COVID-19 Registry in Japan

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COVIREGI-JP
COVID-19 REGISTRY JAPAN

Research for clinical response method development for emerging and re-emerging respiratory infections such as Middle East Respiratory Syndrome (MERS)

(Number：H27-新興- 指定- 006 Period: H27－28)

Observation in endemic countries

Observation to South Korea (Korean CDC, Seoul University Hospital etc.), U.S. (NIH, Emory university etc.), and Thailand

Observation of medical care systems to medical institutions designated for type II infectious diseases in Japan

Public health measures

Epidemiology / Public Health Responses:

- Discussions for contact tracing survey methods (Contact data management surveys in South Korea)
- Model development of contact tracing survey tools

Medical systems:

- Proposals to divide functions of medical institutions designated for type II infectious diseases (Diagnosis only / Complete treatments)

Medical supports:

- Establishing a system for dispatching experts to medical institutions. Dispatching two experts from NCGM.

Development of medical care and infection prevention measures

Intensive care guidelines:

Establishment of a medical guidance of intensive care for serious cases

Treatment guidelines：

- Creating antiviral treatment guidelines for treatment for MERS
- Establishing a multicenter prospective observational study system to collect epidemiological information on MERS patients
- Establishing a treatment system using recovery plasma

Infection prevention measures：

- Providing infection control videos and home handbooks for healthcare professionals and the general public
- Creating guidelines for infection prevention measures when emerging respiratory infections such as MERS occur

Offer information

Workshops for medical professionals, Edification by E-learning

Epidemiol. Infect. (2010), **138**, 1531–1541.
doi:10.1017/S0950268810001366

Pandemic (H1N1) 2009 influenza in the UK: clinical and epidemiological findings from the first few hundred (FF100) cases

Outline of Registry

1. **Objective:**

   Clarify the clinical picture and epidemiology of COVID-19 patients

2. **Subjects:**

   Patients diagnosed as COVID-19 and admitted to medical institutions for treatment*

3. **Period:**

   From Jan 2020 (the registry opened in Mar) to the present

4. **Scope of Analysis and Consideration:**

   1. **Clinical picture, clinical course, prognosis**
   2. **Investigation of risk factors that may lead to severe cases**
   3. **Clinical course of and safety for patients receiving drugs**

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ISARIC

ISARIC provides a collaborative platform through which global, patient-oriented clinical studies can be developed, executed and shared.

Protocols addressing the most important questions between and during epidemics of severe acute respiratory infections and other rapidly emerging public health threats are undertaken in order to generate new knowledge, maximise the availability of clinical information, and thereby save lives.

Healthcare professionals in COVID-19 hospital (Photo credit: Professor Bin Cao, China-Japan Friendship Hospital, China)

International Severe Acute Respiratory and emerging Infection Consortium

https://isaric.org/

World Health Organization ISARIC

PARTICIPANT IDENTIFICATION #: [___][___][___][___][___]---[___][___][___][___]

MODULE 1: PRESENTATION/ADMISSION CASE REPORT FORM

CLINICAL INCLUSION CRITERIA

Suspected or confirmed novel coronavirus (COVID-19) infection: O YES O NO

DEMOGRAPHICS

Clinical centre name:_____ **Country:**_____

Enrolment date /first COVID-19 assessment date: [_D_][_D_]/[_M_][_M_]/[_2_][_0_][_Y_][_Y_]

Ethnic group *(check all that apply)*: ☐Arab ☐Black ☐East Asian ☐South Asian ☐ West Asian ☐Latin American ☐White ☐Aboriginal/First Nations ☐Other: _____ O Unknown

Employed as a Healthcare Worker? O YES O NO O Unknown **Employed in a microbiology laboratory?** O YES O NO O Unknown

Sex at Birth: O Male O Female O Not specified/Unknown **Age** [___][___][___]years OR [___][___]months

Pregnant? O YES O NO O Unknown **If YES: Gestational weeks assessment:** [___][___] weeks

POST PARTUM (within 6 weeks of delivery)? O YES O NO O Unknown *(if NO or Unknown skip this section)*

Pregnancy Outcome: O Live birth O Still birth **Delivery date:** [_D_][_D_]/[_M_][_M_]/[_2_][_0_][_Y_][_Y_]

