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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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Abstract

Background. Chronic pain has been extensively explored as a risk factor for opioid misuse, resulting in increased focus on opioid prescribing practices for individuals with such conditions. Physical disability sometimes co-occurs with chronic pain but may also represent an independent risk factor for opioid misuse. However, previous research has not disentangled whether disability contributes to risk independent of chronic pain.

Methods. Here, we estimate the independent and joint adjusted associations between having a physical disability and co-occurring chronic pain condition at time of Medicaid enrollment on subsequent 18-month risk of incident opioid use disorder (OUD) and non-fatal, unintentional opioid overdose among non-elderly, adult Medicaid beneficiaries (2016–2019).

Results. We find robust evidence that having a physical disability approximately doubles the risk of incident OUD or opioid overdose, and physical disability co-occurring with chronic pain increases the risks approximately sixfold as compared to having neither chronic pain nor disability. In absolute numbers, those with neither a physical disability nor chronic pain condition have a 1.8% adjusted risk of incident OUD over 18 months of follow-up, those with physical disability alone have an 2.9% incident risk, those with chronic pain alone have a 3.6% incident risk, and those with co-occurring physical disability and chronic pain have a 11.1% incident risk.

Conclusions. These findings suggest that those with a physical disability should receive increased attention from the medical and healthcare communities to reduce their risk of opioid misuse and attendant negative outcomes.

Introduction

The drug overdose epidemic continues to pose a substantial health threat in the United States (Centers for Medicare & Medicaid Services, 2020). People with opioid use disorder (OUD) are at high risk of drug overdose (Hser et al., 2017) and >10 times the risk of death from any cause (Degenhardt et al., 2011; Hser et al., 2017). Between 1999 and 2021, more than 1 million people died from a drug overdose; opioids contributed to nearly 700 000 of those deaths (Cerdá et al., 2021; National Institute on Drug Abuse, 2023).

Chronic pain has been extensively explored as a risk factor for opioid misuse (Cerdá et al., 2021; Dunn et al., 2010; Marshall, Bland, Hulla, & Gatchel, 2019; Orhurhu et al., 2019; Volkow & McLellan, 2016); many people who experience opioid-related adverse events were initially exposed to opioids via a prescription (Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008). Chronic pain (often defined as pain that occurs on most days and lasts ≥3 months) affects a growing proportion of the population (Case, Deaton, & Stone, 2020), an estimated 21% of US adults in 2021 (Rikard, Strahan, Schmit, & Guy, 2023). Although rates of prescription opioid use to manage acute and chronic pain have declined in recent years (Maestas, Sherry, & Strand, 2021), their use remains common – 50% of Medicare beneficiaries with chronic pain were estimated to have received an opioid prescription in 2017 (Mikosz et al., 2020). In particular, longer opioid prescription duration, higher doses, greater dose variability, and having multiple opioid prescribers have been implicated in increasing the risk of opioid misuse, development of OUD, and overdose (Cho et al., 2020; Edlund et al., 2014; Glanz, Binswanger, Shetterly, Narwaney, & Xu, 2019; Ozturk, Hong, McDermott, & Turk, 2021; Peirce, Smith, Abate, & Halverson, 2012; Peters, Durand, Monteiro, Dumenco, & George, 2018; Rose et al., 2018; Savych, Neumark, & Lea, 2019; Volkow & McLellan, 2016). Exposure to opioids, particularly over extended periods of time, may increase pain sensitivity,

thereby making perceived pain worse, and in turn, resulting in higher opioid doses, creating a feedback loop (Angst & Clark, 2006; Covington, 2000; Kidner, Mayer, & Gatchel, 2009; Mao, Price, & Mayer, 1994; Mao, Sung, Ji, & Lim, 2002). In addition, anxiety and depression are frequently comorbid with chronic pain (Cohen, Vase, & Hooten, 2021; Fox & Reichard, 2013; Marshall et al., 2019; Mills, Nicolson, & Smith, 2019; Whitney, Hurvitz, & Peterson, 2018), which can increase the risk of taking medications that can negatively interact with opioids, such as benzodiazepines and other sedative hypnotics (Cho et al., 2020; Gressler, Martin, Hudson, & Painter, 2018; Rose et al., 2018), and increase the risk of opioid misuse directly (Sullivan, 2018).

Disability, which sometimes co-occurs with chronic pain (termed 'high-impact chronic pain') (Interagency Pain Research Coordinating Committee, 2016; Pitcher, Von Korff, Bushnell, & Porter, 2019), may also be an independent risk factor for opioid misuse, OUD, and overdose. Disability rates among working-aged adults have increased over the past two decades (Choi, Schoeni, & Martin, 2016; Lakdawalla, Bhattacharya, & Goldman, 2004; Martin, Freedman, Schoeni, & Andreski, 2010); an estimated 30% of US adults now live with a disability (Taylor, 2018). However, examining disability as a risk factor for opioid misuse has received far less attention than chronic pain. Moreover, the limited literature that has examined disability as a risk factor for opioid misuse has not attempted to disentangle it from chronic pain (Hong, Geraci, Turk, Love, & McDermott, 2019; 2022; Lauer, Henly, & Brucker, 2019; Ozturk et al., 2021; Reif et al., 2021).

People with disabilities are a heterogeneous group, encompassing those with visual impairments, hearing and communication-related impairments, physical disabilities, intellectual disabilities, cognitive impairments, or developmental disorders, and mental disorders (Gómez-Zúñiga, Pousada, & Armayones, 2023). Although vulnerabilities to opioid misuse are necessarily unique for every individual, the vulnerabilities of those within one of the above categories are likely more similar than across categories. However, most prior literature examining the relationship between disability and opioid misuse considered individuals with disabilities as a single group (Hong et al., 2022; Nicholson, Valentine, Ledingham, & Reif, 2022), compromising the 'well-defined exposure' requirement of casual inference (Hernan & Robins, 2023). Having a well-defined exposure is necessary for: (1) understanding and identifying causal mechanisms, (2) external validity, and (3) linking counterfactuals to real-world observed data (called 'consistency'), which is fundamental for inferring causal relationships from observed data (Hernan & Robins, 2023; Pearl, 2018).

