Appendix 1 (as supplied by the authors): Supplementary material

Diagnostic codes for exclusions and covariates

Supplementary Table S1. Cancer diagnostic codes for exclusions

Description	ICD codes
ICD-9 codes:	
Malignant neoplasm of lip, oral cavity, and pharynx	140–149
Malignant neoplasm of digestive organs and peritoneum	150-159
Malignant neoplasm of respiratory and intrathoracic organs	160-165
Malignant neoplasm of bone, connective tissue, skin, and breast	170-175
Kaposi's sarcoma	176
Malignant neoplasm of genitourinary organs	179-189
Malignant neoplasm of other and unspecified sites	190-199
Malignant neoplasm of lymphatic and hematopoietic tissue	200-208
Neuroendocrine tumors	209
ICD-10 codes:	
Malignant neoplasms of lip, oral cavity and pharynx	C00-C14
Malignant neoplasms of digestive organs	C15-C26
Malignant neoplasms of respiratory and intrathoracic organs	C30-C39
Malignant neoplasms of bone and articular cartilage	C40-C41
Melanoma and other malignant neoplasms of skin	C43-C44
Malignant neoplasms of mesothelial and soft tissue	C45-C49
Malignant neoplasm of breast	C50
Malignant neoplasms of female genital organs	C51-C58
Malignant neoplasms of male genital organs	C60-C63
Malignant neoplasms of urinary tract	C64-C68
Malignant neoplasms of eye, brain and other parts of central nervous system	C69-72
Malignant neoplasms of thyroid and other endocrine glands	C73-C75
Malignant neoplasms of ill-defined, secondary and unspecified sites	C76-C80
Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue	C81-C96

Supplementary Table S2. Chronic non-cancer pain covariates

Chronic pain condition	Diagnostic codes (ICD-9, ICD-10)	Definition (algorithm)
Nociceptive pain:		
Mechanical neck and back problems (excluding low back pain)	ICD-9: 721.0, 721.1, 721.2, 721.3, 721.4, 721.5, 721.6, 721.7, 721.8, 721.9, 722.0, 722.1, 722.2, 722.3, 722.4, 722.5, 722.6, 722.7, 722.8, 722.9, 723.0, 723.1, 723.2, 723.3, 723.4, 723.5, 723.7, 723.8, 723.9, 737.1, 737.2, 738.2, 738.4, 738.5, 739.1, 739.2, 739.3, 739.4, 756.1, 846.0, 846.1, 846.2, 846.3, 846.8, 846.9, 847.0, 847.1, 847.2, 847.3, 847.9 ICD-10: M47, M48.1, M48.2, M48.3, M48.9	>=1 healthcare encounter with any of the ICD codes listed during previous 365 days [Adapted from an algorithm created by Lavis et al, 1998,[7] and validated by Lacasse et al, 2015][8]
Low back pain, mechanical	ICD-9: 724.0, 724.1, 724.2, 724.3, 724.5, 724.6, 724.8, 724.9, ICD-10: M43.2, M43.5, M48.0, M53.2, M53.8, M53.9, M54.5	>=1 healthcare encounter with any of the ICD codes listed during previous 365 days [Adapted from an algorithm validated by Lacasse et al, 2015]
Osteoarthritis	ICD-9: 715.00–715.99 ICD-10: M15, M16, M17, M18, M19	>=1 hospital admission or >=3 physician visits with any of the ICD codes listed during previous 365 days [Adaptation of an algorithm of Harrold et al, 2000,[9] who tested >=3 ambulatory visits]
Rheumatoid arthritis	ICD-9: 714 ICD-10: M05-M06	>=1 hospital admission or >=3 physician visits with any of the ICD codes listed during previous 365 days [Adaptation of algorithms of Widdifield et al, 2013,[10] who tested 1 hospitalization ever as one algorithm and >=3 physician visits as another algorithm]
Neuropathic pain:		
Diabetic neuropathy	ICD-9: 250.6, 357.2 ICD-10: E10.4, E11.4	>=1 hospital admission or >=2 physician visits with any of the ICD codes listed during previous 365 days [Cf. Dworkin et al, 2010;[11] Berger et al, 2003;[12] Kostev et al, 2014][13]
Peripheral neuropathy (excluding diabetic neuropathy)	ICD-9: 354.5, 356.0, 357.0, 357.1, 357.3, 357.4, 357.5, 357.6, 357.7, 357.8, 357.9 ICD-10: G58.7, G60.0, G61.0, G61.9, G63, G62.0, G62.1, G62.2, G62.8	>=1 hospital admission or >=2 physician visits with any of the ICD codes listed during previous 365 days [Adaptation of algorithm of Callaghan et al, 2015][14]
Lumbar radiculopathy	ICD-9: 724.4 ICD-10: M54.16	>=1 hospital admission or >=2 physician visits during previous 365 days [Adapted from Schoenfeld et al, 2012][15]