Baby tested for COVID-19/SARS-CoV-2 infection? O YES O NO O Unknown

If YES, result of test: O Positive O Negative O Unknown (If Positive, complete a separate CRF for baby)

INFANT – Less than 1 year old? O YES O NO *(If NO skip this section)*

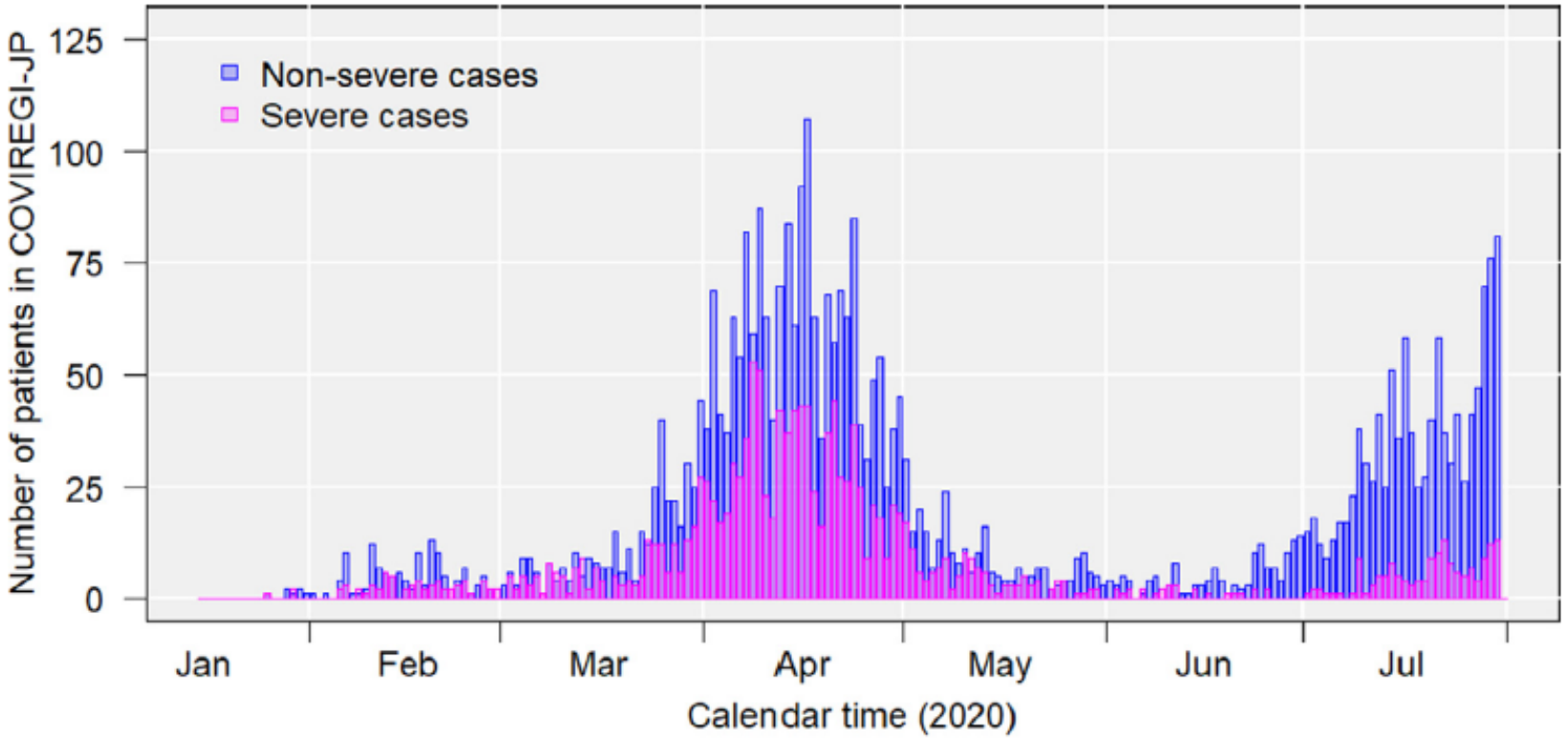
Birth weight: [___][___].[___] O kg or O lbs O Unknown

