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**Supplementary Methods**

**Outcomes**

Three indicators of opioid prescribing practices, focusing on persons newly receiving opioid prescriptions, were examined over time.

1) The monthly rate of incident opioid prescriptions. An incident prescription was defined as an opioid prescription fill for a patient who had not filled an opioid prescription in the prior six months. The numerator for the rate included the number of incident prescriptions each month; the denominator included all persons who were currently insured that month without an observed opioid prescription in the previous six months (i.e., opioid naïve persons, the population “at risk” of an incident opioid prescription). Rates were reported per 10,000 person-months (PM).

2) The days’ supply of the incident opioid prescription dispensed. Days’ supply was taken directly from the prescription record.

3) The daily morphine milligram equivalents (MME) of the incident opioid prescription prescribed. The daily MME was calculated based on the prescription’s National Drug Code. First, the total MME of the prescription was calculated by multiplying the strength in milligrams (mg) per unit and the number of units dispensed and an MME conversion factor from CDC tables.1 We then divided the total MME by the days’ supply of the prescription (i.e., the number of days the prescription was intended to last) as recorded in the paid insurance claim. The days’ supply and MME were calculated at the individual level in a person-day-level file prior to aggregation for analyses.

*Control series*

The rate of incident benzodiazepine prescriptions and days’ supply of incident prescriptions were calculated in the same manner as described above.

**Pain indication and cancer history groupings**

Among opioid-naïve patients, trends in opioid prescribing were examined for three distinct pain indication groups based on the apparent type of indication for the initial opioid prescription: 1) postsurgical, 2) acute, and 3) chronic pain. We used a hierarchical algorithm to assign a derived clinical indication for the index opioid prescription, assuming that 1) patients with a surgical indication received an opioid prescription related to that surgery, 2) patients without an indication of surgery who had a diagnosis of acute pain received an opioid prescription related to the acute pain diagnosis, and 3) patients without evidence of surgery or acute pain who had a chronic pain diagnosis received the prescription for the chronic pain condition.

Postsurgical pain was defined as patients undergoing invasive surgery as classified by the Healthcare Cost and Utilization Project (HCUP) using Current Procedural Terminology (CPT) codes.2 A new opioid prescription was determined to be associated with an invasive surgery if it was billed to insurance ≤14 days before the date of outpatient surgery or first day of an inpatient stay for an inpatient surgery event (presurgical), or if the first opioid prescription was billed to insurance ≤14 days after the date of outpatient surgery or final day of an inpatient stay for an inpatient surgery event (postsurgical). Presurgical prescriptions ≤14 days before an invasive surgery were assumed to be intended for management of postsurgical pain.

Both acute and chronic pain were defined using International Classification of Diseases, 9th Revision (ICD-9-CM) and 10th Revision (ICD-10-CM), Clinical Modification (**Supplementary Tables 2 & 3**).3–6 A new opioid prescription was determined to be associated with an acute pain diagnosis if it was billed to insurance ≤14 days after the acute pain diagnosis; a new opioid prescription was determined to be associated with a chronic pain diagnosis if it was billed to insurance ≤14 days after the chronic pain diagnosis.

Approximately 45% (mean: 5,158; range: 3,465–6,663) of new opioid prescriptions overall per month did not meet any of the above three criteria and were therefore excluded from analyses.

Trends for each of these pain indication groups were also examined separately for persons *with a history of cancer* and those *without a history of cancer*. A history of a malignant cancer was defined as a diagnosis of cancer using International Classification of Diseases, 9th Revision (ICD-9-CM) and 10th Revision (ICD-10-CM), Clinical Modification, excluding 1) benign neoplasm, 2) non-melanoma skin cancer, 3) neoplasm of uncertain or unspecified behavior, and 4) carcinoma in situ. This definition uses an all-available lookback, meaning that each person’s entire insurance history was reviewed for presence of cancer codes*.* Cancer history was treated as a time-varying stratification variable. Incident prescriptions were assigned to the cancer history stratum if the patient had a cancer indication before the date of prescription and were assigned to the no cancer history stratum if the patient never had a cancer indication or only had their first cancer indication after the prescription date. The denominator (person-time at risk) was separated in any given month into those who had never had a cancer indication as of that month and those who have had a cancer indication as of that month. The month in which a cancer indication occurred was evenly divided between the two strata.