Consequently, in this paper, we focus on those with a likely physical disability to result in a more well-defined exposure. Musculoskeletal injuries are the most common federally compensated physical disability (Kidner et al., 2009; Melhorn & Kennedy, 2005; Social Security Administration, 2015; Theis, Roblin, Helmick, & Luo, 2018) and the most common type of work-related disability in the United States; they account for much of the increase in worker compensation claims and growth in disability insurance applications and beneficiaries since 2000 (Burkhauser & Daly, 2012; David & Duggan, 2006; Maestas, 2019; Social Security Administration, 2015).

Although physical disability has not been previously considered as an independent risk factor for opioid misuse, there are several reasons why it could contribute to risk. First, those with a disability have more contact with the health care system, in part due to Medicaid and Medicare access through Social Security Disability Insurance (SSDI/SSI) (Ghertner, 2021; King, Strumpf, & Harper, 2016). Greater insurance access among those with disability may increase their access to a larger number of providers (Meara et al., 2016), and both of these factors may, in turn, contribute to an increased likelihood of being prescribed opioids (Gebauer, Salas, Scherrer, Burge, & Schneider, 2019; Lauer et al., 2019; Reif et al., 2021; Stover et al., 2006), or other medications that may negatively interact with opioids (Cho et al., 2020; Ford, Hinojosa, & Nicholson, 2018; Gressler et al., 2018; Rose et al., 2018), including for longer periods and at higher doses than those without a disability (Hong et al., 2019; Liaw, Kuo, Raji, & Baillargeon, 2020; Meara et al., 2016; Morden et al., 2014; Ozturk et al., 2021; Savych et al., 2019). Second, individuals with a physical disability are also at higher risk of having anxiety and depression (Cree, Okoro, Zack, & Carbone, 2020; Morden et al., 2014; Turner & Turner, 2004; Whitney et al., 2018), which independently increase the likelihood of: (1) being prescribed opioids (Davis, Lin, Liu, & Sites, 2017), (2) being prescribed benzodiazepines that may interact with opioids (Ford et al., 2018), and (3) misusing opioids (Dasgupta, Beletsky, & Ciccarone, 2018; Krueger, 2017; Ledingham, Adams, Heaphy, Duarte, & Reif, 2022; McLean, 2016; Monnat, 2018; Zoorob & Salemi, 2017). Relatedly, physical disability may create barriers to participating in work activities, worsening socioeconomic status (De Souza & Oliver Frank, 2011; Hughes & Avoke, 2010) and social connectedness (Hughes & Avoke, 2010; Wilson, 2011), which may, in turn, further worsen emotional well-being (Turner & Turner, 2004; Wilson, 2011), and ultimately increase risk of non-medical opioid use (Dasgupta et al., 2018; Krueger, 2017; McLean, 2016; Monnat, 2018; Zoorob & Salemi, 2017). In terms of opioid-related outcomes, individuals with disabilities are reportedly at high risk of opioid misuse (Martin, Jin, Bertke, Yiin, & Pinkerton, 2020), non-fatal and fatal opioid overdose (Kuo, Raji, & Goodwin, 2019; Meara et al., 2016; Peters et al., 2018; Song, 2017), and developing OUD (Hong et al., 2022). Finally, even if individuals with a physical disability do not initially have co-occurring chronic pain, they could develop a chronic pain condition later if their disability worsens or initial opioid use increases pain sensitivity over time.

We estimate the independent and joint adjusted associations between having a physical disability and/or chronic pain condition at time of Medicaid enrollment and subsequent risk of incident OUD and non-fatal, unintentional opioid overdose.

Methods

Data and cohort

The study was approved by the Columbia University Institutional Review Board. We used data from the following Medicaid T-MSIS Analytic Files (TAF): Demographics, Other Services, Inpatient, and Pharmacy claims, for years 2016–2019. The study includes non-pregnant adults aged 35–64 years who were Medicaid beneficiaries enrolled 2016–2019 from the following 26 states that implemented Medicaid expansion under the Affordable Care Act in or prior to 2014: ND, VT, NH, CA, OR, MI, IA, NV, OH, IL, NY, MD, MA, RI, HI, WV, WA, KY, DE, AZ, NJ, MN, NM, CT, CO, AR (Kaiser Family Foundation, 2020). We focus on expansion states, because within these states Medicaid covers: (1) nearly all non-elderly disabled individuals during their initial 24 months receiving disability insurance (after that, individuals transition to Medicare [Rupp & Riley, 2012]), (2) nearly all low-

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income (up to 138% of the federal poverty limit), non-elderly adults under the Affordable Care Act (ACA) expansion (Kaiser Family Foundation, 2020), and (3) nearly 40% of those with OUD (Kaiser Family Foundation, 2019). We note that we used 35 as the minimum age to make our exposure groups more comparable, which we discuss further in Section S1 of the online Supplementary Materials. We subsequently excluded beneficiaries from Maryland due to unreliable diagnosis code data as determined by the Medicaid Data Quality Atlas (Centers for Medicare & Medicaid Services, 2023).

Cohort

Cohort enrollment began after a 6-month look-back or washout period to determine eligibility criteria. Because individuals who are disabled and receive SSDI transition to Medicare after 24 months (Rupp & Riley, 2012), we used a follow up period of 18 months, thereby including individuals for a maximum of 24 months (6 month washout + 18 month follow-up). A timeline of the study is shown in Fig. 1 and additional details are in Section S1 of the Supplementary Materials.

Figure 2 depicts the cohort exclusion/inclusion criteria. Using the above-described washout periods, we excluded those who were dual-eligible for Medicare, because Medicare would typically be the primary payer, and we did not have access to Medicare claims. Individuals who did not have an eligibility code during the washout period, or whose disability status could not be determined by their eligibility code were also excluded, as well as those with any OUD diagnosis during the washout period. In defining the rest of the exclusion criteria, we prioritized internal validity, more well-defined exposure groups, and more interpretable potential causal mechanisms. We provide rationale for each criterion in Section S1 of the Supplementary Materials. All codes used for these exclusion criteria, as well as code to implement the exclusion criteria are in a Github repository at https://github.com/CI-NYC/disability-chronic-pain.

