

## Supporting Information

**Table S1** Definitions of substance categories, appendicitis, and corresponding ICD-10 codes (WHO)

| Substance Category          | ICD-10 codes              |
|-----------------------------|---------------------------|
| Cannabis                    | F12, T407                 |
| Stimulants (except cocaine) | F15, T436                 |
| Alcohol                     | F10, T510, T518, T519     |
| Sedatives <sup>1</sup>      | F11, F13, T401-T404, T406 |
| Nicotine                    | F17, T652                 |
| Volatile solvents           | F18, T52                  |
| Hallucinogens               | F16, T408, T409           |
| Cocaine                     | F14, T405                 |
| Appendicitis                | K35-K37                   |

<sup>1</sup> Including opioids, sedatives, and narcotics

## Statistical Analysis

### Pre-legalization model selection

We used an interrupted time-series (ITS) design with forecast-based counterfactuals: for each substance, models were trained **exclusively on the pre-legalization periods**, and then used to generate counterfactual trajectories against which observed post-legalization hospitalizations were compared.

To identify the model that best represented the pre-legalization data-generating process, we follow a three-stage workflow: candidate model specification, diagnostic evaluation, and performance-based selection.

#### *Candidate model specification*

For each substance category, weekly hospitalization counts ( $Y_t$ ) were modeled using generalized linear models with a log-link and adolescent population offset. Given potential overdispersion in count data, we included both Poisson and negative binomial (NB) families as candidates. Zero-inflated variants (ZIP and ZINB) were pre-specified as possible choices if the observed proportion of zero weeks exceeded the expectation under the empirical NB model by more than 5 percentage points; however, this criterion was not met for any substance, and thus zero-inflated models were not included in the candidate pool.

$$Y_t \sim \text{Poisson}(\mu_t) \text{ or } \text{NB}(\mu_t, \theta)$$

Here,  $\mu_t$  is the expected number of hospitalizations in the week  $t$ , and  $\theta$  is the dispersion parameter of the negative binomial distribution. The linear predictor was structured to allow for increasing complexity across nested sets of covariates, with each set evaluated both with and without COVID-19 terms. The general model form was:

$$\log \mu_t = \underbrace{\underbrace{\beta_0 + \beta_1 t + \beta_2 Y_{t-1} + \log N_t + f_{\text{season}}(t)}_{\text{Set B: seasonality}} + \overbrace{\beta_{H_1} I_t^{\text{NY}} + \beta_{H_2} I_t^{\text{Songkran}}}^{\text{Set C: holidays}} + \underbrace{\beta_3 I_t^{\text{COVID}} + \beta_4 (t - t_{\text{COVID}}) I_t^{\text{COVID}}}_{\text{COVID terms}}$$

Where  $t$  is epidemiologic week,  $Y_{t-1}$  is the previous week's count (lag-1 term), and  $N_t$  is the mid-year adolescent population (offset). The function  $f_{\text{season}}(t)$  represents within-year seasonality captured using natural splines with six degrees of freedom.  $I_t^{\text{NY}}$  and  $I_t^{\text{Songkran}}$  are indicator variables for major Thai holiday periods (New Year and Songkran, respectively).  $I_t^{\text{COVID}}$  denotes the post-COVID lockdown period beginning July 18, 2021, and  $t_{\text{COVID}}$  is the time in weeks since the lockdown period.

In more intuitive terms, we constructed a nested set of predictors. Set A (trend) included a baseline linear time trend, the lag-1 outcome term to capture short-term dependence, and the population offset. Set B (seasonality) added spline terms to reflect Thailand’s three seasonal cycles. Set C (holidays) further incorporated indicators for the New Year and Songkran periods, which are known to influence some substance-related hospitalization patterns. Finally, we evaluated each of these sets with and without COVID-19 terms, which allows the model to adjust for the abrupt disruption and altered trajectory of admissions following mid-2021. To avoid unstable estimation due to sparse data, candidate specifications with fewer than five events per parameter were excluded.