**Statistical analyses**

*Controlled interrupted time series analysis*

To build our time series ARIMA models, we examined the need for differencing, autoregressive (AR) and moving average (MA) parameters, and the lag order of each parameter for seasonality.7,8 We performed white noise diagnostics by examining time series plots of the data and autocorrelation function plots and statistics of the residuals for each model. When needed, we compared candidate models (with the same timeframe) using AIC to assess model fit. Our final models for the outcome new opioid prescription rates included a first-order MA component (q = 1) with a seasonal lag of eight months. Our final models examining the outcome of mean days’ supply included a second-order AR component (p = 2).

The model for the CITS analyses is as follows:

outcomet = β0 + β1(timet)

+ β2(initiative level) + β3(initiative trendt)

+ β4(legislation level) +β5(legislation trendt)

+ β6(group)

+ β7(group x timet)

+ β8(group x initiative level) + β9(group x initiative trendt)

+ β10(group x legislation level) + β11(group x legislation trendt) + εt,

where *time* (t) is a continuous variable representing months from January 2012 through August 2018, ranging from 1 to 80; *initiative level* and *legislation level* are dichotomous variables indicating time before (0) and after (1) each policy change; *initiative trend* and *legislation trend* are continuous variables set to 0 before the respective policy change and time in months after each policy change; *group* is a dichotomous variable set to 0 for benzodiazepine prescriptions (the control series) and 1 for opioid prescriptions; *group x time*, *group x initiative level*, and *group x legislation level* are dichotomous product terms between the respective variables; and *group × initiative trend* and *group x legislation trend* are product terms between the respective variables, resulting in continuous variables set to zero for a) the entire benzodiazepine group and b) the time before each respective policy change for the opioid group, or to the time in months after each policy change for the opioid group only.

With this specification, β0 through β5 describe benzodiazepine prescribing patterns where β0 estimates the monthly benzodiazepine outcome at baseline; β1 estimates the pre-medical board initiative time trend of the benzodiazepine outcome; β2 and β4 estimate the absolute change in benzodiazepine outcome immediately after the enactment of the medical board initiative and legislation, respectively; and β3 and β5 estimate the change in trend in the benzodiazepine outcome after each policy.

The remaining terms, β6 through β11, then estimate the opioid level, trend, changes in level, and changes in trend before and after each policy, controlling for the benzodiazepine time trend. Thus, β6 represents the pre-medical board initiative difference between opioid and benzodiazepine prescription outcomes;β7 represents the pre-medical board initiative difference in trend between opioid and benzodiazepine prescription outcomes; β8 and β10 estimate the difference in absolute change in outcome immediately after the enactment of each policy (medical board initiative and legislation, respectively) between opioid and benzodiazepine prescriptions; and β9 and β11 estimate the difference in trend change of the outcome for each policy between opioid and benzodiazepine prescriptions.

*Single-series interrupted time series analysis*

For opioid prescription rates and days’ supply outcomes analyzed using ARIMA models for a single-series ITS analysis without a control group, we built our models according to the procedures described above in CITS analyses. Our final models for the outcome new opioid prescription rates included a first-order AR component (p = 1) with a seasonal lag of twelve months. Our final models examining the outcome of mean days’ supply included a first-order AR component (p = 1). The opioids MME outcome did not require additional parameters. The model for these analyses is as follows:

outcomet = β0 + β1(timet)

+ β2(initiative level) + β3(initiative trendt)

+ β4(legislation level) +β5(legislation trendt) + εt,

where *time (t)* is a continuous variable representing months since January 2012; *initiative level* and *legislation level* are dichotomous variables indicating time before and after each policy change; and *initiative trend* and *legislation trend* are continuous variables set to 0 before the respective policy change and time in years after each policy change. With this specification, β1 estimates the medical board initiative trend of the outcome; β2 and β4 estimate the absolute change in outcome immediately after the enactment of each policy; and β3 and β5 estimate the difference in the pre- and post-policy trajectories of the outcome for each policy.