Beneficiaries with incomplete study follow up, who turned 65, or who became Medicare-eligible during follow-up were censored at the point of these events.

Measures

Exposure

The exposure consisted of four mutually exclusive categories regarding health status at time of enrollment, ascertained during the 6-month washout period: (1) physical disability and co-occurring chronic pain, (2) physical disability only (without chronic pain), (3) chronic pain only, and (4) neither disability nor chronic pain. After using eligibility codes and exclusions to identify the subgroup of those with a likely physical disability, we confirmed most individuals (66%) had claims for a physically disabling condition. Another 16% did not have claims for a physically disabling condition but did have claims for a serious mental illness without psychosis, suggesting some across-category heterogeneity in our disability exposure group remained (online Supplementary Table S1, Supplementary Materials). We refer to this exposure as 'physical disability' throughout for brevity but note that it is more accurately defined as having a likely physical disability or serious mental illness without psychosis. However, given the prevalence of depressive, bipolar, and anxiety disorders in the adult Medicaid population (Chapel, Ritchey, Zhang, & Wang, 2017; Han et al., 2022; Thomas et al., 2005), we chose not to exclude these individuals, because it would have resulted in exclusion of many who likely also had a physical disability. Instead, we control the mental health conditions as covariates.

Chronic pain status was identified using previously described non-cancer diagnoses (ICD-10 codes) typically associated with chronic pain (with modifications based on consultation with clinicians) (Mayhew et al., 2019), occurring at least two times for the same condition and at least 90 days apart during the washout period, to align with the common definition of pain lasting ≥3 months while excluding conditions potentially representing distinct acute pain diagnoses (Miller, Guy, Zhang, Mikosz, & Xu, 2019). We include more detail on the diagnoses used to define chronic pain status in Section S2 of the Supplementary Materials and in the Github repository.

Outcomes

Outcomes were ascertained in the 18 months following the washout period. The primary outcome of interest was incident OUD diagnosis, as defined by ICD-10 diagnosis codes indicating opioid abuse or dependence (Samples, Williams, Olfson, & Crystal, 2018, 2022). As a secondary OUD outcome, we defined OUD using the more expansive definition of Cochran et al. (2017), which indicates presence of any of four components: OUD ICD-10 codes; non-fatal, unintentional opioid overdose ICD-10 codes; MOUD treatment (methadone, buprenorphine, or naltrexone); or probable opioid misuse (Sullivan et al., 2010) (a composite score summed over rolling 6-month periods, detailed in the Supplementary Materials). Another secondary outcome included incident non-fatal, unintentional opioid overdose, identified using ICD-10 codes. All relevant ICD codes and each outcome's implementation using these codes are detailed in the Github repository.

In a secondary analysis on a subset of beneficiaries without chronic pain, we also examined incident chronic pain (defined as detailed above), incident depressive and anxiety disorders using ICD codes, and opioid prescriptions for pain using NDC codes (Samples et al., 2018).

Covariates

We used the washout period to characterize each beneficiary's baseline covariates: age in years, sex, race/ethnicity, English as

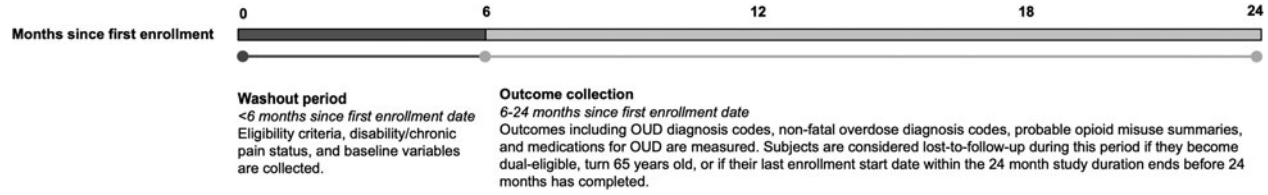

Figure 1. Study timeline for variable collection.

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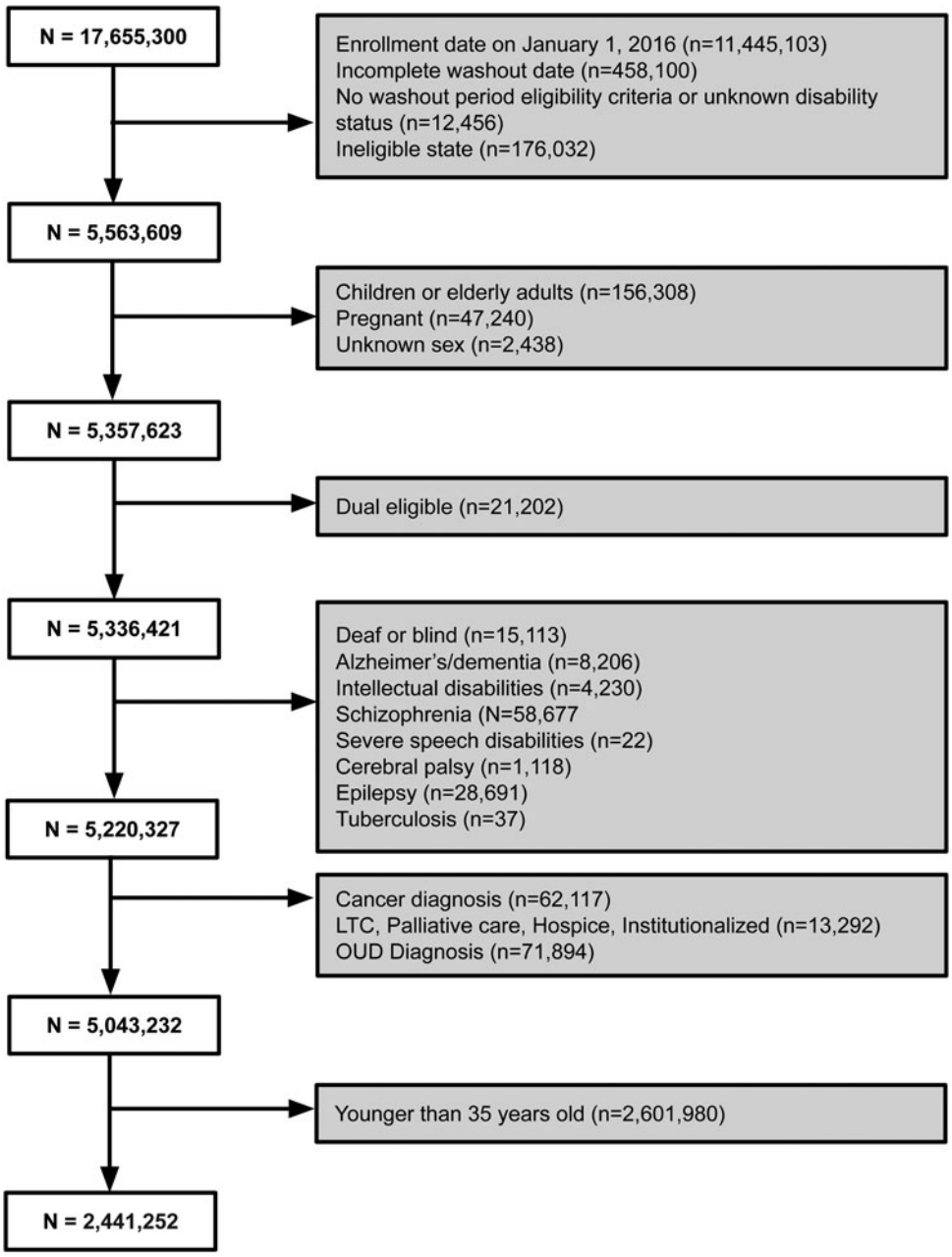