### *Diagnosis evaluation*

In the second stage, each model specifications were fitted and subjected to diagnostic screening. We assess convergence criteria (positive definite Hessian matrices) and model misspecification tests using DHARMA simulated residuals for uniformity, overdispersion, zero-inflation adequacy, and temporal autocorrelation. Models failing any of these criteria at a conservative threshold ( $p$ -values  $< 0.001$ ) were excluded. Models with borderline results ( $0.001 \leq p < 0.05$ ) were retained for visual inspection and subsequent evaluation. The evaluation result was shown in Table S2-10.

### *Performance-based selection.*

In the third stage, models passing diagnostic screening were tested for their predictive performance. We first ranked candidates by corrected Akaike Information Criterion (AICc) and retained all specifications within 10 AICc units of the model with the lowest AICc. These contended models were then evaluated using rolling-origin cross-validation, with a minimum 104-week training window, a 4-week forecast horizon, and 4-week step increments. The model achieving the lowest out-of-sample negative log-likelihood was selected as the final counterfactual model for each substance. The results of this performance screening, including AICc values, candidate status, cross-validation metrics, and the selected model for each substance, are reported in Table S2-10.

## **Counterfactual Prediction**

For each selected model, we generated counterfactual trajectories using a parametric bootstrap. We drew 1,000 parameter sets from the multivariate normal distribution of the maximum likelihood estimates, resampling dispersion from a log-normal distribution for negative binomial models. For each draw, the weekly series was generated recursively from the first observation ( $t_0$ ) through the end of the study period. At each week  $t$ , the expected mean ( $\mu_t$ ) was computed from the linear predictor combining the observed covariates, the sampled parameters, and the lagged outcome ( $Y_{t-1}$ ). We then sampled  $Y_t \sim \text{Poisson/NB}(\mu_t, \theta)$ , which was in turn carried forward as  $Y_{t-1}$  for the next step. This procedure yielded 1,000 counterfactual paths per substance, with only the post-legalization portions compared against the observed series to estimate policy effects

**Table S2** Diagnostic and Performance screening for cannabis models

| Counterfactual Model |               |                     |           |                |               |              |              | Performance Test      |         |           |                                 |                |   |
|----------------------|---------------|---------------------|-----------|----------------|---------------|--------------|--------------|-----------------------|---------|-----------|---------------------------------|----------------|---|
| Family               | Predictor set | Diagnostic Criteria |           |                |               |              |              | Information Criterion |         |           | Rolling Origin Cross-validation |                |   |
|                      |               | Adequate EPP        | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc                  | ΔAICc   | Candidate | NLL                             | Selected Model |   |
| Poisson              | COVID         | A                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1463.99 | 7.92      | ✓                               | 11.11          | ✗ |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1467.59 | 11.52     | ✗                               | –              | – |
|                      | No COVID      | A                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1464.79 | 8.71      | ✓                               | 10.4           | ✗ |
|                      |               | C                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
| Negative Binomial    | COVID         | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | 1456.37               | 0.3     | ✓         | 10.5                            | ✗              |   |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1456.27 | 0.2       | ✓                               | 10.66          | ✗ |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1460.13 | 4.06      | ✓                               | 10.74          | ✗ |
|                      | No COVID      | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1460.61 | 4.53      | ✓                               | 10.19          | ✓ |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1456.08 | 0         | ✓                               | 10.24          | ✗ |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1459.92 | 3.85      | ✓                               | 10.32          | ✗ |

Abbreviations: COVID, models including COVID-19 period effects; Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods; EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; ✗ indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, ✗ = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation

**Table S3** Diagnostic and Performance screening for stimulant models

| Counterfactual Model |               |                     |           |                |               |              |              | Performance Test      |         |           |                                 |                |   |
|----------------------|---------------|---------------------|-----------|----------------|---------------|--------------|--------------|-----------------------|---------|-----------|---------------------------------|----------------|---|
| Family               | Predictor set | Diagnostic Criteria |           |                |               |              |              | Information Criterion |         |           | Rolling Origin Cross-validation |                |   |
|                      |               | Adequate EPP        | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc                  | ΔAICc   | Candidate | NLL                             | Selected Model |   |
| Poisson              | COVID         | A                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
|                      |               | B                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
|                      |               | C                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
|                      | No COVID      | A                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
|                      |               | B                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
|                      |               | C                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |         |           |                                 |                |   |
| Negative Binomial    | COVID         | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1941.89 | 0         | ✓                               | 14.35          | ✓ |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1950.17 | 8.28      | ✓                               | 14.53          | ✗ |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1954.27 | 12.38     | ✗                               | –              | – |
|                      | No COVID      | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1994.84 | 52.95     | ✗                               | –              | – |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 2005.6  | 63.71     | ✗                               | –              | – |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 2009.84 | 67.95     | ✗                               | –              | – |

Abbreviations: COVID, models including COVID-19 period effects; Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods; EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; ✗ indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, ✗ = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation

**Table S4** Diagnostic and Performance screening for alcohol models

| Counterfactual Model |               |                     |           |                |               |              |              |                       | Performance Test |           |                                 |                |   |
|----------------------|---------------|---------------------|-----------|----------------|---------------|--------------|--------------|-----------------------|------------------|-----------|---------------------------------|----------------|---|
| Family               | Predictor set | Diagnostic Criteria |           |                |               |              |              | Information Criterion |                  |           | Rolling Origin Cross-validation |                |   |
|                      |               | Adequate EPP        | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc                  | ΔAICc            | Candidate | NLL                             | Selected Model |   |
| Poisson              | COVID         | A                   | ✓         | ✓              | X             | X            | ✓            | X                     |                  |           |                                 |                |   |
|                      |               | B                   | ✓         | ✓              | X             | X            | ✓            | X                     |                  |           |                                 |                |   |
|                      |               | C                   | ✓         | ✓              | ✓             | X            | ✓            | X                     |                  |           |                                 |                |   |
|                      | No COVID      | A                   | ✓         | ✓              | X             | X            | ✓            | X                     |                  |           |                                 |                |   |
|                      |               | B                   | ✓         | ✓              | X             | X            | ✓            | X                     |                  |           |                                 |                |   |
|                      |               | C                   | ✓         | ✓              | X             | X            | ✓            | X                     |                  |           |                                 |                |   |
| Negative Binomial    | COVID         | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1897.45          | 41.06     | X                               | –              | – |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1885.02          | 28.62     | X                               | –              | – |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1856.4           | 0         | ✓                               | 13.74          | ✓ |
|                      | No COVID      | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1905.23          | 48.83     | X                               | –              | – |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1899.68          | 43.29     | X                               | –              | – |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1879.28          | 22.88     | X                               | –              | – |

Abbreviations: EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; X indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, X = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation; COVID, models including COVID-19 period effects. Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods.

**Table S5** Diagnostic and Performance screening for sedative models

| Family            | Predictor set | Counterfactual Model |           |                |               |              |              | Performance Test      |               |                                 |       |                |
|-------------------|---------------|----------------------|-----------|----------------|---------------|--------------|--------------|-----------------------|---------------|---------------------------------|-------|----------------|
|                   |               | Diagnostic Criteria  |           |                |               |              |              | Information Criterion |               | Rolling Origin Cross-validation |       |                |
|                   |               | Adequate EPP         | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc                  | $\Delta$ AICc | Candidate                       | NLL   | Selected Model |
| Poisson           | COVID         | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1431.47               | 4.99          | ✓                               | 11.3  | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1426.91               | 0.44          | ✓                               | 11.45 | X              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1430.74               | 4.27          | ✓                               | 11.49 | X              |
|                   | No COVID      | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1428.87               | 2.4           | ✓                               | 9.95  | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1427.36               | 0.89          | ✓                               | 10.1  | X-             |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1431.13               | 4.65          | ✓                               | 10.14 | X              |
| Negative Binomial | COVID         | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1429.34               | 2.86          | ✓                               | 11.2  | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1427.02               | 0.54          | ✓                               | 11.38 | X              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1430.93               | 4.46          | ✓                               | 11.42 | X              |
|                   | No COVID      | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1426.48               | 0             | ✓                               | 9.9   | ✓              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1426.9                | 0.43          | ✓                               | 10.07 | X              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 1430.76               | 4.28          | ✓                               | 10.11 | X              |

