Delayed timing of physical therapy initiation increases the risk of future opioid use in individuals with knee osteoarthritis: a real-world cohort study

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ABSTRACT

Objective We assessed whether late versus early initiation of physical therapy (PT) was related to greater risk of future opioid use in people with knee osteoarthritis (OA) who receive PT.

Methods We used Commercial and Medicare Advantage claims data from 1999 to 2018 from American adults with incident knee OA referred for PT within 1 year of diagnosis. We categorised people as opioid naïve or opioid experienced based on prior prescriptions. We examined the association of timing of PT initiation with any and chronic opioid use over 1 year.

Results Of the 67 245 individuals with incident knee OA, 35 899 were opioid naïve and 31 346 were opioid experienced. In the opioid naïve group, compared with PT within 1 month, PT 1 to <3, 3 to <6, 6 to <9, 9–12 months from diagnosis was associated with adjusted risk ratio (aRR (95% CIs)) for any opioid use of 1.18 (1.10 to 1.28), 1.49 (1.37 to 1.61), 1.73 (1.58 to 1.89) and 1.93 (1.76 to 2.12), respectively; aRRs (95% CIs) for chronic opioid use were 1.25 (1.01 to 1.54), 1.83 (1.48 to 2.26), 2.29 (1.82 to 2.89) and 2.50 (1.96 to 3.19). Results were similar among opioid experienced; aRRs (95% CIs) for any opioid use were 1.19 (1.14 to 1.24), 1.32 (1.26 to 1.37), 1.39 (1.32 to 1.45) and 1.54 (1.46 to 1.61); aRRs (95% CIs) for chronic opioid use were 1.25 (1.17 to1.34), 1.43 (1.33 to 1.54), 1.53 (1.41 to 1.66) and 1.65 (1.51 to 1.80).

Conclusion Compared with PT initiation within 1 month, delayed PT initiation was associated with higher risk of opioid use in people with incident knee OA. The longer the delay in PT initiation, the greater was the risk.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Exercise and education, commonly delivered as part of physical therapy (PT), are the first line recommended interventions for people with chronic pain due to knee osteoarthritis (OA).

WHAT THIS STUDY ADDS

⇒ Delayed initiation of PT (ie, >1 month after diagnosis) versus early initiation (ie, within 1 month of diagnosis) is associated with increased future risk of any opioid use and chronic opioid use in people with incident knee OA. The longer the delay in PT initiation, the greater is the risk.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ In people referred to PT after a diagnosis of knee OA, earlier initiation of care could lead to more effective pain management and reduce reliance on opioids.

INTRODUCTION

The global opioid crisis has been partly fueled by the need to manage chronic musculoskeletal pain.[1–4] Osteoarthritis (OA) is a leading cause of chronic pain in middle-age and older-age adults, and knee OA accounts for over half of the global burden of OA.[5 6] In the USA, joint pain due to OA is the second most common reason for patients to seek medical care[7] and prescriptions for arthritis pain represent over 50% of all opioid prescriptions.[8 9] Hence, interventions that could reduce utilisation of opioids in people with knee OA are needed.

Exercise, usually delivered as part of physical therapy (PT) care, is recommended as first-line intervention for knee OA across the world.[10–14] However, in individuals undergoing knee replacement, utilisation of PT has remained variable and suboptimal in countries where such data have been reported.[15 16] Contrary to treatment guidelines, intra-articular and oral analgesics are the most common initial interventions for knee OA.[10 11 17–19] In fact, there has been an increase in prescription analgesics over time.[1 3 20] Early versus late initiation of active exercise-based PT interventions after knee OA diagnosis could improve pain management and function leading to reduced utilisation of prescription opioids, as has been reported for people with low back pain or patellofemoral pain.[21 22] These studies may guide clinicians to use PT as an early strategy to reduce or prevent opioid use in people with knee OA.

While there is some evidence from clinical trials that greater number of PT sessions are related with better outcomes, whether this is true in real-world practice is not known.[23 24] Further, while passive interventions (eg, heat and cold) should only be provided with active PT interventions that require patient participation (eg, self-management training, exercise, gait retraining), it is not known if active interventions protect against opioid use.[10 11] Information on optimal dose and type of PT interventions could guide clinical practice for knee OA.