All analyses of opioid prescribing practices were stratified by pain indication and also by pain indication within cancer status. Benzodiazepine prescribing practices are reported for the full population in prescription rate and days’ supply models. Analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

**Supplementary Results**

**Overall**

In this sample of North Carolina residents privately insured between January 2012 and August 2018, there was a monthly mean of 796,199 persons without an observed opioid prescription in the previous six months (**Supplementary Table 4**). A minority of the study population (mean of 35,195 persons per month) had a previous or current cancer diagnosis. Among those with cancer history, a monthly average of 469 persons with postsurgical pain, 197 persons with acute pain, and 272 persons with chronic pain indications were newly prescribed an opioid. Among those with no cancer history (mean of 761,003 per month), a monthly average of 1,871, 1,595, and 1,820 persons were newly prescribed an opioid for postsurgical, acute, and chronic pain, respectively (**Supplementary Table 4**).

On average per month, 838,340 persons had not received a benzodiazepine prescription in the previous six months and 4,398 persons received a new benzodiazepine prescription. A monthly mean of 197 persons with acute pain and 272 persons with chronic pain received an incident benzodiazepine prescription (**Supplementary Table 4**).

At the start of the study, the rates of new opioid prescriptions were 31.67, 31.11, and 24.52 per 10,000 person-months (PM) among patients with chronic, postsurgical, or acute pain, respectively (**Figure 1**). The rate of new benzodiazepines prescriptions was 57.39 per 10,000 PM. These rates remained stable until 2015, a year before the medical board initiative, when the rates for acute and chronic pain indications and benzodiazepines began a slow decline; postsurgical rates remained stable and started increasing after the initiative. Immediately following the legislative action, there was no notable change in the rate of new opioid prescriptions for acute pain, a small decline for chronic pain, and a larger decline for postsurgical pain; at the same time, the rate of benzodiazepine prescriptions also showed a small decline. Persons with a cancer history had more than double the rates of new opioid prescriptions within all pain groups compared to those with no cancer history (at the start of the study period, postsurgical pain: 158.70 vs. 26.44; chronic pain: 97.63 vs. 29.26; and acute pain: 64.18 vs. 23.07 per 10,000 person months) (**Figure 1**). Compared to the unstratified patterns in the study population, notable differences among persons with a cancer history are evident in the rates of new prescriptions for postsurgical and chronic pains, which appear to fall at the implementation of the state legislation. Among persons with no cancer history, rates of new opioid and benzodiazepine prescriptions were similar to overall (non-stratified) trends throughout the study period (**Figure 1**).

From 2012 to the introduction of the state legislation in 2018, mean days’ supply was fairly constant within all prescription groups, at 16 to 17 days’ supply for benzodiazepines, just under 10 days’ supply among persons who were prescribed opioids for chronic pain, and 4 to 6 days’ supply for those prescribed opioids for postsurgical or acute pain (**Figure 2**). When stratifying mean days’ supply by persons with and without a cancer history, similar visual observations were observed for all pain groups.

At the start of the study, mean daily MME of initial opioid prescriptions ranged from 59.42 for postsurgical pain to 36.87 for acute pain and 30.66 for chronic pain, and declined gradually in all groups throughout the study period (**Figure 3**). Persons with a cancer history and those without such history experienced trends in daily MME that were very similar to the unstratified analysis.

**Sensitivity Analysis**

When advancing the start date of the legislative action by three months to align with the date of the insurer’s internal policy, an immediate sharp decline in days’ supply of initial opioid prescriptions was observed in persons with chronic pain overall and by cancer status, relative to benzodiazepines (overall cRD: -3.39 [95% CI: -4.18, -2.61]; history of cancer cRD: -3.01 [95: CI: -4.41, -1.61]; no history of cancer cRD: -3.49 [95% CI: -4.28, -2.70] mean days’ supply), with slight to no declines observed in other pain groups immediately after policy implementation (postsurgical overall cRD: -0.30 [95% CI: -1.11, 0.51]; acute overall cRD: -0.39 [95% CI: -1.19, 0.42] mean days’ supply) (**Supplementary Table 5**).

**Supplementary Table 1. Prescription opioids**

|  |
| --- |
| **Opioid Ingredient** |
| Codeine  |
| Dihydrocodeine  |
| Fentanyl |
| Hydrocodone |
| Hydromorphone |
| Morphine |
| Oxycodone |
| Oxymorphone |
| Pentazocine |
| Propoxyphene |
| Tapentadol |
| Tramadol |

Excluding formulations used to treat cough, cold, and allergies. This includes opioids in combination with: chlorpheniramine, gauifenesin, bromodiphenhydramine, pseudoephedrine, brompheniramine, calcium, pryilamine, phenylpropanolamine, phenylephrine, promethazine, dexbrompheniramine, diphenhydramine, chlorcyclizine, terpin, phosphate/guaifenesin, triprolidine, homatropine, carbinoxamine.

