence limits corrected by bias terms that are the product of the PD and RD.

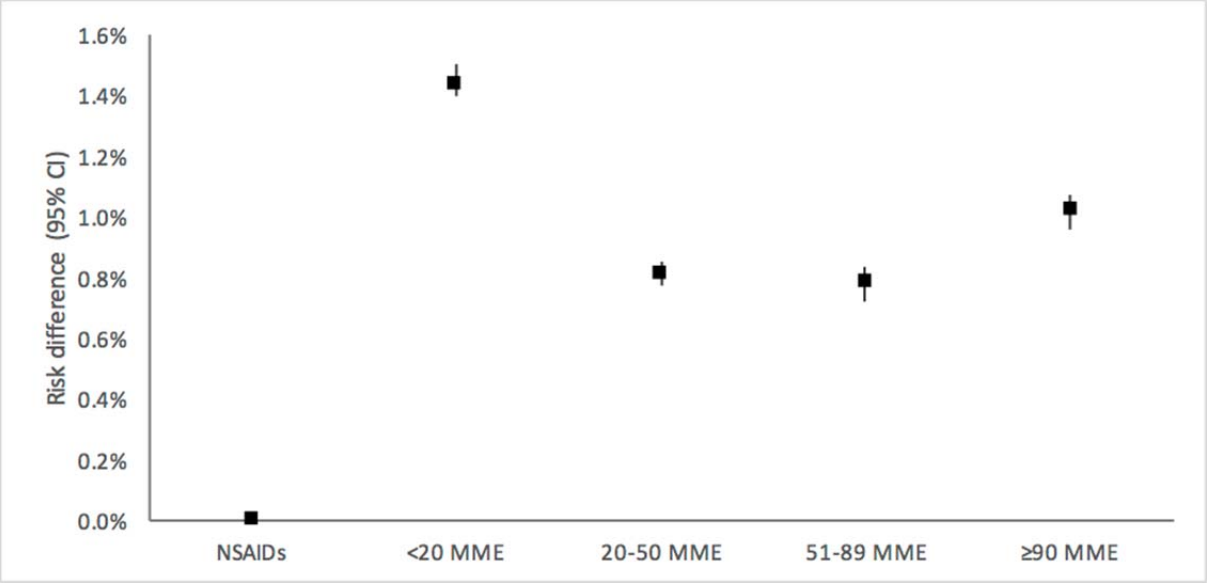
eTable 3. Distribution of index prescriptions for opioids.

Opioid	n	%
Hydrocodone	3,384,920	58
Oxycodone	836,960	14
Codeine	819,595	14
Tramadol	339,637	6
Propoxyphene	323,701	6
Other	166,190	3

eFigure 1. Inverse probability weighted 1-year opioid initiation risk differences and 95% confidence intervals among household members by year of cohort entry, MarketScan Commercial Claims and Encounters 2000-2014. Estimates adjusted for household size, region, family history of substance abuse, age, sex, baseline pain and psychiatric co-morbidities, use of scheduled and unscheduled prescription medications, and healthcare utilization.



eFigure 2. Inverse Probability-Weighted 1-Year Opioid Initiation Risk Differences and 95% CIs Among Household Members by Opioid Daily Dose MarketScan Commercial Claims and Encounters, 2000-2014



Estimates adjusted for household size, region, year of cohort entry, family history of substance abuse, age, sex, baseline pain and psychiatric comorbidities, use of scheduled and unscheduled prescription medications, and health care utilization. MME indicates morphine milligrams equivalent.

eMethods for Constructing inverse probability of treatment weights (IPTW) and inverse probability of censoring weights (IPCW)

We used inverse probability weighted Kaplan Meier estimators to approximate a study where household members were randomized at baseline to be exposed to household opioids or household NSAIDs. Weights were the product of inverse probability of treatment and inverse probability of censoring weights that were estimated using logistic regression models. The model for the treatment weights included confounders and prognostic factors. The model for the censoring weights included predictors of disenrollment (i.e., dropout). Age, number of outpatient visits during baseline, and household size were modeled using restricted quadratic splines[31] and calendar year as a categorical variable with each year as a separate category. Treatment weights were calculated as the complement of the propensity score (PS) for members of opioid households and (1-PS) for members of NSAID households and stabilized by the marginal probability of household exposure to opioids in the cohort. Censoring weights were calculated as the complement of the probability of dropout (Pr(D)) for those who disenrolled, and (1-Pr(D)) for those who remained under observation and stabilized by the marginal probability of disenrollment in the cohort.

eMethods for Sensitivity Analysis to Assess Potential Influence of Unmeasured Confounder.

We examined the potential influence of an unmeasured confounder (e.g., socioeconomic status, healthcare provider, or prescription drug monitoring) by applying bias formulas under simplifying assumptions.[1] Assuming homogeneity of the prevalence difference of an unmeasured binary confounder between household exposure groups in all inverse probability weighted strata, and homogeneity of the difference in opioid initiation risk between levels of the confounder within all inverse probability weighted strata, we evaluated a range of bias factors that could potentially reduce our observed risk difference for the household opioid availability-opioid initiation relationship (0.71%) to the null. Bias factors were applied to bootstrapped samples to obtain 95% confidence limits.

Vanderweele TJ, Arah OA. Bias formulas for sensitivity analysis of unmeasured confounding for general outcomes, treatments, and confounders. *Epidemiology.* 2011;22(1):42-52.