Our primary objective was to determine the association of timing of PT initiation with subsequent opioid use in individuals with incident knee OA who receive PT who were opioid naïve and those

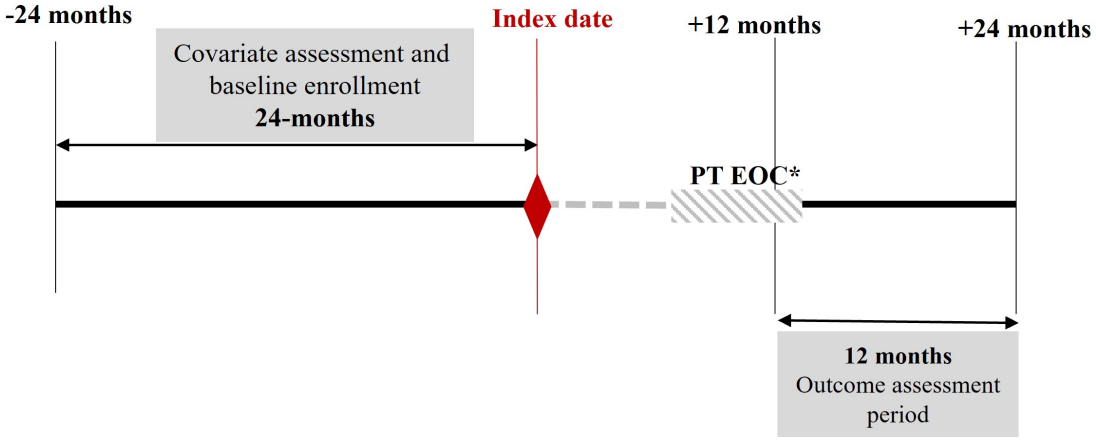


Figure 1 Study design. EOC, episode of care; PT, physical therapy. *The *PT EOC* can start anytime within the 12-month period following the index date. In cases where the *PT EOC* is initiated close to the end of the 12-month period, it may extend into the outcome assessment period.

with prior opioid use. We also assessed the associations of dose and type (ie, active vs passive) of PT with any and chronic opioid use in this population.

METHODS

Study design

We conducted a longitudinal cohort study in individuals with incident knee OA who received PT within 1 year of diagnosis (figure 1). We assessed the relation of the PT timing, dose and type after diagnosis with future opioid use over a 1-year period.

Study sample

We used data from the Optum Labs Data Warehouse (OLDW, Eden Prairie, USA), which includes deidentified medical and pharmacy claims, PT claims, laboratory results and enrolment records for commercial and Medicare Advantage enrollees. Members in the database had full insurance coverage for physician, hospital and prescription drug services.[25] The database contains longitudinal health information on patients representing a diverse mix of ages, ethnicities and US geographical regions.

We included data from individuals ≥40 with incident knee OA between 2001 and 2016. Incident knee OA was defined by knee OA diagnosis (International Classification of Diseases (ICD), code 715.x6 (9th revision) or M17.x (10th revision)) with no claims for a diagnosis of knee OA during the prior 24 months. The date of knee OA diagnosis was defined as the index date. To be included in the analyses, individuals were required to have continuous medical and pharmacy claims from 24 months prior to and following the index date. We excluded individuals with history of total knee replacement, other knee surgery, cancer or rheumatoid arthritis. We also excluded individuals who received PT in the 12 months preceding the index date and individuals with missing information for sex, geographical region or insurance type.

We categorised included individuals as those with any prior opioid use (opioid experienced) and those without prior opioid use (opioid naïve) as done in prior studies.[26 27] Since single opioid prescription for acute medical issues is related to greater risk of future use, prior opioid use was defined as 1 or more filled opioid prescriptions within 2 years prior to index date[28–32]; opioid naïve individuals had no opioid prescription within the 2 years.

Exposures

Our primary exposure was timing of PT initiation relative to the index date. Secondary exposures were PT dose and type (described in next paragarph). Exposures were defined by first identifying the initial outpatient PT episode of care (EOC) in the 12-month period following the index date (figure 1). The initial PT visit was identified by a current procedural terminology (CPT) evaluation code for PT (online supplemental eTable 1) from an outpatient facility. A PT EOC was considered to have ended when there were no PT claims ≥12 weeks. To ensure that PT was for knee OA, all ICD codes from the initial PT visit were reviewed (DK) to identify those indicating knee OA. Individuals with ICD codes that did not suggest PT for knee OA were excluded. We also excluded individuals who only underwent PT evaluation but no intervention.