Gestational outcome: O Term birth (≥37wk GA) O Preterm birth (<37wk GA) O Unknown

Breastfed? O YES-currently breastfeeding O YES-breastfeeding discontinued O NO O Unknown

Vaccinations appropriate for age/country? O YES O NO O Unknown

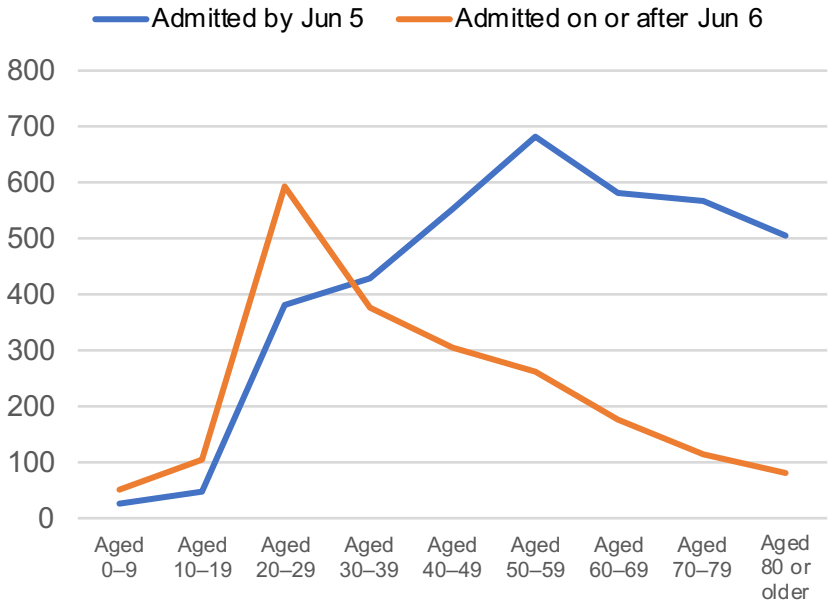
The second wave had a smaller proportion of severe cases (12.0% vs 33.1%) in Japan

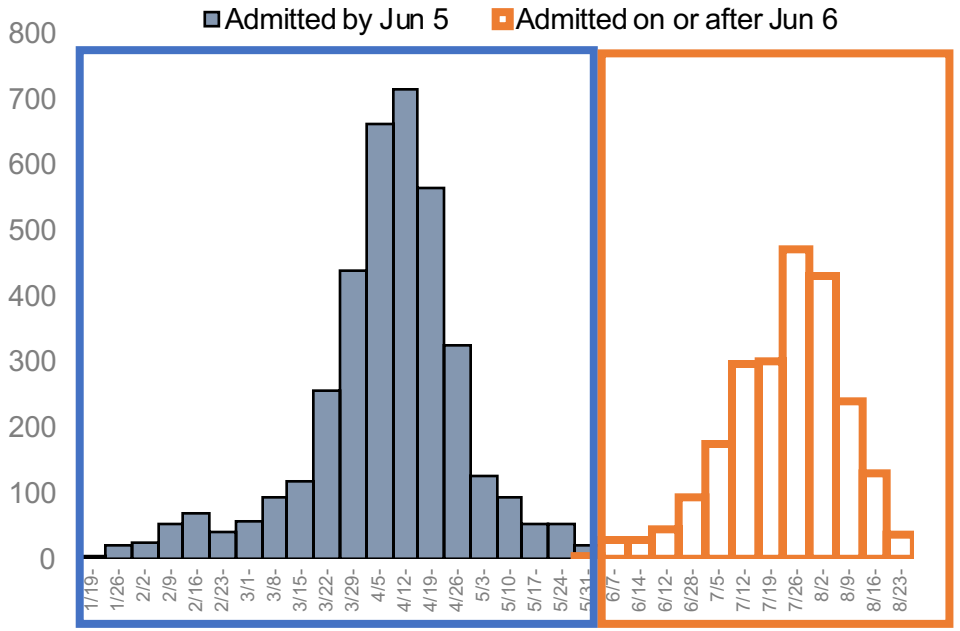


https://doi.org/10.1016/j.jinf.2020.10.033

Clinical Characteristics of Inpatients

- For cases registered from collaborating medical institutions, the proportion of elderly patients is lower in cases admitted on and after Jun 6 than in cases admitted by Jun 5.





