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Prescription Patterns for COVID-19 before the Availability of Antiviral Drugs Using the National Database of Health Insurance Claims in Japan

HSD77

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Background

- Early during the COVID-19 pandemic, antiviral drugs were not available. Guidelines for COVID-19 treatment evolved and changed frequently including off-label use of particular prescription drugs [1,2]. Therefore, we expect treatment patterns for COVID-19 to have changed as guideline recommendations were updated.
- Remdesivir was approved for COVID-19 treatment on May 7, 2020, listed in the National Formulary on August 12, 2021, and began normal distribution on October 18, 2021. In addition, other drugs listed in the National Formulary were approved for COVID-19 treatment and may also have affected prescribing patterns.
- Using a comprehensive Japanese health claims database, we examined whether prescription drug use patterns changed in response to the changes in COVID-19 treatment approval and guidelines.

Methods

Study design and data source

- Cross-sectional study using the National Database of Health Claims (NDB; January 2020—June 2021) owned by the Japanese Ministry of Health, Labour and Welfare.
  - ❖ The database included all health claims data issued in Japan.

Study population

- Patients with COVID-19 were defined as those who had a record of a COVID-19 diagnosis indicated by the standard disease name and a code for healthcare expenses by the government.
  - ❖ Since all healthcare expenses for COVID-19 were paid by the government during the data period, we used the code for the payments to identify medical practice for COVID-19.

Analysis

1. Monthly number of newly diagnosed patients with COVID-19 was calculated and compared to the monthly number of new positive cases reported by government [3].
2. Prescription patterns were analyzed for drugs approved or included in the guidelines for COVID-19 treatment during the study period (Table 1).
   - ❖ Prescriptions for COVID-19 treatment were defined as those with a COVID-19 diagnosis in the same month and with the code for healthcare expenses by the government.
   - ❖ Since the government's policy for using NDB prohibits reporting a specific number if the total number is 1-9, 5 was imputed if the quarterly number of patients was 1-9.

Table 1. List of COVID-19 treatment drugs analyzed in this study

Classification / Name	Quarterly [a] '20 Q1	Q2	Q3	Q4	'21 Q1	Q2	Q3	Q4	'22 Q1	Q2
Listed in the National Formulary in January 2020										
Steroids										
Ciclesonide	△	△	△	△	△	△	△	△	△	△
Dexamethasone	×	△	○	○	○	○	○	○	○	○
Prednisolone[b]	×	△	△	△	△	△	△	△	△	△
Other steroids[c]	×	△	△	△	△	△	△	△	△	△
Other Drugs										
Lopinavir/ritonavir	△	△	△	×	×	×	×	×	×	×
Hydroxychloroquine	×	△	△	×	×	×	×	×	×	×
Azithromycin	×	△	△	×	×	×	×	×	×	×
Tocilizumab	×	△	△	△	△	△	△	△	○	○
Nafamostat	×	△	△	△	△	△	△	△	△	△
Ivermectin	×	△	△	△	△	△	△	△	△	△
Sarilumab	×	△	△	△	△	△	△	△	△	△
Camostat	×	△	△	△	△	△	×	×	×	×
Baricitinib	×	×	×	△	△	○	○	○	○	○
Not listed in the National Formulary in January 2020, but listed later										
Remdesivir[d]	△	○	○	○	○	○	○	○	○	○

Note: [a]○: approved for COVID-19 treatment, △: not approved for COVID-19 treatment, but included in COVID-19 treatment guidelines, ×: not approved for COVID-19 treatment nor included in COVID-19 treatment guidelines.
[b]Prednisolone includes methylprednisolone.
[c]Other steroids include steroids excluding dexamethasone, prednisolone, and methylprednisolone.
[d]Remdesivir was listed in the National Formulary in August 2021.

Results

Monthly number of newly diagnosed patients with COVID-19

- The dataset included 6,612,147 patients diagnosed with COVID-19 for the analysis.
- Monthly number of newly diagnosed patients with COVID-19 showed a pattern of mostly increasing until August 2021 when there was a significant decrease in newly diagnosed patients and thereafter a significant increase in newly diagnosed patients starting January 2022. The monthly number of newly diagnosed patients in each month was similar to the monthly number of new positive cases reported by the government [3] (Fig. 1).

Prescription patterns of COVID-19 treatment drugs

- Steroids were the most frequently prescribed drugs throughout the study period (Fig. 2A). The proportion of patients receiving steroids changed from approximately 50% in Q1 and Q2 2020 to 70%–80% from Q3 2020 to Q4 2021, and then decreased to approximately 60%.
- Among the steroids, ciclesonide, which was guideline recommended early on, was the most commonly prescribed in Q1 2020, but decreased later (Fig. 2B) The use of dexamethasone increased notably when it was approved for COVID-19 treatment in Q3 2020 and later(Fig. 2B).
- The number of patients prescribed drugs other than steroids continued to increase each quarter until Q3 2021 (Fig. 2A). A wide range of drugs were prescribed in Q1 and Q2 2020, and the mix od drugs changed each period (Fig. 2C). After the approval of baricitinib for the treatment of COVID-19 in Q2 2021, the use of unapproved drugs gradually decreased while the use of approved drugs increased (Fig. 2A).
- The use of remdesivir was first identified in Q3 2021 when it was listed in the National Formulary, but the use was very low even after it became normal distribution in Q4 2021 (Fig. 2A). The proportion prescribed this drug increased significantly in Q1 2022.