We categorised PT timing as the time (in months) between index date and the initial PT visit (ie, <1 month (reference), 1 to <3 months, 3 to <6 months, 6 to <9 months, 9 to 12 months). Guided by clinical practice, PT dose was categorised as the number of unique sessions on unique dates (ie, 1–5 (reference), 6–12, 13+) during the PT EOC. PT type was defined as active or passive (reference) based on CPT codes during the PT EOC (online supplemental eTable 1). Active PT interventions were defined as ≥50% of codes being active interventions during the PT EOC, as per prior studies.[33]

Outcomes

Outcomes of interest were as follows: (1) any opioid use and (2) chronic opioid use over a 12-month period starting 1 year after index date (ie, outcome assessment period) (figure 1). We included oral/enteral opioid formulations as selected by a rheumatologist investigator (MD) (online supplemental eTable 2). Any opioid use was defined as ≥2 filled prescriptions of an opioid during the outcome assessment period.[34] Chronic opioid use was defined as ≥90 days of filled opioid prescriptions as defined previously in non-surgical cohorts.[35]

Potential confounders

We selected confounders based on factors that could influence both our exposures and outcomes. All analyses were adjusted for age, sex, race, obesity, type of insurance (commercial or Medicare Advantage), geographical location, physical and mental health comorbidities. Comorbidities were identified throughout

24 months prior to the index date using the Elixhauser Index.[36 37] Physical comorbidities were included as the count of physical comorbidities, except for: obesity, alcohol abuse, drug abuse, psychoses, depression.[21 37] Bipolar disorder, post-traumatic stress disorder and schizophrenia disorder that were combined because of the potential collinearity. Other psychological disorders, obesity and sleep disorders were included individually.[36–38] Healthcare utilisation was calculated as number of outpatient claims ≥7 days apart within the 2 years prior to index date. Calendar year was added as a covariate for all models to account for secular trends.

Statistical analysis

We evaluated the relations of the exposures to the outcomes in the opioid experienced and naïve cohorts separately, using Poisson regression with a robust variance.[39] We report risk ratios adjusted for the covariates (adjusted risk ratio, aRR). Analyses were conducted using SAS V.9.4 (SAS Institute). We calculated E-values to examine the robustness of the findings to unmeasured confounding.[40] The E-value reflects the minimum strength of association needed between an unmeasured confounder and both the exposure and the outcome to nullify the observed effect estimate. Sensitivity analyses were as follows: (A) redefined opioid experienced individuals as those with two or more filled opioid prescriptions within 24 months prior to index date to avoid inclusion of single prescriptions for acute medical or dental issues,[34] (B) redefined chronic opioid use outcome as at least 90 days of filled prescriptions without ≥30 days break in supply and (C) additionally included prior non-steroidal anti-inflammatory drugs (NSAIDs) use as a covariate. We also performed sensitivity analyses for PT type by redefining active PT as each PT visit having at least one active code.

Equity, diversity and inclusion statement

We used data from OLDW, which includes persons of all genders, race/ethnicities and geographical regions in the USA. The research team included four women (senior author is a woman) and four men, of whom three are early career researchers. The author's disciplines include PT, rheumatology, epidemiology and biostatistics. We considered sex and race as covariates in our analyses. We also considered geographical region and type of insurance as covariates which may partially capture socioeconomic status. However, since we only included data from persons with insurance, those who are underinsured or uninsured are not captured in this study.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

We identified 2 194 144 individuals with an incident knee OA diagnosis between 2000 and 2016 of whom 67 245 met the study criteria (figure 2). Of these 35 899 were opioid naïve and 31 346 were opioid experienced (table 1). Opioid experienced individuals had greater prevalence of obesity, NSAIDs use and other health conditions.

The mean duration of PT EOC was 6.2±7.5 weeks and the mean intensity of PT was 2.4±1.9 visits/week. Overall, in the opioid naïve cohort, the prevalence of any opioid use and chronic opioid use during the outcome assessment period was 12.3% and 1.9% in the opioid naïve cohort and 35.0% and 15.0% in the opioid experience cohort.

