Supplementary Materials for: Independent and joint contributions of physical disability and chronic pain to incident opioid use disorder and opioid overdose among Medicaid patients

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S1 Additional detail on cohort definition and exclusion criteria

In an effort to capture the initial 24 months of enrollment we only allowed beneficiaries to enter the study if they had an enrollment date after January 1, 2016, because it was unknown if a January 1, 2016 enrollment date was a re-enrollment from December 2016. The washout period comprised the first six calendar months since the beneficiary's first enrollment date, and the study duration lasted the first 18 months after the washout period ended.

Chronic pain and physical disability were our two exposures of interest; we considered them alone and together in reference to individuals with neither. As discussed in the Introduction, having well-defined exposure groups are important for understanding and identifying the causal mechanisms responsible for the exposure's effect on an outcome and for external validity. In the chronic pain literature, those with cancer pain are typically excluded for such reasons. Here, we excluded individuals with a cancer diagnosis or in hospice or palliative care from our cohort.

Identifying beneficiaries with a likely physical disability was impeded by not having access to the beneficiary's qualifying disability coupled with extensive missingness on whether the beneficiary was receiving Medicaid due to SSDI/SSI. Consequently, we used eligibility codes to identify beneficiaries who likely qualified for Medicaid due to a disability, then, used a combination of eligibility codes and exclusion criteria as a means for identifying those with a likely physical disability, thereby reducing heterogeneity and creating a more well-defined exposure group. We excluded those who were disabled due to hearing, vision, severe speech, dementia, epilepsy, severe intellectual impairments, dementias, intellectual disabilities, cerebral palsy, tuberculosis, epilepsy, and schizophrenia and other serious mental illness (SMI) with psychosis. We chose to exclude the above subgroups instead of putting them the "neither" reference exposure group in an effort to create exposure groups that would more likely be exchangeable conditional on covariates—in other words, to have exposure

groups that differ from each other in terms of the exposure itself and the distribution of measured covariates but are similar to each other in terms of other possible confounding factors. Those with hearing, vision, intellectual disabilities, dementia, and mental illnesses with psychoses are likely different from those who do not have such disabilities on numerous confounding factors that we do not measure, so would not be able to control for. Thus, including all these individuals in the reference group would likely create additional imbalance in confounding factors across the exposure groups that we would not be able to correct. Thus, we chose to apply our exclusion criteria across the entire cohort to optimize internal validity.

Lastly, we want to include individuals who, conditional on observed values of their confounding variables (e.g., age, marital status), have a nonzero probability of being in each of the exposure groups (i) disability and co-occurring chronic pain, ii) disability alone, iii) chronic pain alone, and iv) neither); which is sometimes discussed as positivity, data support, or appropriate choice of reference group.[1,2] To this end, we included community-dwelling adults, excluding those who were in jail, prison, or long-term care homes, as institutionalized individuals would likely be less likely to be partnered and live in single-family households. Relatedly, due to large age differences between the exposure groups, we subset the cohort to those greater than or equal to 35 years old so as to not violate positivity.[1]

S2 Additional detail on measures

S2.1 Exposure

Probable physical disability status was determined using the latest eligibility code occurring within the washout period that had disability as the basis for eligibility (detailed in the Github repository).

Table S1: Chronic conditions among those with probable disability in order of frequency, as determined by inpatient and outpatient ICD codes during the entire 24 months of enrollment. Note that rows are exclusive, meaning that for the first row, the percentage is out of the total number of individuals with disability; for the second row, the percentage is out of the total number of individuals with disability and without musculoskeletal conditions; for the third row, the percentage is out of the total number of individuals with disability and without musculoskeletal conditions or injuries; etc.

Condition	Percentage
Diseases of the musculoskeletal system and connective tissue	58.44
Injury	7.40
Chronic kidney disease	1.03
Cerebral infarction	0.58
Mental, Behavioral and Neurodevelopmental disorders	16.28
Diseases of the respiratory system	3.62
Diseases of the circulatory system	2.88

S2.2 Outcome

Probable opioid misuse was operationalized by Sullivan et al.[3] as follows: ≤2 opioid prescribers=0, 3-4 prescribers=1, ≥5 prescribers=2); ≤2 pharmacies used for medication filling=0, 3-4 pharmacies=1, ≥5 pharmacies=2; and for each of short-acting and long-acting opioids, ≤185 days supplied=0, 186-240 days=1, >240 days=2; with a score ≥5 categorized as probable misuse).

