Opioids and Psychotropic Medications Co-Prescribing for Chronic Non-Cancer Pain Patients in Taiwan Before and After Medication Guideline Changes: An Interrupted Time Series Analysis

EPH17

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KEY MESSAGE

- The 2018 TFDA guideline revision was associated with an immediate reduction in opioid–BZD co-prescribing.
- The effect was not sustained and rebounded within 12 months.
- Increases in several non-BZD psychotropics suggest substitution/ spillover and limited policy durability.

BACKGROUND / OBJECTIVE

CNCP patients on LTOT are often co-prescribed psychotropics, increasing safety risk. Taiwan revised the TFDA LTOT guideline on 4 Dec 2018 to discourage routine opioid–BZD co-prescribing.

Objective: assess the impact on BZD co-prescribing and potential substitution/ spillover to other psychotropics.

METHODS

Data source: Taiwan NHIRD

Study period: Oct 2017–Dec 2019
Analysis window: Jan 2018–Dec 2019
Washout: late 2017

Population: Adults with chronic non-cancer pain receiving newly initiated long-term opioid therapy (LTOT)

Outcomes: Monthly proportion co-prescribed opioids with BZDs, antidepressants, antiepileptics, anxiolytics, sedative-hypnotics, antipsychotics, muscle relaxants, and any psychotropic

Intervention: TFDA guideline revision (4 Dec 2018), modeled at Jan 2019; sensitivity Oct 2018

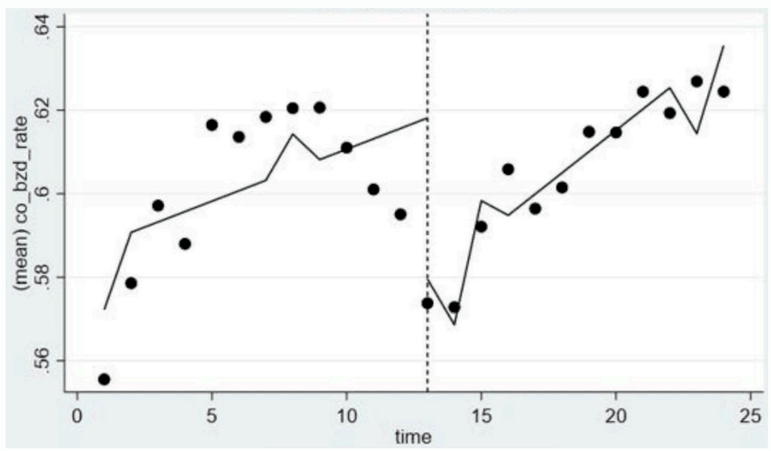
Analysis: Segmented generalized linear interrupted time series with Newey–West robust standard errors

STUDY POPULATION SNAPSHOT

- **22,258** New LTOT recipients
- **127,808** Total visits
- **2018** 61,170 visits
- **2019** 66,638 visits
- **56.6%** Age ≥65 years
- **61.0%** Female

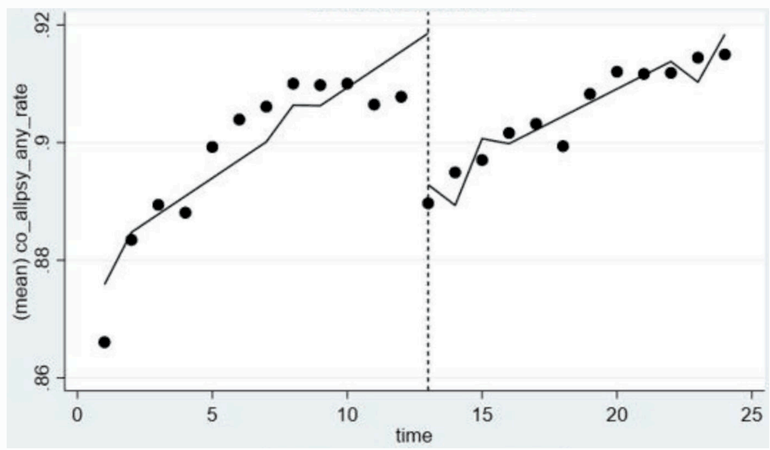
RESULTS: INTERRUPTED TIME SERIES ANALYSIS OF CO-PRESCRIBING RATES

A. Opioids + Benzodiazepines (BZDs) – Primary Policy Target



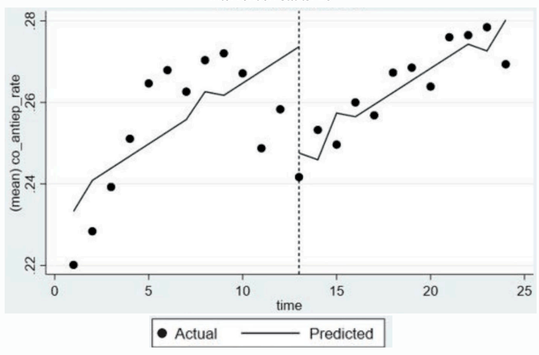
Dashed line indicates intervention (Jan 2019).

H. Opioids + Any Psychotropic – Overall Signal



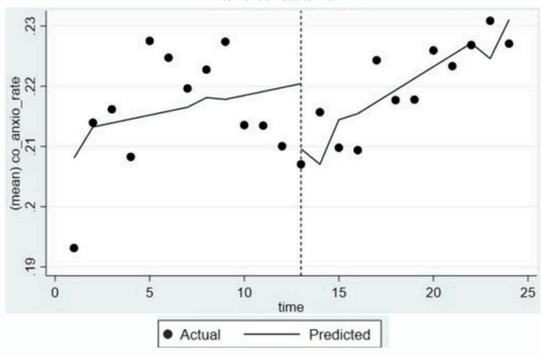
Dashed line indicates intervention (Jan 2019).