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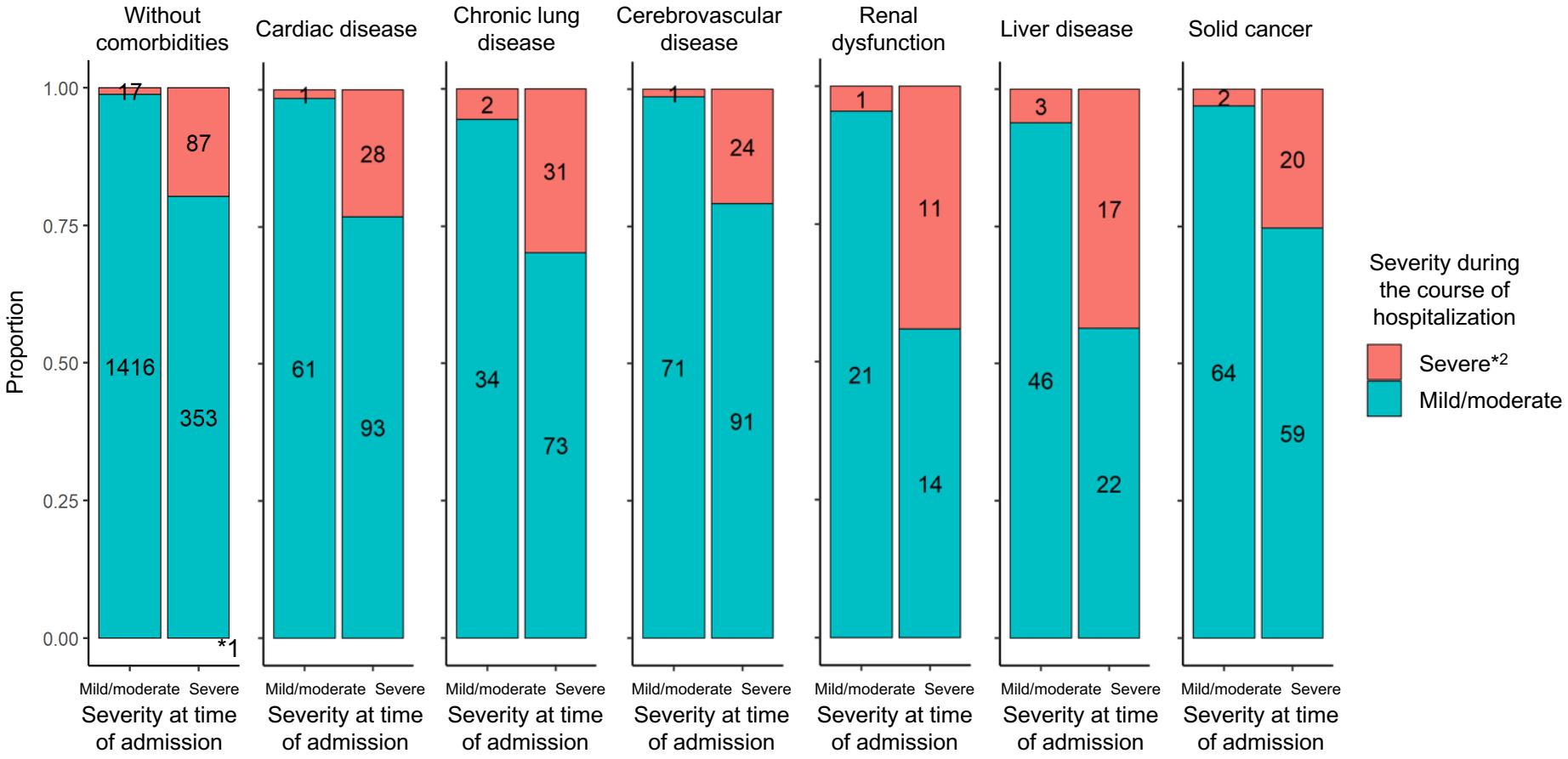
Factors Leading to Severe Cases After Admission

○ In cases with renal dysfunction, liver disease, obesity, hyperlipemia, hypertension, or diabetes, symptoms tend to become severe after admission compared to in cases without comorbidities.