Abbreviations: EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; X indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, X = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation; COVID, models including COVID-19 period effects. Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods.

**Table S6** Diagnostic and Performance screening for volatile solvent models

| Family            | Predictor set | Counterfactual Model |           |                |               |              |              | Performance Test      |               |                                 |      |                |
|-------------------|---------------|----------------------|-----------|----------------|---------------|--------------|--------------|-----------------------|---------------|---------------------------------|------|----------------|
|                   |               | Diagnostic Criteria  |           |                |               |              |              | Information Criterion |               | Rolling Origin Cross-validation |      |                |
|                   |               | Adequate EPP         | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc                  | $\Delta$ AICc | Candidate                       | NLL  | Selected Model |
| Poisson           | COVID         | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 761.92                | 3.52          | ✓                               | 6.84 | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 769.6                 | 11.19         | X                               | –    | –              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 773.25                | 14.84         | X                               | –    | –              |
|                   | No COVID      | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 758.41                | 0             | ✓                               | 4.76 | ✓              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 766.31                | 7.9           | ✓                               | 4.91 | X              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 769.9                 | 11.49         | X                               | –    | –              |
| Negative Binomial | COVID         | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 763.78                | 5.37          | ✓                               | 6.58 | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 771.7                 | 13.29         | X                               | –    | –              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 775.41                | 17            | X                               | –    | –              |
|                   | No COVID      | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 760.23                | 1.82          | ✓                               | 4.76 | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 768.37                | 9.96          | ✓                               | 4.91 | X              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 772.01                | 13.61         | X                               | –    | –              |

Abbreviations: EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; X indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, X = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation; COVID, models including COVID-19 period effects. Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods.

**Table S7** Diagnostic and Performance screening for nicotine models

| Counterfactual Model |               |                     |           |                |               |              |              |                       | Performance Test |           |                                 |                |   |
|----------------------|---------------|---------------------|-----------|----------------|---------------|--------------|--------------|-----------------------|------------------|-----------|---------------------------------|----------------|---|
| Family               | Predictor set | Diagnostic Criteria |           |                |               |              |              | Information Criterion |                  |           | Rolling Origin Cross-validation |                |   |
|                      |               | Adequate EPP        | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc                  | ΔAICc            | Candidate | NLL                             | Selected Model |   |
| Poisson              | COVID         | A                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |                  |           |                                 |                |   |
|                      |               | B                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |                  |           |                                 |                |   |
|                      |               | C                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |                  |           |                                 |                |   |
|                      | No COVID      | A                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |                  |           |                                 |                |   |
|                      |               | B                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |                  |           |                                 |                |   |
|                      |               | C                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗                     |                  |           |                                 |                |   |
| Negative Binomial    | COVID         | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1237.27          | 0         | ✓                               | 8.91           | ✗ |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1246.06          | 8.79      | ✓                               | 9.07           | ✗ |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1250.17          | 12.91     | ✗                               | –              | – |
|                      | No COVID      | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1239.84          | 2.57      | ✓                               | 8.55           | ✓ |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1247.64          | 10.38     | ✗                               | –              | – |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓                     | 1251.74          | 14.47     | ✗                               | –              | – |

Abbreviations: EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; ✗ indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, ✗ = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation; COVID, models including COVID-19 period effects. Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods.