Figure 2. Participant flow diagram for the enrollment cohort used for analyses.

their primary language, marriage/partnership status, household size, veteran status, income likely >133% of the Federal Poverty Level, any inpatient or outpatient diagnosis of bipolar disorder, any anxiety disorder, attention deficit hyperactivity disorder (ADHD), any depressive disorder, or other mental disorder (e.g. anorexia, personality disorders [Samples et al., 2018]). We report missingness for each variable in online Supplementary Table S2 (Supplementary Materials).

Statistical analysis

We first computed descriptive statistics for all covariates and outcomes across the four exposure strata in the cohort. Then, we estimated adjusted associations comparing: (1) physical disability and co-occurring chronic pain, (2) physical disability only, and (3) chronic pain only *v.* the 'neither' category on each outcome of interest, adjusting for all baseline confounders and incorporating right censoring.

We estimated all adjusted analyses with collaborative targeted minimum loss-based estimation (TMLE) (Benkeser, Cai, & van der Laan, 2020; Van der Laan et al., 2011). TMLE uses regressions for the outcome, exposure, and censoring models to produce an estimate that is robust to misspecification of at most one of these models, i.e. it is a doubly robust estimator. We used an ensemble of flexible machine learning algorithms to fit the outcome, exposure, and censoring regressions using the Superlearning algorithm with twofold cross-validation. Our candidate algorithms included generalized linear models, multivariate adaptive regression splines (MARS) (Milborrow, 2011), and gradient boosting (Ke et al., 2017). Superlearning optimally combines

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predictions from these candidate algorithms via weighting (van der Laan, Polley, & Hubbard, 2007).

Sensitivity analyses

We implemented several sensitivity analyses. We first used a 12-month washout period followed by a 12-month follow-up period. This sensitivity analysis may more completely capture the exposure categories by using more time to detect disability, chronic pain, and their co-occurrence. For example, chronic pain was defined as at least two diagnosis codes for pain in the same anatomical location, at least 90 days but less than 12 months apart. In the second sensitivity analysis, instead of considering chronic pain, we considered any pain during the initial 6 month washout period.

In another exploratory secondary analysis, we examined potential risk factors contributing to the increased OUD and overdose risk for individuals with physical disability alone. We estimated associations between having physical disability alone *v.* neither on the following incident outcomes: chronic pain, any depressive disorder, any anxiety disorder, and any opioid prescription for pain (see Section S3 in the Supplementary Materials).

Finally, we performed a negative control outcome analysis to detect possible bias, and did not find any evidence of such bias (see Section S4 in the Supplementary Materials).

Code for all data cleaning and statistical analyses is available at https://github.com/CI-NYC/disability-chronic-pain.

Results

The cohort contained $N = 2\,441\,252$ beneficiaries (Fig. 2, Table 1). Overall, these beneficiaries were 49% female-identifying, 51% male-identifying, and 49% reported their race as white, non-Hispanic. The exposure groups included $n = 6736$ beneficiaries with both physical disability and chronic pain, $n = 77\,834$ with chronic pain only, $n = 51\,015$ with physical disability only, and $n = 2\,305\,667$ with neither condition. These groups had notably different characteristics observed during both baseline and study duration (Table 1). For example, compared to beneficiaries with chronic pain and/or physical disability, beneficiaries with neither condition were younger (median: 47, interquartile range [IQR] 40–54), with higher rates of non-white, non-Hispanic races reported (51%). In contrast, beneficiaries with both chronic pain and physical disability were oldest (median: 55, IQR 50–59) and had higher proportions of females (60%) and individuals of white, non-Hispanic race (60%). They had the highest rates of mental disorder diagnoses and were more likely to receive a prescription for antidepressants (40%), benzodiazepines (28%), antipsychotics (12%), mood stabilizers (35%), stimulants (1.7%), and opioids for pain (66%) during the washout period than those with one or neither physical disability nor chronic pain condition.

Adjusted analyses

After adjusting for baseline confounders and right-censoring, an estimated 11.13% (95% confidence interval [CI] 9.85–12.41%) of individuals with physical disability and chronic pain had an incident OUD diagnosis within 18 calendar months (Fig. 3). The estimated adjusted incident risk of OUD was 3.64% (95% CI 3.43–3.85%) and 2.89% (95% CI 2.66–3.13%) for individuals with chronic pain only or physical disability only, respectively. The estimated incidence was lowest for individuals with neither physical disability nor chronic pain: 1.78% (95% CI 1.76–1.80). The adjusted incidence rates for OUD using the composite criteria were similar (Fig. 3).