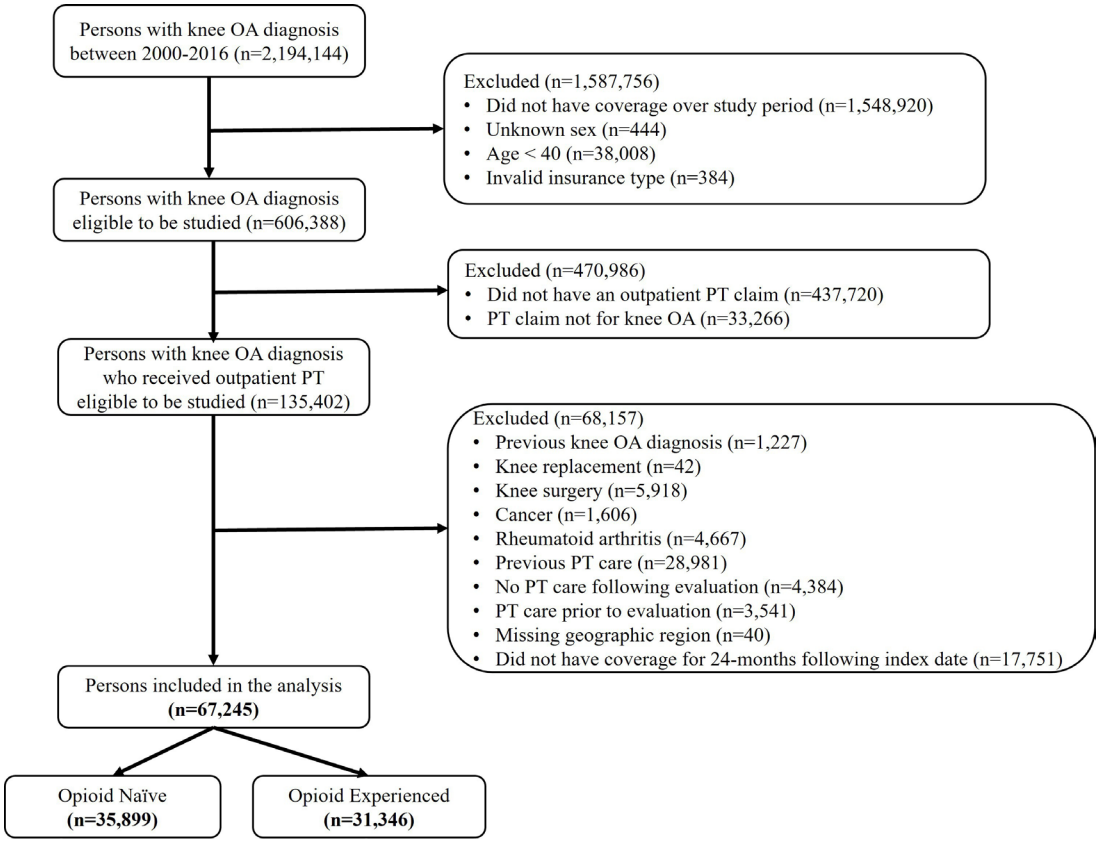


Figure 2 Participant flow diagram. OA, osteoarthritis; PT, physical therapy.

Table 1 Cohort characteristics

Characteristics	Opioid naïve (n=35 899)	Opioid experienced (n=31 346)	All subjects (n=67 245)
Age (years), mean (SD)	61.9 (11.1)	61.1 (10.9)	61.5 (11.0)
Female, n (%)	21 360 (59.5%)	19 548 (62.4%)	40 908 (60.8%)
Obesity, n (%)	4332 (12.1%)	6161 (19.7%)	10 493 (15.6%)
Race/ethnicity, n (%)			
Asian	1018 (2.8%)	453 (1.4%)	1471 (2.2%)
Black	3261 (9.1%)	3697 (11.8%)	6958 (10.3%)
Hispanic	2292 (6.4%)	1971 (6.3%)	4263 (6.3%)
White	28 234 (78.6%)	24 454 (78.0%)	52 688 (78.4%)
Missing	1094 (3.0%)	771 (2.5%)	1865 (2.8%)
US Region, n (%)			
Midwest	12 379 (34.5%)	9984 (31.9%)	22 363 (33.3%)
Northeast	5599 (15.6%)	3165 (10.1%)	8764 (13.0%)
South	12 995 (36.2%)	13 753 (43.9%)	26 748 (39.8%)
West	4926 (13.7%)	4444 (14.2%)	9370 (13.9%)
Insurance type, n (%)			
Commercial	26 352 (73.4%)	22 844 (72.9%)	49 196 (73.2%)
Medicare advantage	9547 (26.6%)	8502 (27.1%)	18 049 (26.8%)
NSAID use, n (%)	10 932 (30.5%)	17 284 (55.1%)	28 216 (42.0%)
Neck pain, n (%)	4059 (11.3%)	6372 (20.3%)	10 431 (15.5%)
Shoulder pain, n (%)	1350 (3.8%)	2303 (7.3%)	3653 (5.4%)
Low back pain, n (%)	7203 (20.1%)	12 684 (40.5%)	19 887 (29.6%)
Elixhauser physical (counts), mean (SD)	1.9 (1.9)	2.6 (2.3)	2.2 (2.1)
Fibromyalgia/chronic pain/fatigue, n (%)	1270 (3.5%)	3072 (9.8%)	4342 (6.5%)
ADHD, n (%)	116 (0.3%)	244 (0.8%)	360 (0.5%)
Depression, n (%)	3488 (9.7%)	5806 (18.5%)	9294 (13.8%)
Substance use disorder, n (%)	53 (0.1%)	296 (0.9%)	349 (0.5%)
Alcohol use disorder, n (%)	172 (0.5%)	332 (1.1%)	504 (0.7%)
Anxiety, n (%)	1717 (4.8%)	2879 (9.2%)	4596 (6.8%)
Bipolar disorder/ Schizophrenia/PTSD, n (%)	368 (1.0%)	741 (2.4%)	1109 (1.6%)
Dementia, n (%)	207 (0.6%)	186 (0.6%)	393 (0.6%)
Sleep disorder, n (%)	3341 (9.3%)	4901 (15.6%)	8242 (12.3%)
Healthcare utilisation, n (%)			
0–3	9154 (25.5%)	3951 (12.6%)	13 105 (19.5%)
4–6	10 583 (29.5%)	7247 (23.1%)	17 830 (26.5%)
7–10	9474 (26.4%)	9686 (30.9%)	19 160 (28.5%)
11+	6688 (18.6%)	10 462 (33.4%)	17 150 (25.5%)