**Table S8** Diagnostic and Performance screening for hallucinogen models

| Family            | Predictor set | Counterfactual Model |           |                |               |              |              | Performance Test      |               |                                 |      |                |
|-------------------|---------------|----------------------|-----------|----------------|---------------|--------------|--------------|-----------------------|---------------|---------------------------------|------|----------------|
|                   |               | Diagnostic Criteria  |           |                |               |              |              | Information Criterion |               | Rolling Origin Cross-validation |      |                |
|                   |               | Adequate EPP         | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc                  | $\Delta$ AICc | Candidate                       | NLL  | Selected Model |
| Poisson           | COVID         | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 691.3                 | 0             | ✓                               | 4.8  | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 700.18                | 8.87          | ✓                               | 4.86 | X              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 702.45                | 11.15         | X                               | –    | –              |
|                   | No COVID      | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 691.88                | 0.58          | ✓                               | 4.6  | ✓              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 700.28                | 8.98          | ✓                               | 4.65 | X              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 702.45                | 11.15         | X                               | –    | –              |
| Negative Binomial | COVID         | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 693.39                | 2.08          | ✓                               | 4.8  | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | ✓            | 702.35                | 11.05         | X                               | –    | –              |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | X            |                       |               |                                 |      |                |
|                   | No COVID      | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 693.93                | 2.63          | ✓                               | 4.6  | X              |
|                   |               | B                    | ✓         | ✓              | ✓             | ✓            | X            |                       |               |                                 |      |                |
|                   |               | C                    | ✓         | ✓              | ✓             | ✓            | ✓            | 704.63                | 13.33         | X                               | –    | –              |

Abbreviations: EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; X indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, X = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation; COVID, models including COVID-19 period effects. Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods.

**Table S9** Diagnostic and Performance screening for cocaine models

| Family            | Predictor set | Counterfactual Model |           |                |               |              |              | Performance Test      |               |                                 |      |                |
|-------------------|---------------|----------------------|-----------|----------------|---------------|--------------|--------------|-----------------------|---------------|---------------------------------|------|----------------|
|                   |               | Diagnostic Criteria  |           |                |               |              |              | Information Criterion |               | Rolling Origin Cross-validation |      |                |
|                   |               | Adequate EPP         | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc                  | $\Delta$ AICc | Candidate                       | NLL  | Selected Model |
| Poisson           | COVID         | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 227.77                | 4.3           | ✓                               | 4.21 | X              |
|                   |               | B                    | X         | ✓              | –             | –            | X            |                       |               |                                 |      |                |
|                   |               | C                    | X         | ✓              | –             | –            | X            |                       |               |                                 |      |                |
|                   | No COVID      | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 225.52                | 2.05          | ✓                               | 1.38 | X              |
|                   |               | B                    | X         | ✓              | –             | –            | X            |                       |               |                                 |      |                |
|                   |               | C                    | X         | ✓              | –             | –            | X            |                       |               |                                 |      |                |
| Negative Binomial | COVID         | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 225.94                | 2.46          | ✓                               | 3.98 | X              |
|                   |               | B                    | X         | ✓              | –             | –            | X            |                       |               |                                 |      |                |
|                   |               | C                    | X         | ✓              | –             | –            | X            |                       |               |                                 |      |                |
|                   | No COVID      | A                    | ✓         | ✓              | ✓             | ✓            | ✓            | 223.48                | 0             | ✓                               | 1.35 | ✓              |
|                   |               | B                    | X         | ✓              | –             | –            | X            |                       |               |                                 |      |                |
|                   |               | C                    | X         | ✓              | –             | –            | X            |                       |               |                                 |      |                |

Abbreviations: EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; X indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, X = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation; COVID, models including COVID-19 period effects. Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods.