*1 Severe at time of admission: cases that fall under any of the following at the time of admission: oxygen supply, treatment with an artificial respirator, an SpO2 of 94% or lower, or a breathing rate of 24 per min. or more

*2 Cases requiring intubation or extracorporeal membrane oxygenation (ECMO) during hospitalization

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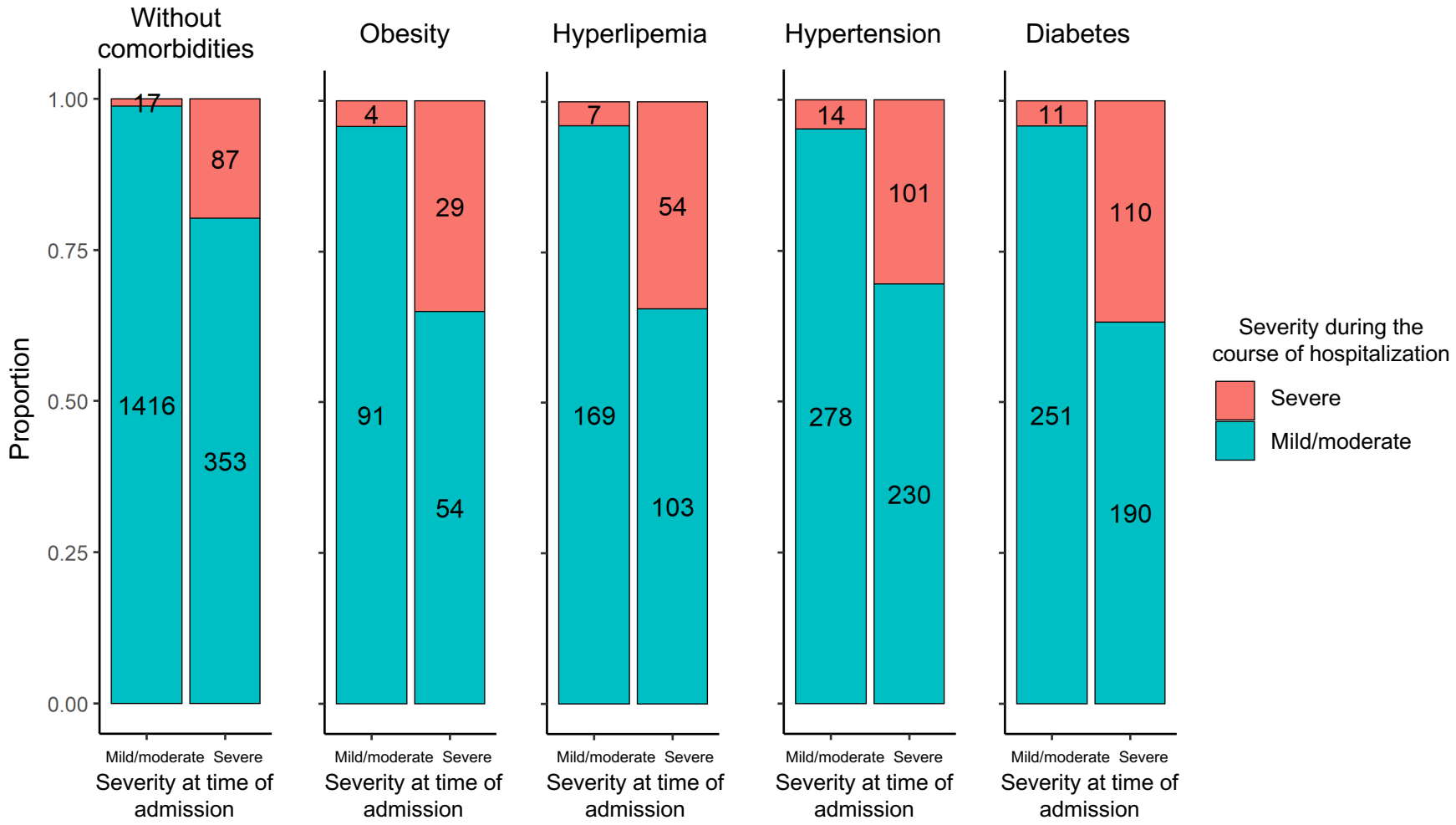
Factors Leading to Severe Cases After Admission