**Supplementary Table 2. ICD-9-CM and ICD-10-CM Diagnostic Codes for Acute Pain**

|  |
| --- |
| **Acute Pain** |
| **ICD-9-CM** | **Description** |  | **ICD-10-CM** | **Description** |
| 282.62 | Sickle cell anemia |  | D57 | Sickle cell anemia |
| 338.11, 338.12, 338.18, 338.19 | Other nervous system disorders |  | G89.11, G89.12, G89.18 | Other nervous system disorders |
| 522.5, 522.7 | Disorders of teeth and jaw |  | K04.6, K04.7 | Disorders of teeth and jaw |
| 574 | Biliary tract disease |  | K80, K87 | Biliary tract disease |
| 577 | Pancreatic disorders (not diabetes) |  | K85-K86 | Pancreatic disorders (not diabetes) |
| 592 | Genitourinary |  | L08.89 | Skin and subcutaneous tissue infections |
| 733 | Pathological fracture |  | M48.5 | Other spondylopathies |
| 800-804, 850-854 | Intracranial injury; skull and face fractures |  | M80, M84.4 | Pathological fracture |
| 805, 807-829 | Fractures |  | M84.75, M99.1, S00-S99, T08, T14-T19, T71, T73, T74.01-T74.02, T75.4, T79 | Injury |
| 830-839 | Joint disorders and dislocations; trauma-related |  | T20-T28, T30-T32 | Burns\*\* |
| 840-848 | Sprains and strains |  | N13.9, N13.2, N20, N22 | Genitourinary\*\* |
| 860-869, 900-904, 925-929 | Crushing injury or internal injury |  | R52 | Pain, not elsewhere classified |
| 870-897 | Open wounds |  | V00-V99, W00-W99, X00-X99, Y00-Y38 | E codes |
| 910-924 | Superficial injury; contusion |  |  |  |
| 930-939, 951-951, 953-959 | Other injuries and conditions due to external causes |  |  |  |
| 940-949 | Burns |  |  |  |
| 806, 952 | Spinal cord injury |  |  |  |
| E800-E999 | E codes |  |  |  |

**Supplementary Table 3. ICD-9-CM and ICD-10-CM Diagnostic Codes for Chronic Pain**

| **Chronic Pain** |
| --- |
| **ICD-9-CM** | **Description** |  | **ICD-10-CM** | **Description** |
| 307.81 | Miscellaneous mental health disorders |  | A18.01, A18.02 | Tuberculosis of other organs |
| 338.21, 338.22, 338.28, 338.29, 338.4 | Other nervous system disorders |  | A52.16 | Late syphilis |
| 346.0-346.5, 346.7-346.9 | Headache, migraine |  | E08.610, E08.618, E09.610, E09.618, E10.610, E10.618, E11.610, E11.618 | Diabetes mellitus with complications |
| 346.6 | Acute cerebrovascular disease |  | G43, G44.209 | Headache, including migraine |
| 710, 725-726, 727-729 | Other connective tissue disease |  | G89.21, G89.22, G89.28, G89.29, R26.2 | Other nervous system disorders |
| 711 | Infective arthritis and osteomyelitis |  | M00.00, M01, M02.1, M02.3-M02.9 | Infective arthritis and osteomyelitis |
| 712 | Gout |  | M02.0, M02.2, M12.1, M13, M14.6, M14.8, M36.1-M36.4, R29.4 | Other non-traumatic joint disorders |
| 713, 716, 718.1-718.9, 719 | Other non-traumatic joint disorders |  | M04.2, M04.8, M04.9 | Immunity disorders |
| 714-715, 720.0 | Rheumatoid arthritis and osteoarthritis |  | M05-M08, M12, M14.6, M14.8, M15-M19, M45, M48.8 | Rheumatoid arthritis and osteomyelitis |
| 716.1, 717-718 | Joint disorders and dislocations, trauma-related |  | M11 | Gout |
| 718.4 | Other acquired deformities |  | M12.5, M22, M23, M24.0-M24.3, M24.6-M24.9, M43.3-M43.5 | Joint disorders and dislocations; trauma-related |
| 720.1, 721-724 | Spondylosis; intervertebral disc disorders; other back problems |  | M20.1, M20.6 | Acquired foot deformities |
| 727.1 | Acquired foot deformities |  | M24.5, M43.8X9 | Other acquired deformities |
|  |  |  | M32-M34, M35, M36.0, M36.8, M60-M62, M63.8, M65-M67, M75-M79, R25.2, R29.898 | Systemic lupus and connective tissue disorders |
|  |  |  | M43.2, M48.0-M48, M49.8, M50, M51, M53, M54, M62.830, M96, M99.2 | Spondylosis; intervertebral disc disorders, other back problems |
|  |  |  | Q68.6 | Other congenital anomalies |