**Table S10** Diagnostic and Performance screening for appendicitis models

| Counterfactual Model |               |                     |           |                |               |              |              |      | Performance Test      |           |     |                                 |   |
|----------------------|---------------|---------------------|-----------|----------------|---------------|--------------|--------------|------|-----------------------|-----------|-----|---------------------------------|---|
| Family               | Predictor set | Diagnostic Criteria |           |                |               |              |              |      | Information Criterion |           |     | Rolling Origin Cross-validation |   |
|                      |               | Adequate EPP        | Converged | Resid. Uniform | No Dispersion | No Autocorr. | Overall pass | AICc | ΔAICc                 | Candidate | NLL | Selected Model                  |   |
| Poisson              | COVID         | A                   | ✓         | ✓              | ✗             | ✗            | ✓            | ✗    |                       |           |     |                                 |   |
|                      |               | B                   | ✓         | ✓              | ✗             | ✗            | ✓            | ✗    |                       |           |     |                                 |   |
|                      |               | C                   | ✓         | ✓              | ✓             | ✗            | ✓            | ✗    |                       |           |     |                                 |   |
|                      | No COVID      | A                   | ✓         | ✓              | ✗             | ✗            | ✓            | ✗    |                       |           |     |                                 |   |
|                      |               | B                   | ✓         | ✓              | ✗             | ✗            | ✓            | ✗    |                       |           |     |                                 |   |
|                      |               | C                   | ✓         | ✓              | ✗             | ✗            | ✓            | ✗    |                       |           |     |                                 |   |
| Negative Binomial    | COVID         | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓    | 2883.05               | 18.03     | ✗   | –                               | – |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓    | 2865.37               | 0.35      | ✓   | 20.3                            | ✓ |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓    | 2865.02               | 0         | ✓   | 20.37                           | ✗ |
|                      | No COVID      | A                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓    | 2897.96               | 32.94     | ✗   | –                               | – |
|                      |               | B                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓    | 2891.18               | 26.16     | ✗   | –                               | – |
|                      |               | C                   | ✓         | ✓              | ✓             | ✓            | ✓            | ✓    | 2890.99               | 25.97     | ✗   | –                               | – |

Abbreviations: EPP, events per parameter; Resid. Uniform, residuals uniformly distributed; No Dispersion, no evidence of overdispersion; No Autocorr., no residual autocorrelation; ✓ indicates criteria met; X indicates criteria not met; – indicates criteria not tested; AICc, Akaike Information Criterion corrected for small sample sizes; Candidate, models within 10 AICc units of the best model (✓ = Yes, X = No); NLL, Negative Log-Likelihood from rolling-origin cross-validation; COVID, models including COVID-19 period effects. Predictor sets: A, trend models including linear time trends, lag-1 autoregressive terms, and population offsets; B, seasonality models adding natural splines (6 degrees of freedom) for within-year seasonality; C, holiday models incorporating indicators for New Year and Songkran periods.

**Table S11** Estimated hospitalisation due to appendicitis among adolescents aged 10–19 years in the post-legalisation period, comparing observed and counterfactual scenarios.

| Excess admissions   | Excess weekly admissions per week | Relative change       |
|---------------------|-----------------------------------|-----------------------|
| Median [95% PI]     | Median [95% PI]                   | % [95% PI]            |
| -4436 [-11358, 294] | -64.3 [-164.6, 4.3]               | -16.4% [-33.4%, 1.3%] |

PI, Prediction interval from 1,000 bootstrap draws of counterfactual simulations

Hospitalisation due to appendicitis among adolescents aged 10-19 years did not differ statistically from the counterfactual predictions.