S2.3 Covariates

We use the 6-month washout period to characterize the beneficiary's baseline covariates: age in years, sex, race/ethnicity (non-Hispanic Asian; non-Hispanic American Indian and Alaska Native (AIAN) or Hawaiian/Pacific Islander; non-Hispanic Black; Hispanic, all races; non-Hispanic White; and non-Hispanic Multiracial or unknown), English as their primary language, marriage/partnership status (currently partnered vs. not), household size (1, 2, and > 2), veteran status (yes/no), income likely >133% FPL (yes/no, determined using the latest washout eligibility code and demographic income information), any inpatient or outpatient DSM-5 diagnosis of: bipolar disorder, any anxiety disorder, attention deficit disorder/ attention deficit hyperactivity disorder (ADD/ADHD), any depressive disorder, or other mental illness (e.g., Anorexia, personality disorders, as operationalized by Samples et al.[4]). All relevant ICD codes and operationalizatons are detailed in the Github repository. We report missingness for each variable in Table S2. In the analyses that follow, we use an indicator for missingness for each variable.

Table S2: Missingness numbers of confounders among cohort used for adjusted analysis.

Characteristic	**N = 2,440,932**[1]
Age	0 (0%)
Sex	0 (0%)
Race/ethnicity	585,067 (24%)
Married/partnered	1,698,394 (70%)
Prim. Language English	329,985 (14%)
Household size	1,733,075 (71%)
Veteran	1,937,042 (79%)
Bipolar Disorder	0 (0%)
Anxiety	0 (0%)
ADD/ADHD	0 (0%)
Depression	0 (0%)
Other Mental Illness	0 (0%)

[1] n (%)

S3 Additional detail on sensitivity analyses

For this analysis, we subset the cohort to those without chronic pain (i.e. those in the "physical disability alone" and "neither" exposure strata), and without the risk factor of interest during the 6-month washout period (e.g., for the outcome of incident depressive disorder we excluded those with a depressive disorder during the washout period). As described above, we used TMLE to estimate the association between disability and each of the risk factors of interest using the same adjustment covariate sets.

S4 Negative control outcome analysis

We implemented a negative control outcome analysis to help detect potential bias in our analysis[5]. A negative control outcome is a variable that is not causally affected by the exposure and that shares the same unobserved confounding mechanism that is of primary concern for the exposure-outcome relationship[6]. We chose acute appendicitis (defined using inpatient hospital ICD-10 admitting diagnosis codes) as our negative control outcome, as we believe it is unlikely to be appreciably affected by an individual's disability and chronic pain status. However, we note that this negative control outcome may still be imperfect, as there is evidence that having a disability increases risk of complicated appendicitis, so those with a disability may be more likely to have an inpatient acute appendicitis code[7]. As we lacked a better-suited alternative negative control outcome, we proceeded with acute appendicitis. Our analytical methods were identical to our primary outcome analysis; that is, we looked at the independent and joint effects of disability and chronic pain, adjusting for the same baseline covariates as our primary analysis, with the dependent outcome of acute appendicitis. The estimated 18-month incidence of acute appendicitis for those with both disability and chronic pain was 0.08% (95% CI: 0.03-0.13). The estimated incidences for those with chronic pain only and disability only were 0.08% (95% CI: 0.05-0.10) and 0.12% (95% CI: 0.05-0.18), respectively. The estimated incidence for those with neither disability nor chronic pain was 0.07% (95% CI: 0.06-0.08). As hypothesized, these did not yield significant incident differences between groups, thereby supporting the validity of our study.

Figure S1: Sensitivity analyses results: instead of a window of 6 months for chronic pain, a window of 12 months is used to classify the exposure groups. The eligibility criteria and baseline characteristics also occur within an expanded 12 month period.