Adjusted incidence rates of non-fatal, unintentional opioid overdose were smaller, but followed a similar pattern as above. An estimated 0.40% (95% CI 0.00–0.80%) of individuals with physical disability and chronic pain at study entry had an incident opioid overdose within 18 calendar months (Fig. 3). The incidence rates were the same for the chronic pain only and disability only groups, 0.14% (95% CI 0.09–0.19%) and 0.14% (95% CI 0.08–0.20%), respectively. Again, the estimated incidence was lowest for individuals with neither physical disability nor chronic pain: 0.05% (95% CI 0.05–0.06%).

We then estimated the average risk differences of incident OUD and incident non-fatal, unintentional opioid overdose comparing those with (1) co-occurring chronic pain and physical disability, (2) physical disability alone, and (3) chronic pain alone to the neither exposure group. All risk differences and their 95% CIs are shown in Fig. 3. Risk ratios, reflecting associations on the multiplicative scale are given in Table 2.

For OUD, co-occurring physical disability and chronic pain conferred a 9.35 percentage point (95% CI 8.07–10.63) increased additive risk as compared to neither, which translated to a 625% relative risk (RR = 6.25). Having a chronic pain disorder alone conferred a 1.86 percentage point (95% CI 1.65–2.07) increased risk, and having a physical disability alone conferred a 1.11 percentage point (95% CI 0.88–1.35) increased risk. There were also significant joint effects of co-occurring physical disability and chronic pain on incident OUD in comparison to disability only (8.24 percentage points; 95% CI 6.94–9.54) and chronic pain only (7.49 percentage points; 95% CI 6.19–8.79). The same pattern was seen for the secondary, composite OUD definition.

For non-fatal, unintentional opioid overdose events, co-occurring physical disability and pain conferred a 0.35 percentage point (95% CI −0.05 to 0.75) increased additive risk compared to neither, which translated into a 757% relative risk (RR = 7.57). Having physical disability alone or chronic pain alone conferred identical increased additive risk as compared to neither, with risk differences (RD) of 0.08 (95% CI 0.03–0.14). There were also positive joint effects of co-occurring physical disability and pain on incident opioid overdose in comparison to either physical disability only or chronic pain only; however, confidence intervals were wide (RD: 0.26; 95% CI −0.14 to 0.67; and 0.26; 95% CI −0.14 to 0.66).

Sensitivity analyses

Online Supplementary Fig. S1 (Supplementary Materials) presents adjusted incidence risk estimates and incident risk differences for the sensitivity analysis considering a 12-month washout. Although incidence rates were lower, as expected given the 50% shorter follow-up time, results resembled the primary analysis. The main difference between this and the primary analysis was that the confidence intervals for the co-occurring physical disability and chronic pain and physical disability alone exposure groups were wide in the case of the overdose outcome, crossing the null.

Online Supplementary Fig. S2 (Supplementary Materials) presents adjusted incidence risk estimates and incident risk differences for the sensitivity analysis including any pain ICD code (i.e. not restricted to chronic pain). Again, results were generally similar as for the primary analysis. The main difference between

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Table 1. Analytical cohort characteristics stratified by physical disability and chronic pain status

Characteristic[a]	Physical disability and chronic pain *N* = 6736	Chronic pain *N* = 77834	Physical disability *N* = 51 015	Neither *N* = 2 305 667
Age	55 (50, 59)	50 (44, 56)	54 (46, 59)	47 (40, 54)
Sex				
Female	4032 (60%)	42 017 (54%)	25 322 (50%)	1 129 271 (49%)
Male	2704 (40%)	35 817 (46%)	25 693 (50%)	1 176 396 (51%)
Race/ethnicity				
AIAN[b], non-Hispanic	77 (1.3%)	1446 (2.3%)	543 (1.3%)	26 697 (1.5%)
Asian, non-Hispanic	65 (1.1%)	3232 (5.1%)	1055 (2.6%)	181 314 (10%)
Black, non-Hispanic	1596 (27%)	9006 (14%)	9802 (24%)	268 278 (15%)
Hawaiian/Pacific Islander	36 (0.6%)	510 (0.8%)	288 (0.7%)	14 299 (0.8%)
Hispanic, all races	563 (9.6%)	10 362 (16%)	6125 (15%)	371 631 (21%)
White, non-Hispanic	3538 (60%)	38 439 (61%)	22 412 (56%)	884 871 (51%)
Other/ Unknown	861	14 839	10 790	929 127
Primary language English	5260 (95%)	59 948 (89%)	36 616 (91%)	1 635 187 (82%)
Unknown	1170	10 310	10 868	307 637
Married/partnered	558 (13%)	7872 (27%)	3350 (15%)	203 157 (30%)
Unknown	2553	48 334	28 146	1 619 361
High income	152 (2.3%)	1934 (2.5%)	1552 (3.0%)	69 694 (3.0%)
Household size				
1	1497 (74%)	19 315 (72%)	12 101 (77%)	432 221 (65%)
2	293 (14%)	3932 (15%)	1832 (12%)	95 110 (14%)
2+	246 (12%)	3742 (14%)	1721 (11%)	136 167 (21%)
Unknown	4700	50 845	35 361	1 642 169
Veteran	*	202 (0.9%)	121 (1.4%)	5378 (1.1%)
Unknown	*	56 226	42 307	1 832 768
TANF[c] Benefits	95 (1.6%)	4561 (7.2%)	1940 (4.7%)	166 323 (8.4%)
Unknown	763	14 369	9416	336 978
SSI[d] Benefits				
Mandatory or optional	502 (12%)	161 (0.6%)	4260 (18%)	1753 (0.2%)
Not applicable	3691 (88%)	25 515 (99%)	19 548 (82%)	884 172 (100%)
Unknown	2543	52 158	27 207	1 419 742
Chronic pain (ever)	–	–	10 065 (20%)	211 915 (9.2%)
Psychiatric conditions				
Bipolar	446 (6.6%)	1565 (2.0%)	1698 (3.3%)	16 026 (0.7%)
Anxiety	1706 (25%)	16 255 (21%)	6175 (12%)	176 358 (7.6%)
ADD/ADHD[e]	59 (0.9%)	851 (1.1%)	248 (0.5%)	10 114 (0.4%)
Depression	1599 (24%)	11 321 (15%)	4777 (9.4%)	97 781 (4.2%)
Other mental illness	673 (10.0%)	5592 (7.2%)	2164 (4.2%)	51 423 (2.2%)
Prescriptions				
Antidepressant	2694 (40%)	19 315 (25%)	7984 (16%)	162 768 (7.1%)
Benzodiazepine	1890 (28%)	14 125 (18%)	4661 (9.1%)	103 069 (4.5%)
Anti-psychotic	821 (12%)	2643 (3.4%)	2920 (5.7%)	24 568 (1.1%)
Stimulant	114 (1.7%)	1251 (1.6%)	370 (0.7%)	16 096 (0.7%)