**Table S12** Estimated excess adolescent substance-related hospitalisations under alternative pre-legalisation trend assumptions (linear vs natural spline)

| Substance category | Excess weekly admissions per week <sup>1</sup> |                             | ΔNLL (relative to primary model) |
|--------------------|------------------------------------------------|-----------------------------|----------------------------------|
|                    | Median [95% PI]                                |                             |                                  |
|                    | Primary counterfactual model <sup>2</sup>      | Spline counterfactual model |                                  |
| Cannabis           | 25.5 [23.5, 27.2]*                             | 23.0 [8.6, 27.3]*           | +0.3                             |
| Stimulants         | 9.1 [0.3, 15.4]*                               | 9.0 [-0.7, 15.7]            | +1.3                             |
| Alcohol            | 1.4 [-8.1, 6.6]                                | 4.5 [-2.3, 8.1]             | +1.2                             |
| Sedatives          | 1.5 [-0.3, 3.1]                                | 1.4 [-7.3, 4.5]             | +0.4                             |
| Nicotine           | 1.4 [0.4, 2.1]*                                | 2.9 [1.5, 3.6]*             | +0.6                             |
| Volatile solvents  | 0.5 [0.3, 0.7]*                                | 0.6 [-0.4, 0.8]             | +0.3                             |
| Hallucinogen       | 0.5 [0.2, 0.7]*                                | 0.8 [0.0, 1.0]*             | +0.2                             |
| Cocaine            | 0.0 [-0.1, 0.1]                                | 0.1 [-4.4, 0.1]             | +0.5                             |

<sup>1</sup> Excess weekly admissions per week, defined as the difference between the total observed and each total simulated counterfactual admissions, divided by 68 post-legalisation weeks.

PI, Prediction interval from 1,000 bootstrap draws of counterfactual simulations

<sup>2</sup> Primary counterfactual model, refer to the best-fit pre-legalisation models of substance-related hospitalisation as presented in Table 2

NLL, negative log-likelihood

\*Indicate statistical significance where 95% prediction intervals exclude zero.

Replacing the linear time trend with a natural spline with 3 degrees of freedom produced directionally consistent excess cases for six of eight substances; while the estimates for stimulants, volatile solvents become non-significant and should therefore be interpreted with caution. Despite that, the rolling cross-validation using the NLL favoured the simpler linear specification for all substance categories.

**Table S13** Estimated excess stimulant-related hospitalisations under alternative counterfactual assumptions (primary model vs pre-COVID trajectory)

|                                                                  | Primary counterfactual model <sup>2</sup> | Pre-COVID counterfactual model <sup>3</sup> |
|------------------------------------------------------------------|-------------------------------------------|---------------------------------------------|
| Excess weekly admissions per week <sup>1</sup> , median [95% PI] | 9.1 [0.3, 15.4]*                          | -14.3 [-20.1, -9.8]*                        |

<sup>1</sup> Excess weekly admissions per week, defined as the difference between the total observed and each total simulated counterfactual admissions, divided by 68 post-legalisation weeks.

PI, Prediction interval from 1,000 bootstrap draws of counterfactual simulations

<sup>2</sup> Primary counterfactual model, refer to the best-fit pre-legalisation models of substance-related hospitalisation as presented in Table 2

