Regional Trends in Favipiravir and Steroid Use in the Treatment of COVID-19

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Background

- COVID-19 remains a global concern, as it has not been conquered even 2.5 years after the epidemic began.
- Effective drugs and vaccines have been developed, and the number of severe cases and deaths have greatly decreased.
- However, **developing evidence-based guidelines requires a long time** because a large amount of clinical data is needed.
- Therefore, various treatments are tried in the early stages of epidemics.
- **Standardization of treatment is important because effective treatment must be available everywhere.**

Aims

- Investigate **how steroid and favipiravir have been administered** in patients over time.
- Examine whether there were **regional differences** in their administration trends.
- Analyze how long it would take for effective treatments to become standard.

Methods

- **Data:**
  - Data from COVIREGI-JP [1,2]
  - Patients tested positive for SARS-CoV-2 and received inpatient treatment
  - Moderate to severe patients admitted between April 2020 and June 2021
  - 10 existing regions + Tokyo + Osaka

- **Statistical method:**
  - Changes in the **proportion of the drugs administered patients** fitted to logistic curve

$$p(m) = \frac{1}{1 + \exp(-(\alpha + \beta\, m))}$$

$p(m)$: the proportion of the drug administered in each month m

Results

Population per wave	1st	2nd	3rd	4th
Patients	1418	1792	4938	2491
Facilities	265	286	340	156

Figure 1. Regional differences in each wave
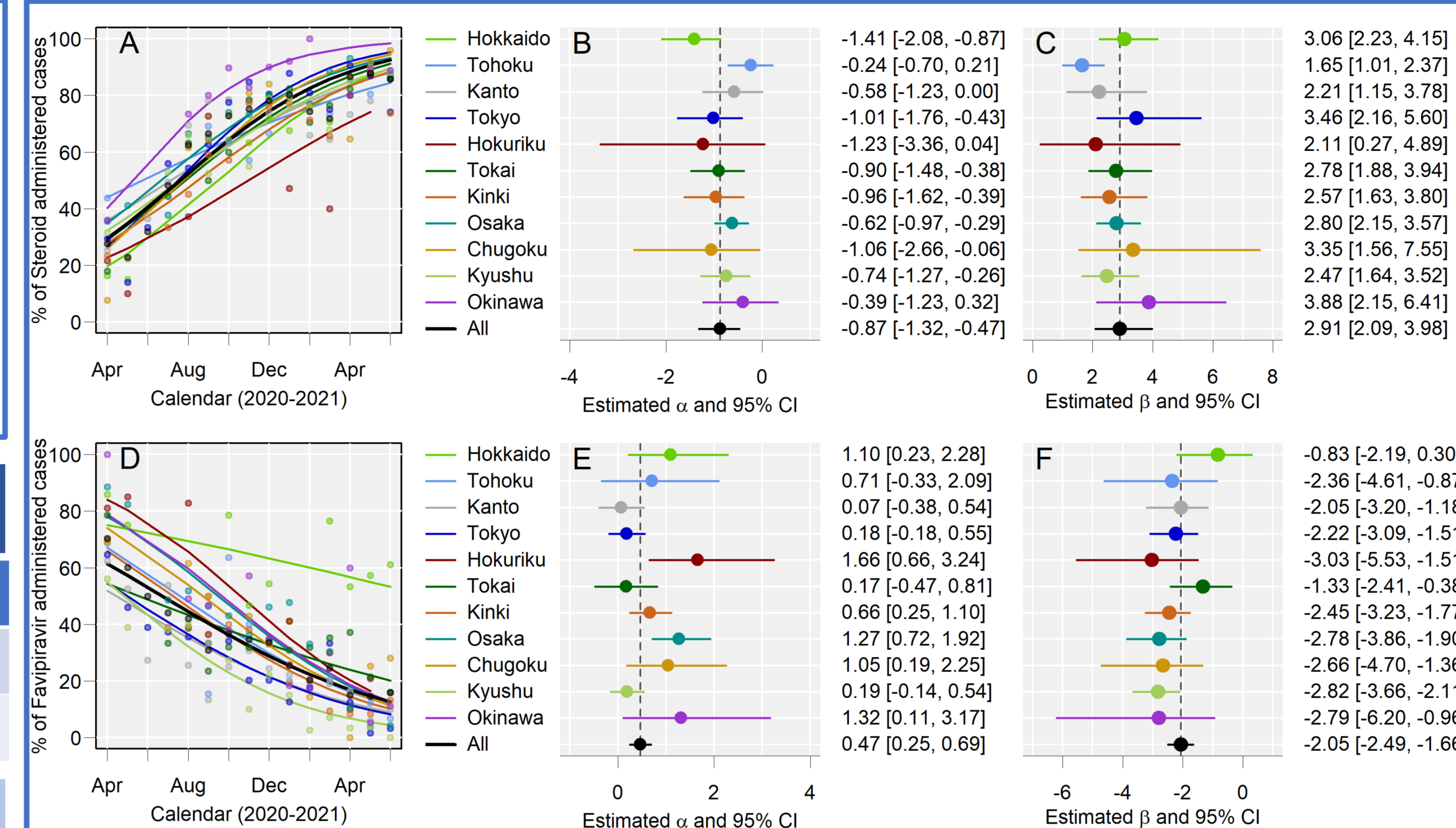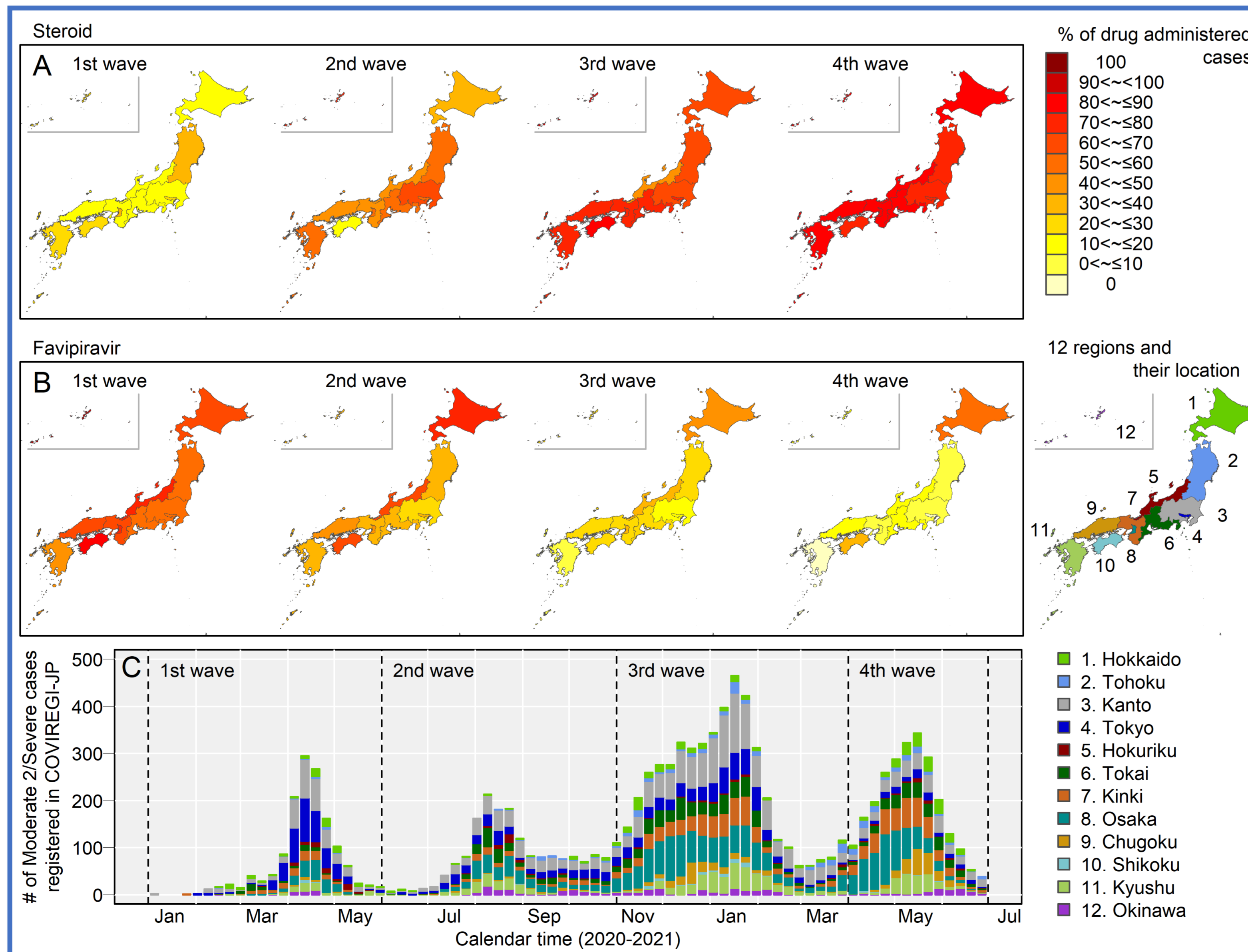