Supplementary Table S3. Diagnostic codes for other covariates

| Description	Subcategory (if applicable)	ICD codes
Opioid use disorder		ICD-9: 304.0 ICD-10: F11
Alcohol dependence or abuse		ICD-9: 303 ICD-10: F10.1, F10.2
Psychiatric illness	Depression	ICD-9: 311, 296.2, 296.3 ICD-10: F32, F33
	Bipolar disorder/ mixed mania	ICD-9: 296.0, 296.1, 296.4, 296.9 ICD-10: F31
	Schizophrenia	ICD-9: 295 ICD-10: F20
	Personality disorders	ICD-9: 301 ICD-10: F60
	Other psychosis	ICD-9: 297 - 299 ICD-10: F21 – F29

Description of statistical analyses with additional detail

We estimated changes in monthly opioid analgesic medication use following the introduction of the standards and guidelines as absolute differences, using a generalized linear model with an identity link function and a normal error distribution. We estimated changes in discontinuation, switching or initiation as odds ratios, using generalized linear models with a logistic link function and a binomial error distribution.

Each statistical model included data for patients in the policy cohort and patients in the historical control cohort. We estimated absolute differences or odds ratios for changes to the level and trend of each outcome following the opioid prescribing standards and guidelines among patients in the policy cohort compared to the historical control cohort by including interactions in each model between cohort status (policy cohort vs historical control cohort) with level effect and trend effect variables. Each model included a binary cohort status variable to associate each observation of an individual with the appropriate cohort, which could differ for different observations of the same individual (if the individual entered both cohorts). In addition, models included a binary level effect variable to indicate the post-policy period, and a linear trend effect variable which incremented by one during the post-policy period; the same values were assigned to analogous periods for the historical control cohort. An interaction between cohort status and level effect in the model tested for level changes in drug utilization, which represented a sudden change following the policy. An interaction between cohort status and trend effect in the model tested for trend (slope) changes, which represented a gradual change in drug utilization occurring in each month of the post-policy period. (Figure S1 in the depicts potential level and trend changes following a change in policy.) We modified our approach for the outcome of monthly opioid use by

including a 3-month transition period and using a shorter post-policy period, because days'

supply from prescriptions pre-dating the opioid prescribing standards and guidelines might

carry forward for approximately 3 months and attenuate this measure.

Supplementary Figure S1. Potential changes in prescription drug utilizaton following a change in drug policy
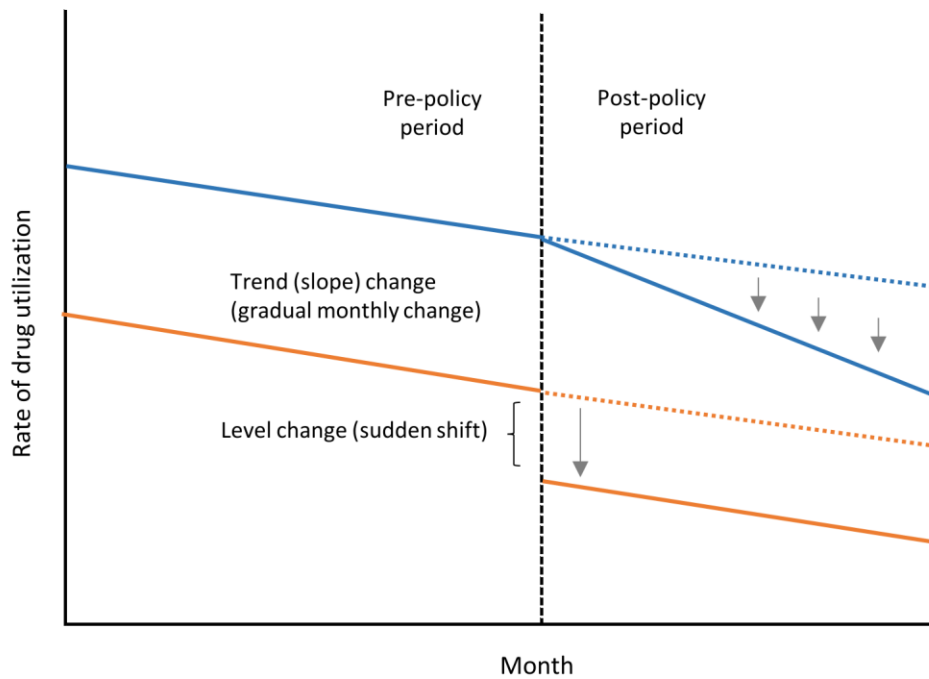
Analyses of concurrent use of opioids and sedative/hypnotic medications

Supplementary Figure S2. Monthly rates of initiation and stopping of concurrent use of opioids and sedative/hypnotic medications, in the policy cohort (PC) vs historical control cohort (HCC).