**Supplementary Table 4. Number of monthly insured prescription opioid- or benzodiazepine- naïve persons and incident prescriptions, by pain indication overall and within cancer status, from a single North Carolina provider of private health insurance, January 2012–August 2018**

|  |  |  |
| --- | --- | --- |
| **Categories per month** | **Number of prescription opioid or benzodiazepine naïve persons per month** | **Number of new prescriptions per month** |
| **Mean (Range)** | **Mean (Range)** |
| **Opioid prescriptions** |  |  |
| Overall | 796,199 (711,440–905,453) |  |
| Postsurgical pain |  | 2,340 (1,909–3,399) |
| Acute pain |  | 1,792 (1,143–2,290) |
| Chronic pain |  | 2,092 (1,307–2,660) |
|  |  |  |
| History of cancer | 35,195 (25,709–42,387) |  |
| Postsurgical pain |  | 469 (347–669) |
| Acute pain |  | 197 (145–261) |
| Chronic pain |  | 272 (178–361) |
|  |  |  |
| No history of cancer | 761,003 (676,278–867,705) |  |
| Postsurgical pain |  | 1,871 (1,504–2,792) |
| Acute pain |  | 1,595 (998–2,040) |
| Chronic pain |  | 1,820 (1,106–2,327) |
|  |  |  |
| **Benzodiazepine prescriptions** |  |  |
| Overall  | 838,340 (746,499–959,345) | 4,398 (3,352–5,453) |

**Supplementary Table 5. Association of a statewide initiative and an insurance reimbursement policy on mean days’ supply of initial opioid prescriptions, by pain indication overall and within cancer status – controlled ITS**

|  | **pre-Medical Board Initiative** | **post-Medical Board** **Initiative** | **post-Reimbursement** **Policy** |
| --- | --- | --- | --- |
| **Outcomes**a | **Trend**b**(95% CI)** | **Absolute difference**c**(95% CI)** | **Change in trend**b,d**(95% CI)** | **Absolute difference**c**(95% CI)** | **Change in trend**b,d**(95% CI)** |
|  | β7 | β8 | β9 | β10 | β11 |
| **Mean days’ supply** |  |  |  |  |  |
|  |  |  |  |  |  |
| **Overall** |  |  |  |  |  |
| Postsurgical pain | 0.16 (0.05, 0.27) | 0.45 (-0.02, 0.92) | -0.23 (-0.61, 0.15) | -0.30 (-1.11, 0.51) | -0.75 (-3.61, 2.11) |
| Acute pain | 0.05 (-0.05, 0.15) | 0.26 (-0.18, 0.70) | 0.02 (-0.33, 0.37) | -0.39 (-1.19, 0.42) | -0.64 (-3.41, 2.14) |
| Chronic pain | 0.13 (0.05, 0.21) | 0.40 (0.04, 0.76) | -0.40 (-0.68, -0.12) | -3.39 (-4.18, -2.61) | -0.14 (-2.81, 2.52) |
|  |  |  |  |  |  |
| **History of cancer** |  |  |  |  |  |
| Postsurgical pain | 0.16 (0.04, 0.27) | 0.55 (0.06, 1.05) | -0.26 (-0.65, 0.13) | -0.08 (-0.98, 0.81) | -1.20 (-4.31, 1.92) |
| Acute pain | 0.06 (-0.07, 0.19) | 0.37 (-0.21, 0.95) | 0.03 (-0.43, 0.49) | -0.54 (-1.65, 0.57) | -1.15 (-4.95, 2.66) |
| Chronic pain | 0.06 (-0.08, 0.19) | 0.65 (0.02, 1.28) | -0.39 (-0.87, 0.10) | -3.01 (-4.41, -1.61) | -1.35 (-6.09, 3.39) |
|  |  |  |  |  |  |
| **No history of cancer** |  |  |  |  |
| Postsurgical pain | 0.16 (0.05, 0.27) | 0.43 (-0.04, 0.90) | -0.23 (-0.60, 0.15) | -0.36 (-1.17, 0.46) | -0.62 (-3.49, 2.26) |
| Acute pain | 0.04 (-0.06, 0.14) | 0.25 (-0.19, 0.69) | 0.01 (-0.33, 0.35) | -0.35 (-1.15, 0.46) | -0.56 (-3.34, 2.22) |
| Chronic pain | 0.14 (0.06, 0.22) | 0.36 (-0.01, 0.72) | -0.40 (-0.68, -0.11) | -3.49 (-4.28, -2.70) | 0.12 (-2.57, 2.81) |