Figure 2. Changes in administration trends

- **Figure 1**
  - Panel A: Administration of **steroid**
    - **Sharp increase throughout Japan**, from 20-41% in 1 st wave to 75% < in the 4th.
    - Same trend was observed in all areas.
  - Panel B: Administration of **favipiravir**
    - Favipiravir tended to be administered nationwide in the 1st wave.
    - Decreasing trend toward the 4th wave
    - **Favipiravir was still administered** to patients in Hokkaido **in the 4th wave.**
- **Figure 2**
  - Upper panels: Trend of **steroid** use
    - β, time coefficients, are more than 1.5, i.e., rapid increase in all regions.
    - Particularly rapid ($\beta > 3.0$) in Hokkaido, Tokyo, Chugoku and Okinawa.

- Lower panels: Trend of **favipiravir** use
  - $\beta < 0$ shows decreasing trend in all region.
  - β = -0.83 [-2.19, 0.30] in Hokkaido. < 60% patients still took favipiravir in June 2021.
  - Other areas shows similar trends
  - **Regional heterogeneity was observed.**

Discussion

- The use of **drugs with proven efficacy was spreading rapidly.**
- The effective treatment was available nationwide after November 2020.
- Favipiravir **was initially expected to be effective** and **continued to be administered**.
- Standardization was not always possible, partly **due to the lack of data**.

Conclusions

- Registry studies have larger populations than clinical trials and can provide real-time information on medication status and trends.
- Registry studies will be **further utilized for standardization of treatment** in the future.

References

1. Matsunaga et al. DOI: 10.1093/cid/ciaa1470
2. Matsunaga et al. DOI: 10.1016/j.lanwpc.2022.100421

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