(*Continued*)

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Table 1. (*Continued.*)

Characteristic[a]	Physical disability and chronic pain *N* = 6736	Chronic pain *N* = 77834	Physical disability *N* = 51 015	Neither *N* = 2 305 667
Mood stabilizer	2325 (35%)	13 806 (18%)	4765 (9.3%)	58 522 (2.5%)
Opioids for pain	4461 (66%)	37 192 (48%)	8705 (17%)	213 224 (9.2%)
Opioid-related measures				
OUD[f] (ICD[g] codes)	549 (8.2%)	2531 (3.3%)	1299 (2.5%)	22 210 (1.0%)
Nonfatal overdose (NFOD)	41 (0.6%)	141 (0.2%)	89 (0.2%)	1317 (<0.1%)
Medication for OUD				
Injection naltrexone	*	70 (<0.1%)	61 (0.1%)	1834 (<0.1%)
Methadone	*	33 (<0.1%)	32 (<0.1%)	581 (<0.1%)
Buprenorphine	*	444 (0.6%)	262 (0.5%)	5487 (0.2%)
Probable opioid misuse	31 (0.5%)	94 (0.1%)	23 (<0.1%)	170 (<0.1%)
Avg. unique providers[h]	1.44 (1.00–2.00)	1.17 (1.00–1.80)	1.00 (1.00–1.63)	1.00 (1.00–1.33)
Avg. unique dispensers[h]	1.00 (1.00–1.35)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
Avg. days supply[h]	63 (15–142)	20 (7–74)	20 (5–72)	7 (4–21)
OUD (composite[i])	595 (8.8%)	2786 (3.6%)	1425 (2.8%)	24 862 (1.1%)

All descriptive statistics are median (interquartile range, IQR) for continuous measures, and *n* (%) for categorical measures.
[a]Median (interquartile range [IQR]); *n* (%).
[b]AIAN = American Indian and Alaska Native.
[c]TANF = temporary assistance for needy families.
[d]SSI = supplemental security income.
[e]ADD/ADHD = attention deficit (hyperactivity) disorder.
[f]OUD = opioid use disorder.
[g]ICD = International classification of diseases.
[h]Among beneficiaries with any opioid prescriptions.
[i]Defined as any abuse or non-fatal overdose diagnosis code, or probable misuse, or medication for OUD treatment.
* Suppressed due to small cell size.

this and the primary analysis was that physical disability alone conferred greater risk than pain alone.

Finally, in an exploratory, secondary analysis, we estimated the adjusted associations between having a physical disability alone and variables that may be mediators of the relationship between physical disability and the outcomes of OUD and opioid overdose. There were positive associations between physical disability and incident chronic pain (RD: 9.65 percentage points, 95% CI 8.44–10.87), incident anxiety disorder (6.78 percentage points, 95% CI 2.90–10.67), incident depressive disorder (6.67, 95% CI 4.33–9.01), and a new opioid prescription for pain (6.92, 95% CI [2.12–11.72]) (online Supplementary Table S3).

Discussion

Our findings from a large cohort of over 2.4 million Medicaid beneficiaries provide some of the first compelling evidence that those with physical disabilities are at increased risk of opioid misuse – even if they do not have co-occurring pain or chronic pain. Having a physical disability significantly increased risk of incident OUD and unintentional opioid overdose – physical disability without chronic pain approximately doubled the risks and physical disability with chronic pain increased the risks approximately sixfold. Those with physical disability and co-occurring chronic pain had 11.1% risk of developing incident OUD over 18 months of follow-up, and those with physical disability without chronic pain had 2.9% risk (as compared to 1.8% risk in the neither group). Those with physical disability and co-occurring chronic pain had 0.4% risk of incident opioid overdose over 18 months of follow-up, and those with physical disability without chronic pain had 0.14% risk (as compared to 0.05% risk in the neither group). Our findings were robust to multiple sensitivity analyses.

It is difficult to put our adjusted incidence rate estimates into context due to a lack of incidence rate estimates in the literature. Prevalence estimates of OUD among individuals aged 12 and older in the United States range from 0.62% to 4.08% (Barocas et al., 2018; Keyes et al., 2022; Substance Abuse & Mental Health Services Administration, 2021). Assuming an average duration of 10–20 years for OUD (Hser, Huang, Chou, & Anglin, 2007; Strang et al., 2020), this would translate to incidence rates over 18 months of 0.05–0.61%. The incidence rates we estimate here are significantly higher, even in neither group. This could be in part due to: (1) our focus on adults 35–64 years as opposed to all individuals ≥12 years and (2) our focus on the Medicaid population, which is a population at much higher risk of OUD – Medicaid covers approximately 40% of those with OUD (Kaiser Family Foundation, 2019) despite covering only 10% of US adults (Center for Medicaid & CHIP Services, 2023).