Abbreviations: Medical Board Initiative = Safe Opioid Prescribing Initiative; Reimbursement Policy = Insurer policy enacted in response to the Strengthen Opioid Misuse Prevention Act; CI = confidence interval.

1. New prescription opioid patient population includes person-months where the individual has been insured continuously for >=6 months and has no opioid prescription in the prior 6 months.
2. Trends calculated per year.
3. Absolute difference in opioid prescribing relative to benzodiazepine prescribing.
4. Change in trend in opioid prescribing relative to benzodiazepine prescribing.

**Supplementary Table 6. Final model Akaike Information Criterion (AIC) results**

|  |  |  |  |
| --- | --- | --- | --- |
| **Final model** | **Single-series ITS****AICa,b** | **Controlled ITS AICb,c** | **Sensitivity analysis AICb,c** |
| **Prescribing rate** |  |  |  |
| **Overall** |  |  |  |
| Postsurgical pain | 319.8261 | 789.3577 | – |
| Acute pain | 273.3665 | 753.1439 | – |
| Chronic pain | 296.9805 | 727.9079 | – |
|  |  |  |  |
| **History of cancer** |  |  |  |
| Postsurgical pain | 592.9414 | 1114.644 | – |
| Acute pain | 510.6515 | 966.0117 | – |
| Chronic pain | 521.5854 | 958.3704 | – |
|  |  |  |  |
| **No history of cancer** |  |  |  |
| Postsurgical pain | 303.329 | 775.4308 | – |
| Acute pain | 266.0745 | 749.0416 | – |
| Chronic pain | 288.8767 | 726.8128 | – |
|  |  |  |  |
| **Mean days’ supply** |  |  |  |
| **Overall** |  |  |  |
| Postsurgical pain | -120.294 | 9.854629 | 10.78294 |
| Acute pain | -75.4956 | 20.49776 | 15.50271 |
| Chronic pain | 94.21092 | 144.9896 | 68.08934 |
|  |  |  |  |
| **History of cancer** |  |  |  |
| Postsurgical pain | -29.217 | 43.2497 | 46.83832 |
| Acute pain | 57.65746 | 113.7941 | 109.7227 |
| Chronic pain | 169.4638 | 261.7904 | 236.247 |
|  |  |  |  |
| **No history of cancer** |  |  |  |
| Postsurgical pain | -108.54 | 12.54672 | 12.47365 |
| Acute pain | -65.4489 | 23.77832 | 19.44019 |
| Chronic pain | 96.81897 | 148.598 | 68.79801 |
|  |  |  |  |
| **Mean daily MME** |  |  |  |
| **Overall** |  |  |  |
| Postsurgical pain | 230.6742 | – | – |
| Acute pain | 148.6881 | – | – |
| Chronic pain | 117.7825 | – | – |
|  |  |  |  |
| **History of cancer** |  |  |  |
| Postsurgical pain | 276.4558 | – | – |
| Acute pain | 313.5634 | – | – |
| Chronic pain | 251.4687 | – | – |
|  |  |  |  |
| **No history of cancer** |  |  |  |
| Postsurgical pain | 250.0172 | – | – |
| Acute pain | 158.8155 | – | – |
| Chronic pain | 129.4726 | – | – |

1. N=80 observations
2. AIC values do not include log determinant
3. N=160 observations with benzodiazepine series

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