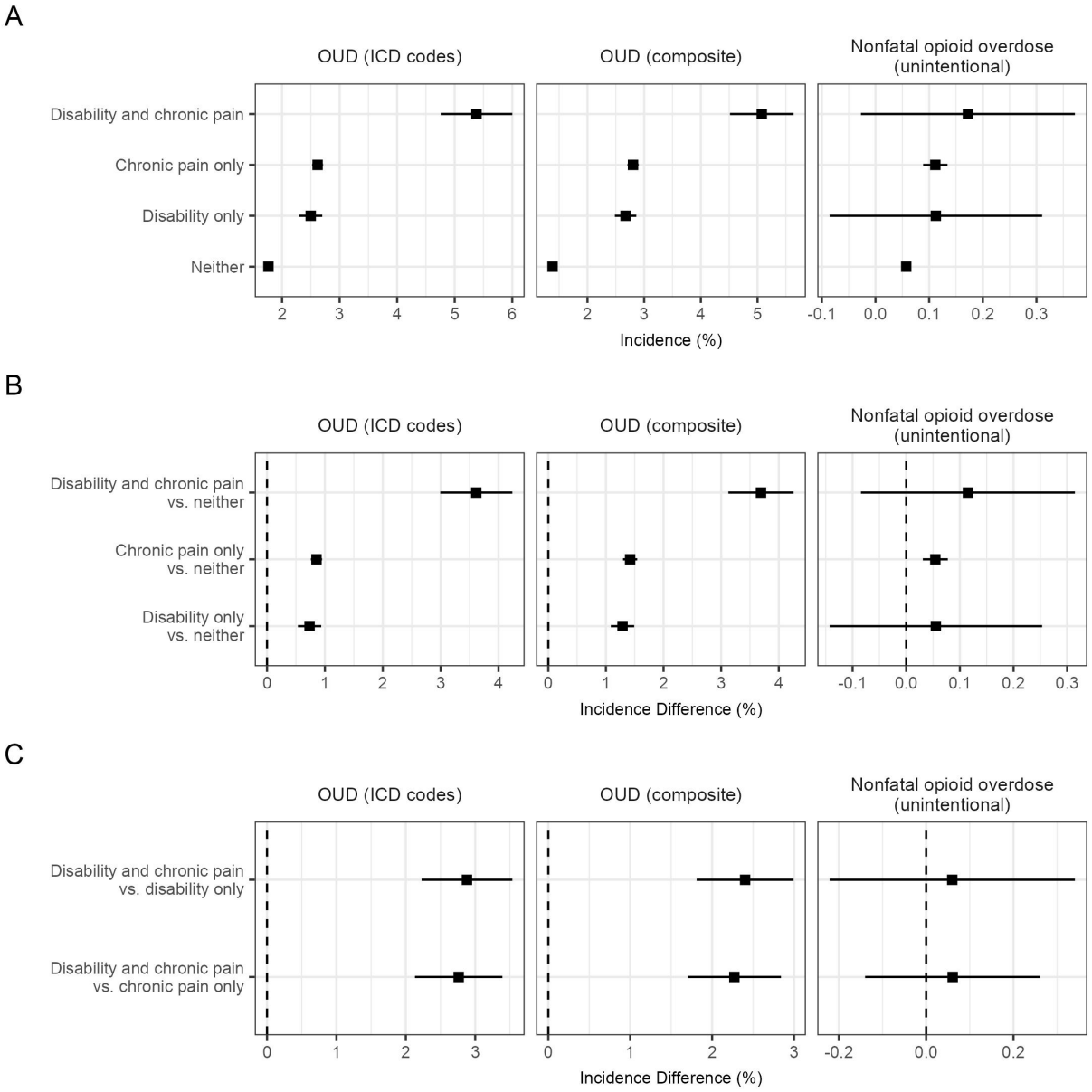

Figure S2: Sensitivity analyses results: instead of chronic pain, any pain ICD code is used to classify the exposure groups.