B. Opioids + Antiepileptics (non-BZDs)



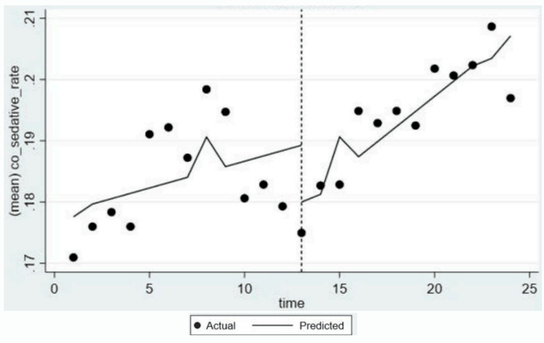
Dashed line indicates intervention (Jan 2019).

C. Opioids + Anxiolytics (non-BZDs)



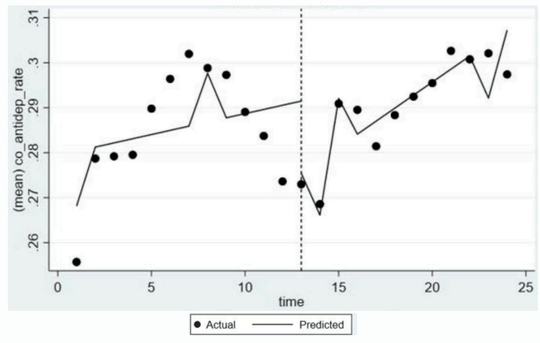
Dashed line indicates intervention (Jan 2019).

D. Opioids + Sedative-Hypnotics (non-BZDs)



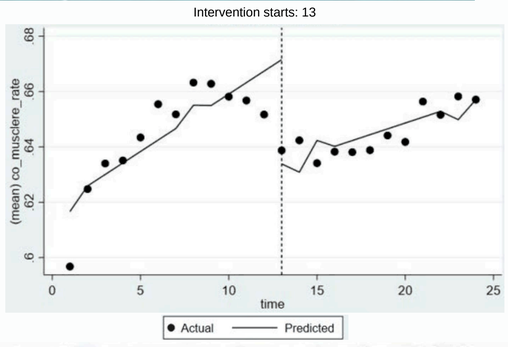
Dashed line indicates intervention (Jan 2019).

E. Opioids + Antidepressants



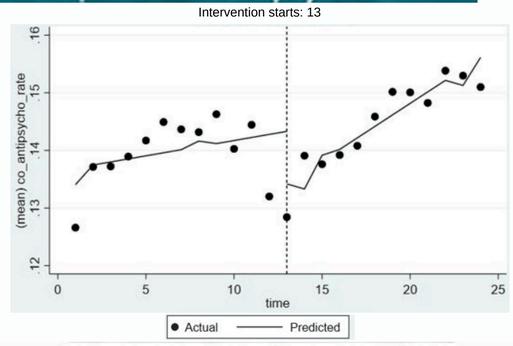
Dashed line indicates intervention (Jan 2019).

F. Opioids + Muscle Relaxants



Dashed line indicates intervention (Jan 2019).

G. Opioids + Antipsychotics



Dashed line indicates intervention (Jan 2019).

ANNUAL CHANGE IN CO-PRESCRIBING RATES

Category	2018 (%)	2019 (%)	Change (pp)
Any psychotropic	86.89	87.26	+0.37
BZDs	54.64	55.21	+0.57
Antidepressants	24.62	25.19	+0.57
Antiepileptics (non-BZDs)	21.36	21.85	+0.49
Sedative-hypnotics (non-BZDs)	16.30	16.69	+0.39
Anxiolytics (non-BZDs)	18.80	19.02	+0.22
Antipsychotics	11.45	11.63	+0.18
Muscle relaxants	60.10	60.30	+0.20

pp = percentage points

SELECTED ITSA ESTIMATES (POST VS PRE)

- **Opioids + BZDs (Primary target):**
  β1 = 0.0025/month; β2 = −0.0386 (95% CI −0.0619, −0.0152);
  β3 = +0.00260/month; post-guideline trend (β1+β3) = 0.0051/month.
- **Opioids + Any psychotropic (Overall):**
  β2 = −0.0257 (95% CI −0.0349, −0.0166);
  post-guideline trend (β1+β3) = 0.0023/month.
- **Opioids + Antiepileptics (non-BZDs):**
  β2 = −0.0261; post-guideline trend = 0.0030/month.
- **Opioids + Antipsychotics:** β2 = −0.0091.
- **Opioids + Muscle relaxants:** β2 = −0.0377.

β1 pre-intervention slope; β2 immediate level change; β3 change in slope.

INTERPRETATION / DISCUSSION

- Immediate reduction in opioid–BZD co-prescribing was observed.
- The effect was not sustained and rebounded within 12 months.
- Increases in several non-BZD psychotropics suggest substitution or spillover.
- Older adults and females remain key groups.

POLICY IMPLICATIONS

- Durable safety gains require more than a single guideline.
- Reinforce medication guidelines.
- CDSS alerts and clinical reminders.
- Pharmacist medication review.
- Academic detailing and provider education.

STRENGTHS / LIMITATIONS

Strengths
- National coverage and large sample.
- Robust ITSA design with Newey–West SEs.
- Subgroup and sensitivity analyses.

Limitations
- No clinical severity or adherence information.
- No direct clinical outcomes.
- Residual confounding.

CONCLUSION

The 2018 TFDA revision produced only a transient reduction in opioid–BZD co-prescribing. Durable safety gains likely require multi-component implementation strategies.

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