ADHD, attention deficit hyperactivity disorder; NSAID, non-steroidal anti-inflammatory drugs; PTSD, post-traumatic stress disorder.

Timing of PT initiation and opioid use

In the opioid naïve group, when compared with initiation of PT intervention within 1 month of knee OA diagnosis, initiation of PT 1 to <3 months, 3 to <6 months, 6 to <9 months, 9 to 12 months from diagnosis was associated with greater risk of any opioid use with aRR of 1.18 (95% CI 1.10 to 1.28), 1.49 (95% CI 1.37 to 1.61), 1.73 (95% CI 1.58 to 1.89) and 1.93 (95% CI 1.76 to 2.12), respectively (figure 3). Similarly, initiation of PT 1 to <3 months, 3 to <6 months, 6 to <9 months, 9 to 12 months from diagnosis was associated with increased risk of chronic opioid use with aRR of 1.25 (95% CI 1.01 to 1.54), 1.83 (95%CI 1.48 to 2.26), 2.29 (95% CI 1.82 to 2.89) and 2.50 (95% CI 1.96 to 3.19), respectively (figure 4).

Similar to the findings in the opioid naïve group, in the opioid experienced group, initiation of PT 1 to <3 months, 3 to <6 months, 6 to <9 months, 9 to 12 months from diagnosis was associated with increased risk of any opioid use with aRR of 1.19 (95% CI 1.14 to 1.24), 1.32 (95% CI 1.26 to 1.37), 1.39 (95% CI 1.32 to 1.45) and 1.54 (95% CI 1.46 to 1.61), respectively (figure 3). Similarly, initiation of PT 1 to <3 months, 3 to <6 months, 6 to <9 months, 9 to 12 months from diagnosis was associated with increased risk of chronic opioid use with aRR of 1.25 (95% CI 1.17 to 1.34), 1.43 (95% CI 1.33 to 1.54), 1.53 (95% CI 1.41 to 1.66) and 1.65 (95% CI 1.51 to 1.80), respectively (figure 4).

Results were largely unchanged when additionally adjusted for prior NSAIDs use in both cohorts (online supplemental eTable 3). Results were also unchanged with more stringent criteria were used to define the opioid experienced cohort (online supplemental eTables4 and 5) and to define the chronic opioid use outcome (online supplemental eTable 6).

The E-values (figures 3 and 4) showed that an unmeasured confounder would have to be associated with both the exposure (timing of PT) and the outcome (any opioid use or chronic opioid use), over and above the measured confounders, by an RR range of 1.64–4.44 (E-value for lower limit of CI ranging from 1.11 to 3.33) in the opioid naïve group. Similarly, the E-value range was 1.67–2.69 (E-value for lower limit of CI ranging from 1.54 to 2.39) for the opioid experienced group.