A natural question is that if there is a unique contribution of physical disability to the development of OUD and opioid overdose, *separate from pain or chronic pain*, what could the contributing mechanisms be? A confluence of mechanisms related to limited social connectedness, loneliness, mental health, more precarious economic conditions, increased access to health insurance but reduced access to behavioral health and substance use treatment services (as compared to those without a disability) could contribute. First, disability of all types, including physical disability, has been found to be associated with substantially constricted

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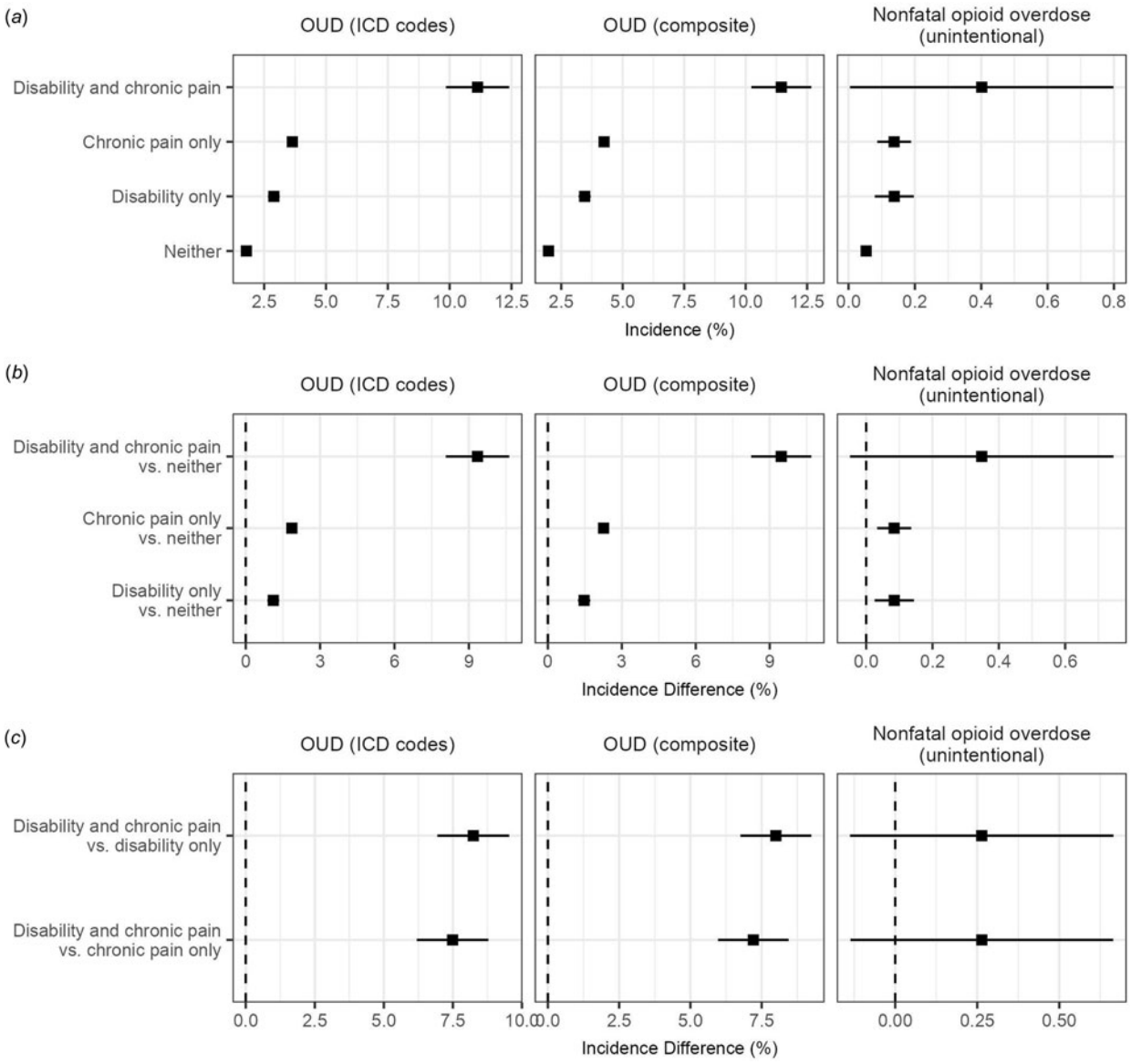

Figure 3. Panel A: Estimated adjusted incidences and 95% CIs of each outcome if the entire cohort were to have each of the four chronic pain and physical disability exposure status. Panel B: Adjusted incidence differences and 95% CIs for disability and chronic pain exposure statuses contrasted with the 'neither' exposure status. Panel C: Adjusted incidence differences 95% CIs for an exposure status of physical disability and chronic pain compared to (1) pain only and (2) disability only.

social networks, decreased social connectedness, and increased social isolation (Emerson, Fortune, Llewellyn, & Stancliffe, 2021a; Gómez-Zúñiga et al., 2023; Krahn, Walker, & Correa-De-Araujo, 2015; Macdonald et al., 2018; Mithen, Aitken, Ziersch, & Kavanagh, 2015). Those with a disability, including a physical disability, are much less likely to live with a partner, less likely to have daily contact with family and friends, less likely to be employed, and less likely to participate in activities outside the home, resulting in many more hours spent alone than people without a disability (Gómez-Zúñiga et al., 2023; Krahn et al., 2015; Macdonald et al., 2018; Mithen et al., 2015). Likely due, at least in part, to reduced social connectedness, those with disabilities experience substantially greater feelings of loneliness (Emerson et al., 2021a, 2021b; Gómez-Zúñiga et al., 2023; Macdonald et al., 2018); worse confidence, self-esteem, overall well-being (Emerson et al., 2021a; 2021b; Gómez-Zúñiga et al., 2023; Turner & Turner, 2004; Wilson, 2011); and increased risks of depression and anxiety (Morden et al., 2014; Whitney et al., 2018), consistent with our findings (online Supplementary Table S3). Loneliness, depression, anxiety, and worse emotional health in general, may all increase risk of substance misuse, including opioid misuse in particular (Cance et al., 2021; Dasgupta et al., 2018; Krueger, 2017; Ledingham et al., 2022; McLean, 2016; Monnat, 2018; Segrin, McNelis, & Pavlich, 2018; Zoorob & Salemi, 2017). A second, albeit related pathway, may operate through financial stress, though we note that all individuals included in this analysis likely were ≤ 133% FPL. However, people with physical disabilities are less likely to be employed (indeed, the primary way that people with disabilities access Medicaid coverage is through SSDI/SSI, which requires that their disability prevents them from working). Labor force exits usually reduce income and socioeconomic status in general,

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Table 2. Estimated risk ratios of each disability and chronic pain exposure group compared to the 'neither' disability nor pain exposure group, for the primary and secondary outcomes