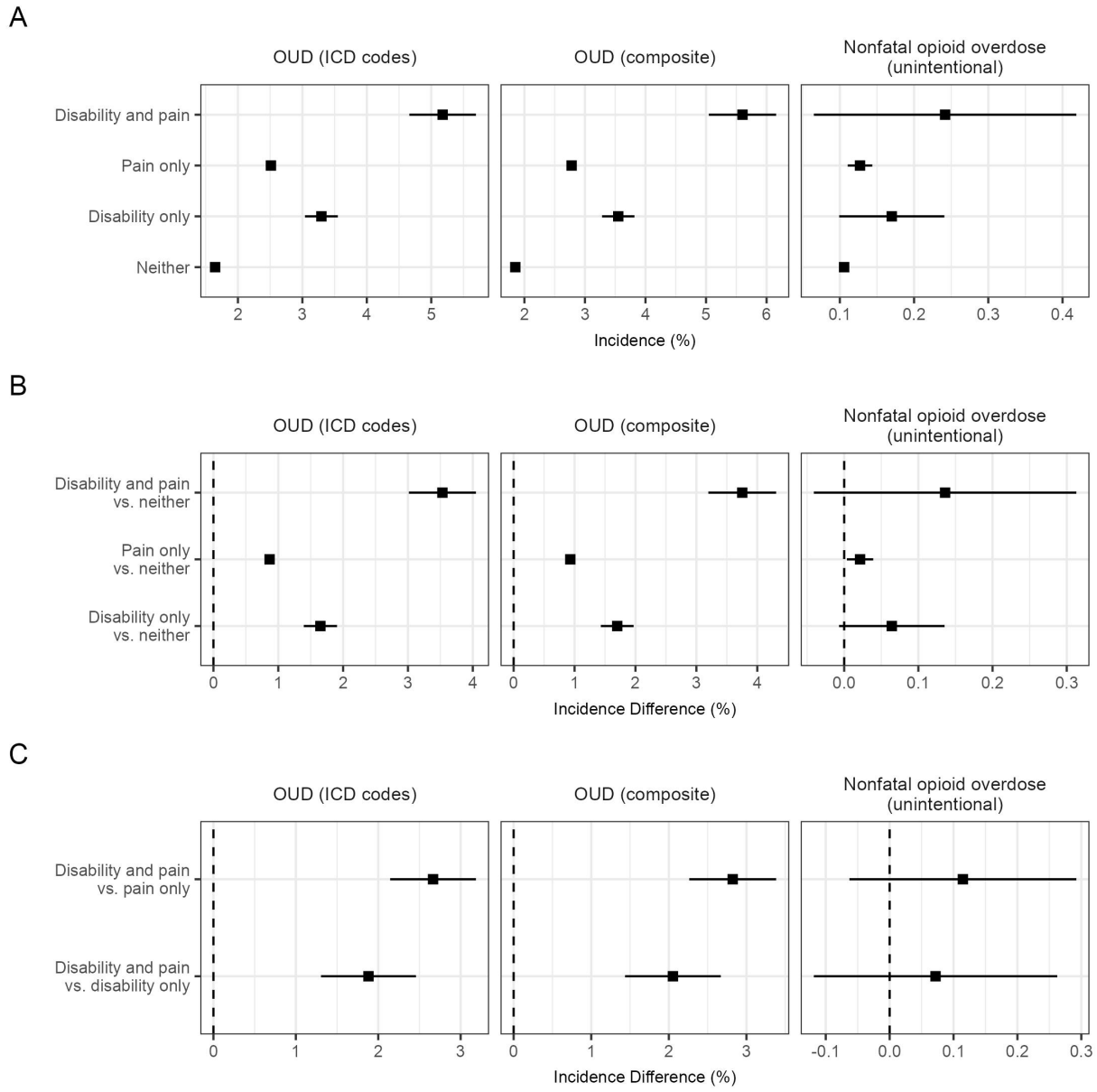

Table S3: Results of secondary analysis examining effects of disability on potential intermediate risk factors for OUD.

	Estimated Incidences		
Outcome	Disability	No disability	Difference

Chronic Pain	26.20 (25.66–26.74)	16.55 (15.46–17.64)	9.65 (8.44–10.87)
Anxiety	19.87 (19.32–20.43)	13.09 (9.25–16.94)	6.78 (2.90–10.67)
Depression	14.89 (14.37–15.41)	8.22 (5.94–10.51)	6.67 (4.33–9.01)
Opioid Prescriptions for Pain	26.85 (26.26–27.45)	19.93 (15.17–24.69)	6.92 (2.12–11.72)

References

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