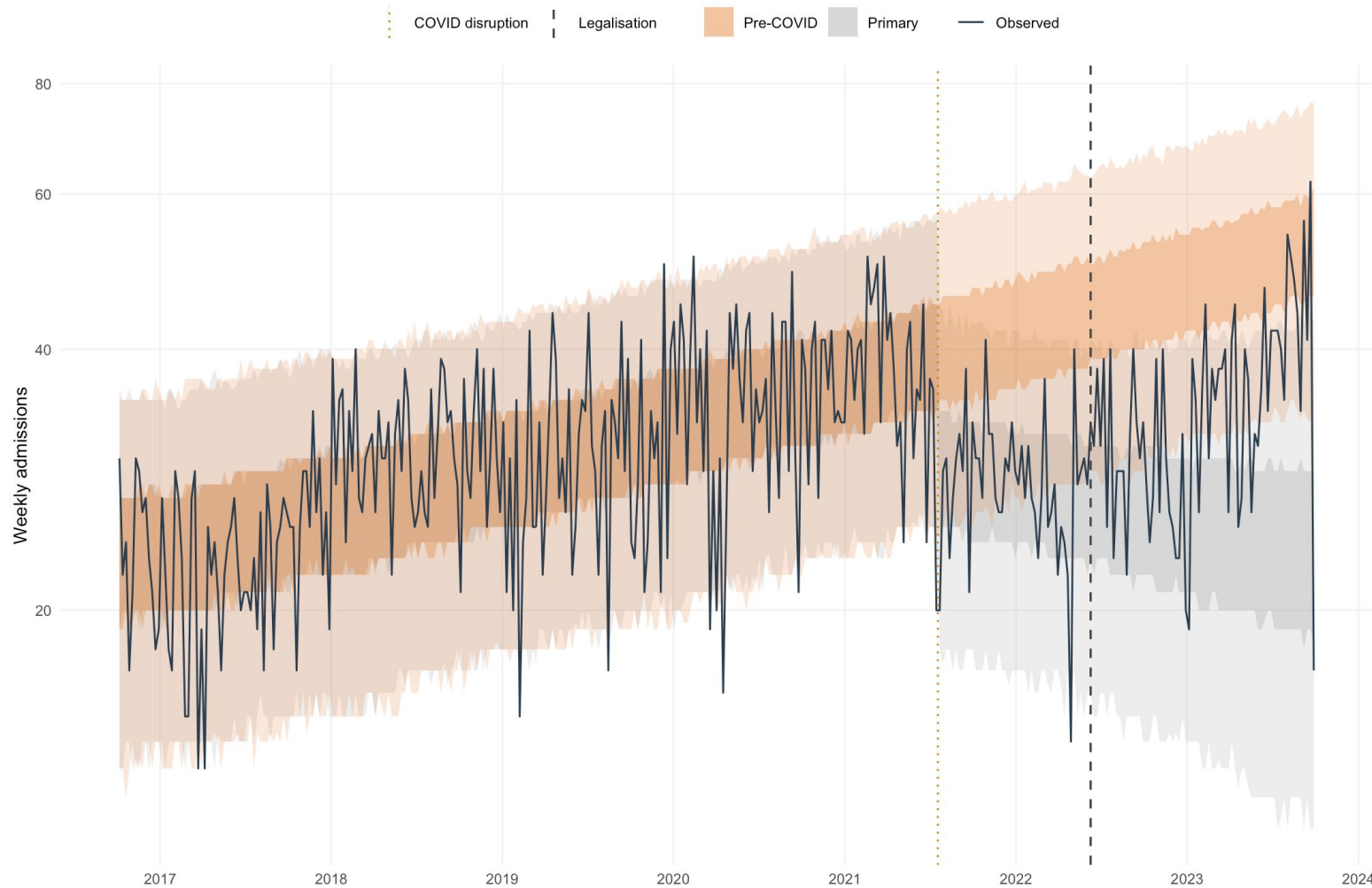
NLL, negative log-likelihood

\*Indicate statistical significance where 95% prediction intervals exclude zero.

<sup>3</sup> Pre-COVID counterfactual trend estimated using pre-COVID data only (1 October 2016 – 17 July 2021)

According to the primary counterfactual model, significant excess stimulant-related hospitalisations were observed during the post-cannabis legalisation period compared with counterfactual predictions. However, additional analysis refitting the stimulant's primary counterfactual model on pre-COVID-19 data only revealed that post-legalisation admissions remained below the pre-pandemic projected trajectory.

## Stimulants



**Figure S1** Counterfactual analysis of stimulant-related hospitalisations. The vertical grey dashed line indicates the legalisation of cannabis (9 June 2022). The vertical orange dotted line indicates the COVID-19 disruption (18 July 2021). The shaded bands represent the 50% and 95% prediction intervals from 1,000 counterfactual simulations based on pre-legalisation data (grey band) and pre-COVID-19 data (orange band). The black solid line represents observed weekly stimulant-related hospitalisation cases across the study period.