PT intervention dose and type, and opioid use

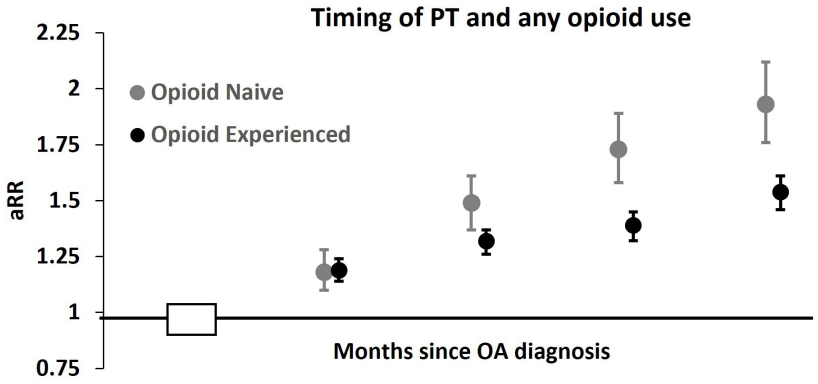
In the opioid naïve group, when compared with 1–5 PT visits, having 6–12 PT visits did not alter the risk for any opioid use (aRR 0.96, 95% CI 0.90 to 1.02), whereas the risk was increased for >12 PT visits (aRR 1.10, 95% CI 1.02 to 1.18) (online supplemental eTable 7). The risk for chronic opioid use was lower for 6–12 PT visits (aOR 0.81, 95% CI 0.68 to 0.97) and was equivocal for >12 PT visits (aOR 1.07, 95% CI 0.89 to 1.28) compared with 1–5 PT visits (online supplemental eTable 7).

In the opioid experienced group, 6–12 visits were associated with a lower risk of any opioid use (aRR 0.93, 95% CI 0.90 to 0.97) and chronic opioid use (aRR 0.88, 95% CI 0.83 to 0.94) than those with 1–5 PT visits (online supplemental eTable 7). Having >12 PT visits compared with 1–5 PT visits was not associated with any opioid use (aRR 1.01, 95% CI 0.98 to 1.05) or chronic opioid use (aRR 0.97, 95% CI 0.91 to 1.03) (online supplemental eTable 7).

For PT type, active PT was associated with lower risk of any opioid use (aRR 0.92, 95% CI 0.86 to 0.98) but not with chronic opioid use (aRR 0.86, 95% CI 0.72 to 1.02) in the opioid naïve group (online supplemental eTable 8). This was also true in the opioid experienced cohort (online supplemental eTable 8). Sensitivity analysis showed similar results except there was a larger protective effect of active PT for chronic opioid use (aRR 0.77, 95% CI 0.62 to 0.95) in the opioid naïve group (online supplemental eTable 9).

DISCUSSION

In this large real-world cohort study of persons with incident knee OA who receive PT, delayed PT initiation versus early initiation was associated with greater risk of opioid use, irrespective of prior experience with opioids. These results provide support for initiation of PT within 1 month of diagnosis for individuals with knee OA who have been referred to PT as being associated with lower risk of opioid use in the subsequent 12 months. However, it is important to note our findings are generalisable



	Timing	<1	1-<3	3-<6	6-<9	9-12
Opioid Naïve	Subjects, n (%)	15,940 (44.4%)	8,816 (24.6%)	5,461 (15.2%)	3,249 (9.1%)	2,433 (6.8%)
	Any Opioid Use, n (%)	1,523 (9.6%)	1,025 (11.6%)	821 (15.0%)	576 (17.7%)	478 (19.6%)
	E-value for effect estimate	-	1.64	2.34	2.85	3.27
	E-value for CI limit closest to null	-	1.43	2.08	2.54	2.92
Opioid Experienced	**Subjects, n (%)**	**12,694 (40.5%)**	**7,941 (25.3%)**	**5,126 (16.4%)**	**3,185 (10.2%)**	**2,400 (7.7%)**
	Any Opioid Use, n (%)	**3642 (28.7%)**	**2753 (34.7%)**	**2051 (40.0%)**	**1365 (42.9%)**	**1149 (47.9%)**
	E-value for effect estimate	**-**	**1.67**	**1.97**	**2.13**	**2.45**
	E-value for CI limit closest to null	**-**	**1.54**	**1.83**	**1.97**	**2.28**