Outcome	Exposure group	Risk ratio estimate (95% CI[a])
	Disability and chronic pain	6.25 (5.57–7.02)
OUD[b] (ICD[c] codes)	Disability only	1.62 (1.50–1.76)
	Chronic pain only	2.04 (1.93–2.17)
	Disability and chronic pain	5.78 (5.19–6.43)
OUD (composite[d])	Disability only	1.74 (1.62–1.87)
	Chronic pain only	2.14 (2.03–2.5)
	Disability and chronic pain	7.57 (2.79–20.48)
Non-fatal opioid overdose (unintentional)	Disability only	2.60 (1.67–4.04)
	Chronic pain only	2.59 (1.76–3.82)

[a]CI, confidence interval.
[b]OUD, opioid use disorder.
[c]ICD, International Classification of Diseases.
[d]Defined as any abuse or non-fatal overdose diagnosis code, or probable misuse, or medication for OUD treatment.

increasing economic stress (De Souza & Oliver Frank, 2011; Hughes & Avoke, 2010; Wilson, 2011), which then increases risk of depression, anxiety, and substance misuse, including the misuse of opioids (Dasgupta et al., 2018; Krueger, 2017; McLean, 2016; Monnat, 2018; Zoorob & Salemi, 2017). Third, in the United States, people with disabilities that qualify for SSDI/SSI are enrolled in Medicaid for the initial 24 months of SSDI/SSI receipt. This population's insured status could, as an unintended consequence, increase access to prescribed opioids, though again, we note that all individuals in this analysis were insured. Finally, focusing on further downstream mechanisms, having a physical disability may create practical barriers to behavioral health and substance use treatment, including treatment for OUD that could increase duration of OUD and risk of overdose (Glazier & Kling, 2013). For example, methadone treatment requires daily or near-daily visits that may be difficult for those with disabilities to access. And nearly all treatment programs offering pharmacotherapy have visit requirements and abstinence requirements that may be prohibitive for someone with a physical disability (Jakubowski & Fox, 2020; Kourounis et al., 2016; West, Graham, & Cifu, 2009). Indeed, a growing body of research finds that people with disabilities are less likely to receive and continue pharmacotherapy for OUD (Lauer et al., 2019; Thomas et al., 2023). The most rigorous way to estimate the contribution of each of these mechanisms is by doing a causal mediation analysis, which we are currently pursuing as a subject of future work.

Although this analysis provides robust evidence of the unique risk conferred by having a physical disability to opioid misuse as measured by the development of OUD and overdose, it is limited in several aspects. First, measurement error is likely, though we took several steps to mitigate its impact. We restricted our analysis to 2016–2019, which allowed us to use only TAF files only ICD-10 codes instead of a mix of ICD-9 and ICD-10 (Yang et al., 2021) and avoid measurement errors and idiosyncrasies introduced by the COVID-19 pandemic. We may expect our effect estimates to be even more pronounced after the start of the COVID-19 pandemic. This is because during this period: (1) Congress required Medicaid beneficiaries to be continuously enrolled (as part of the Families First Coronavirus Response Act), which would reduce the extent of censoring, (2) rates of opioid overdose increased (Ahmad, Rossen, & Sutton, 2021), (3) rates of chronic pain increased (in part due to long COVID) (Shanthanna, Nelson, Kissoon, & Narouze, 2022), and (4) rates of physical disability increased, also likely in part due to long COVID (Roberts, Ives-Rublee, & Khattar, 2022).There are other measurement error concerns with other state-variable combinations, though mostly having to do with missingness, and none which rose to the level justifying their exclusion (Centers for Medicare & Medicaid Services, 2023).

Another limitation was that our 'physical disability' exposure groups were imperfect in that we used eligibility codes to determine probable disability and specific disability types. Ideally, we would be able to link SSDI/SSI approvals with Medicaid claims to identify which beneficiaries received Medicaid through disability insurance and their qualifying disability. However, such linkages were infeasible. Alternatively, we could have used the SSDI receipt variable from the TAF demographics file to determine any SSDI disability, but that variable had high levels of missingness (Table 1). Consequently, our use of eligibility codes combined with exclusion criteria was designed to identify a more well-defined exposure group comprised mostly of those with probable physical disability. Nonetheless, our group of beneficiaries with likely physical disability was still heterogeneous (online Supplementary Table S1), and beneficiaries with disabilities may have an eligibility codes that do not indicate disability. Analogously, our 'chronic pain' exposure groups were also imperfect in that we use diagnosis codes for conditions typically associated with chronic pain, which may miss individuals with chronic pain arising from other conditions as well as individuals who do not have ≥2 claims for their chronic pain condition. In addition, it is plausible that some individuals with such conditions do not have chronic pain. Such mismeasurement means our estimates may be conservative.

Our analysis also benefited from several strengths. First, we analyzed an extremely large cohort of over 2.4 million beneficiaries, which mitigates finite sample bias and also improves the generalizability of our results to the non-elderly, non-pregnant, non-institutionalized Medicaid population in the states that enacted Medicaid expansion. Second, we used a doubly robust, data-adaptive estimator to flexibly adjust for possible confounding variables and non-random right-censoring without relying on correct parametric model specification (Benkeser et al., 2020;

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Van der Laan et al., 2011). Third, we conducted several sensitivity analyses to assess the extent to which our findings were robust to certain judgements in the analytic process and found that our inferences were maintained.

Lastly, as stated above, our work disentangled and quantified the independent and joint contributions of (1) physical disability and (2) chronic pain on incident risk of OUD and opioid overdose. In addition, we sought to reduce heterogeneity in defining our group of beneficiaries with physical disability – a majority of those in this exposure group had a physical disability, and 16% had disability likely due to a serious mental illness. We found robust evidence that individuals with a likely physical disability are at high risk of developing OUD and of opioid overdose – even beneficiaries with no chronic pain were at 174% higher risk of developing OUD (95% CI 162–187%) and 214% of overdose (95% CI 203–225%) over 18 months if they had a physical disability. These findings suggest that those with a physical disability should receive increased focus from the medical and healthcare communities to reduce their risk of opioid misuse and attendant negative outcomes. Future work could examine the mechanisms by which this increased risk is conferred and identify possible points of intervention.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S003329172300332X

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Competing interests. None.

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