Discussions

- Since the monthly number of newly diagnosed patients with COVID-19 in this study is similar to the monthly number of new positive cases reported by the government, the use of claims data appears to be appropriate for the study of patients with COVID-19. PCR testing for COVID-19 was covered by health insurance, making it likely that most patients with COVID-19 were included in the claims database.
- Steroids were frequently used during the entire study period. The use of specific steroid types is likely influenced by the guideline recommendation and approval for COVID-19.
- The guidelines recommended off-label use of particular prescription drugs and were covered by health insurance for COVID-19 treatment earlier when there were no particular drug treatments. When approved drug became available, the use of off-label drugs declined.
- Remdesivir was approved in May 2020, but it was not listed in the National Formulary until later due to the limited supply of the drug. Use of remdesivir did not increase significantly, even after the start of normal distribution of remdesivir in Q4 2021. The number of patients and the proportion of the patients prescribed remdesivir increased in Q1 2022 when the number of new COVID-19 cases increased significantly. The increase in use may be associated with the expanding the indication in early 2022 from use in only severe patients to include patients with mild to moderate and at high risk of progression to severe disease.

Limitations

- Although we confirmed the validity of using claims data compared to the government reported cases, patients with subclinical infection and patients who were not tested were not included in either our study or the government report.
- Since this study used claims data, prescriptions not covered by health insurance, such as those for drugs not approved or not listed in the National Formulary, were not included.

Conclusions

Using real world Japanese data, we demonstrated prescription patterns changed according to change in guideline recommendations and availability of new approved drug therapies for COVID-19 treatment.

Figure 1. Monthly number of newly diagnosed patients with COVID-19

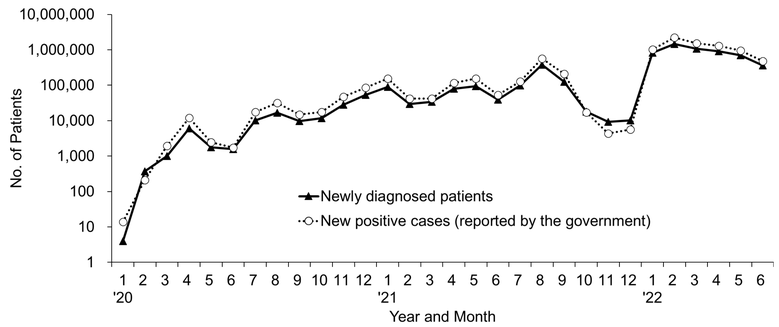
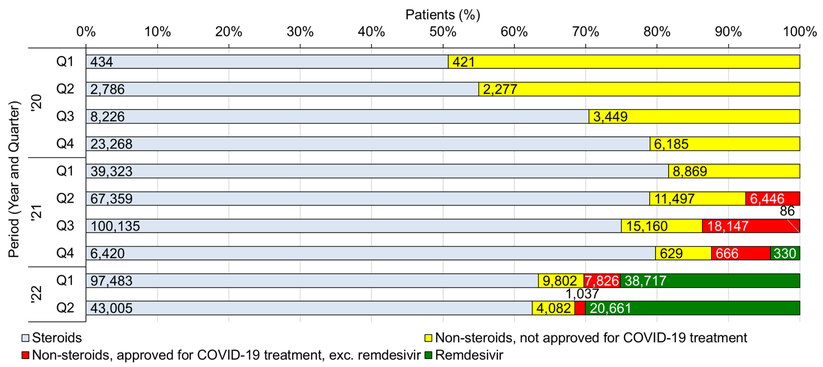
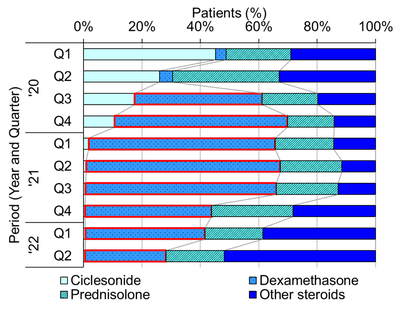


Figure 2. Prescription patterns of COVID-19 treatment drugs by quarterly

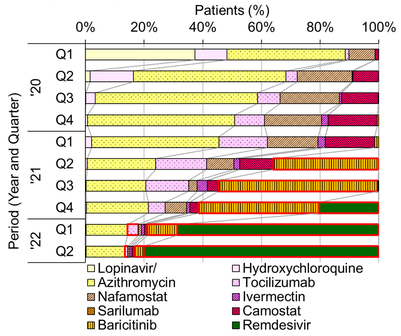
A. Proportion and number of patients categorized by steroids or not and approved or not approved



B. Proportion of patients prescribed each type of drugs among steroids



C. Proportion of patients prescribed each type of drugs among non-steroids



Note: Steroids include both approved and not approved for COVID-19. The percentage in A was calculated by dividing the total number of patients prescribed drugs in each category by the total numbers of patients prescribed each drug listed in Table 1. Numbers on the bars in A represent the number of patients. Red grid lines in B and C indicate that the drug was approved for COVID-19 in the period.

References: 1. The taskforce for COVID-19 drugs of the Japanese association for infectious diseases. Considerations of drug therapy for COVID-19, ver.1.0. February 26, 2020 [in Japanese]. 2. The expert committee of the Ministry of Health, Labour and Welfare. Clinical treatment guideline for COVID-19 ver 1. March 17, 2020 [in Japanese]. 3. Ministry of Health, Labour and Welfare. Visualizing the data: information on COVID-19 infections, Trend in the number of newly confirmed cases (daily). 2023.