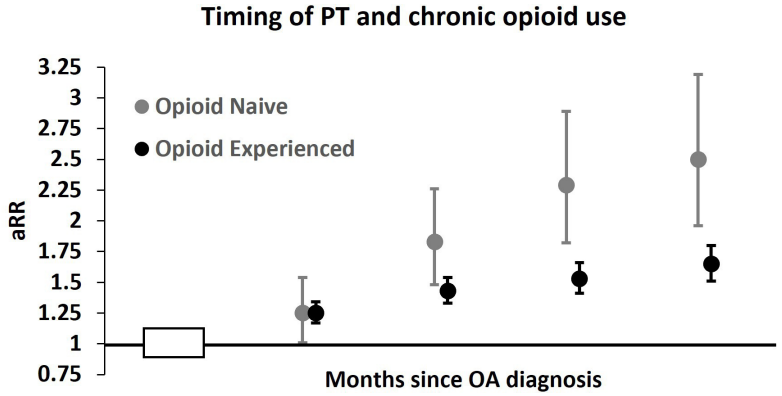
Figure 3 Relation of timing of PT initiation with any opioid use in opioid naïve (grey) and opioid experienced (black) individuals. aRR, adjusted risk ratio; PT, physical therapy.

only to patients with incident knee OA who receive PT and that a majority of the patients typically do not get referred to PT despite clinical practice guidelines.

The association of timing of PT initiation with risk of opioid use was noted in both opioid naïve and experienced groups, with somewhat larger relative effects in those who were opioid naïve, potentially reflecting their lower background risk than those who are opioid experienced. Our findings were robust to adjustment for prior NSAIDs use which may be an indicator of pain severity. Similar findings have been reported in people with new onset low back or neck pain where early initiation of PT care was associated with lower odds of opioid use (effect sizes between 0.15 and 0.84).[21 41–46] In a cohort of people with musculoskeletal pain of different origins, PT initiation within 90 days of the index primary care visit was associated with ~16% lower odds of opioid use in those with knee pain.[47] Our findings (ie, 18%–93% increased risk of any opioid use for later PT initiation) are in line with these previously reported data. In a randomised trial of people with low back pain, early PT initiation compared with usual care was associated with improvements in disability which did not meet minimal important difference criteria.[48] To our knowledge, no randomised trials have specifically investigated early versus late PT in people with knee OA. Our study provides additional important information about the relation of timing of PT to chronic opioid use with increased risk ranging from 25% to 150% depending on the length of delay and prior opioid experience. Our findings were robust even when we used a more stringent definition of chronic opioid use outcome. For a majority of our cohort, PT was initiated more than 1 month after diagnosis; this trend may reflect referral patterns, access to care or patient preferences.[49]

We observed a lower risk of any opioid use with 6–12 PT sessions vs 1–5 PT sessions, but only in the opioid experienced cohort. No further reduction in risk was seen with >12 sessions and in fact, an increased risk of opioid use was seen with >12 sessions in the opioid naïve group. It is possible that requiring >12 PT visits may reflect suboptimal pain management leading to subsequent opioid use. In a meta-analysis of exercise trials in knee OA, more reduction in pain was seen with a greater number of in-person sessions.[50] In contrast, no further benefit was observed for >12 in-person sessions in our study. However, our effect estimates overall were small for the relation of PT dose to opioid use, and clinical meaningfulness of these findings remains unclear. The association of 6–12 sessions of PT with lower risk of chronic opioid use was relatively consistent across both opioid naïve and experienced cohorts. It is worth noting that approximately 45% of patients received ≤6 sessions of PT.

We also observed lower risk of opioid use with active PT interventions in both cohorts. However, the effects observed in our study were small except when active PT was defined as every PT visit having ≥1 active PT code. In this definition of compliant care, active PT was related to a 23% lower risk of chronic opioid use in the opioid naïve cohort. Exercise has beneficial effects in this population.[10 11 51] Real-world data from 16 499 patients with knee or hip OA in Denmark who received a standardised 8-week active intervention (2–3 session of patient education,



	Timing	<1	1-<3	3-<6	6-<9	9-12
Opioid Naïve	Subjects, n (%)	15,940 (44.4%)	8,816 (24.6%)	5,461 (15.2%)	3,249 (9.1%)	2,433 (6.8%)
	Chronic Opioid Use, n (%)	205 (1.3%)	147 (1.7%)	144 (2.6%)	112 (3.4%)	91 (3.7%)
	E-value for effect estimate	-	1.81	3.06	4.01	4.44
	E-value for CI limit closest to null	-	1.11	2.32	3.04	3.33
Opioid Experienced	**Subjects, n (%)**	**12,694 (40.5%)**	**7,941 (25.3%)**	**5,126 (16.4%)**	**3,185 (10.2%)**	**2,400 (7.7%)**
	Chronic Opioid Use, n (%)	**1,418 (11.2%)**	**1,161 (14.6%)**	**940 (18.3%)**	**654 (20.5%)**	**532 (22.2%)**
	E-value for effect estimate	**-**	**1.81**	**2.21**	**2.43**	**2.69**
	E-value for CI limit closest to null	**-**	**1.62**	**1.99**	**2.17**	**2.39**

Figure 4 Relation of timing of PT initiation with chronic opioid use in opioid naïve (grey) and opioid experienced (black) individuals. aRR, adjusted risk ratio; PT, physical therapy.

12 sessions of supervised exercise therapy) across >400 clinics also demonstrated reductions in analgesic use, including opioids (decrease from 7.0% to 4.5%).[52] Our data support and extend these previous findings with an association of active PT interventions with a lower risk of opioid use outside of a highly structured setting with selected patients.

Clinical implications

Guidelines recommend exercise and education, typically delivered as part of PT care, as the first-line intervention for managing pain due to knee OA. However, utilisation of PT for people with knee OA remains low and healthcare providers should consider referral to PT as an early strategy for these patients. In addition, our findings from this large, representative cohort of American adults with incident knee OA suggest that in people referred for PT, strategies to ensure early initiation of PT care are needed to reduce reliance on opioids. Expanded reimbursement of self-referral, telerehabilitation, stepped care treatment protocols and implementation of clinical practice guidelines, are some approaches to improve early access and referral to PT. Also, physicians, insurance providers and PT practices may consider ensuring that 6–12 sessions of PT are provided to people with knee OA. More work is also needed to standardise PT interventions for knee OA and to determine the relation of type of PT interventions and subsequent opioid use.

Limitations

This study was performed using claims data. As such we did not have the ability to validate knee OA definition against diagnostic criteria; however, we combined the claims-based diagnosis with a treatment for the same condition (PT), which would be expected to increase specificity. Also, individuals may have sought care for symptoms related to knee OA prior to the index date. We adjusted for prior healthcare utilisation and NSAIDs use to partly account for this. Given the observational nature of our data, residual confounding is a possibility, though the reported E-values and adjustments for a large number of confounders raise confidence that our finding are unlikely to largely be the result of unmeasured confounding. We did not compare individuals who did and did not receive PT due to concerns with confounding by indication. We did not adjust for access to PT care across different states because regulations regarding access to PT have changed over time and it was not possible to adjust for this variation in our study comprising data from a 15-year period, though we accounted for calendar year to address secular trends. We did not have information on OA severity or clinical outcomes (eg, pain, function); hence, opioid use only serves as a proxy for efficacy of pain management. We used claims data through 2018; lack of substantive changes in OA management guidelines over the recent years and continued evidence of opioid use in this population suggest that our findings are relevant to current practice. We modelled PT timing as a categorical variable and the

effect sizes for future opioid use may be different if PT timing were modelled as a continuous variable. While our cohort was reflective of the racial/ethnic and geographical diversity in the USA, it is unclear if our findings would be generalisable to other countries with different demographic and healthcare utilisation patterns. We also did not have access to data from underinsured or uninsured individuals who typically have a lower socioeconomic status.

In conclusion, we observed that delayed versus early PT initiation after knee OA diagnosis was associated with greater risk of opioid use irrespective of prior experience with opioids. For people with knee OA who are referred for PT, these real-world data provide support for strategies to initiate PT care early. These findings on timing, dose and type of PT interventions may be used by payers and providers for implementing optimal PT interventions to reduce utilisation of opioids in these patients.

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Contributors CP and DK had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. Concept and design: DK, TN, CP, MD, LM, JC and DTF. Acquisition, analysis or interpretation of data: DK, TN, CP, KA, MD, JC, LM and DTF. Drafting of the manuscript: DK, CP and KA. Critical revision of the manuscript for important intellectual content: DK, TN, CP, KA, LM, JC, DTF and MD. Statistical analysis: CP, DK, TN, MD. Obtained funding: DK, TN and DTF. Administrative, technical or material support: DK, MD, DTF and TN. Supervision: DK, TN, DTF and MD.

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Patient consent for publication Not applicable.

Ethics approval Since this study involved analysis of pre-existing, deidentified data, it was exempt from institutional review board review.

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