* Categorized in the same manner as in the previous slide

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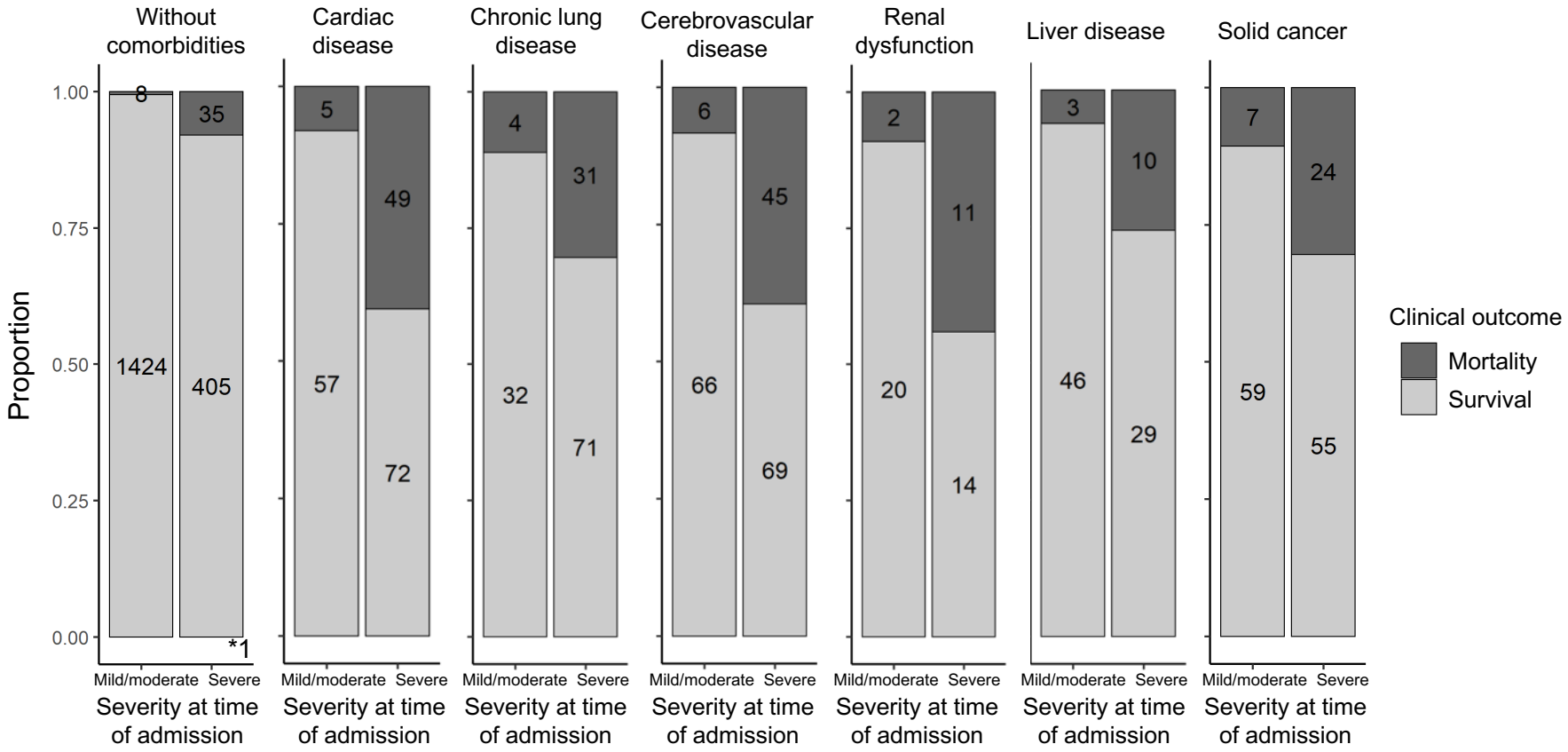
Mortality Factors

- **The mortality rate tends to be high in cases with cardiac disease, chronic lung disease, cerebrovascular disease, or renal dysfunction compared to in cases without comorbidities.**
- **Factors leading to severe cases may be different from mortality factors.**



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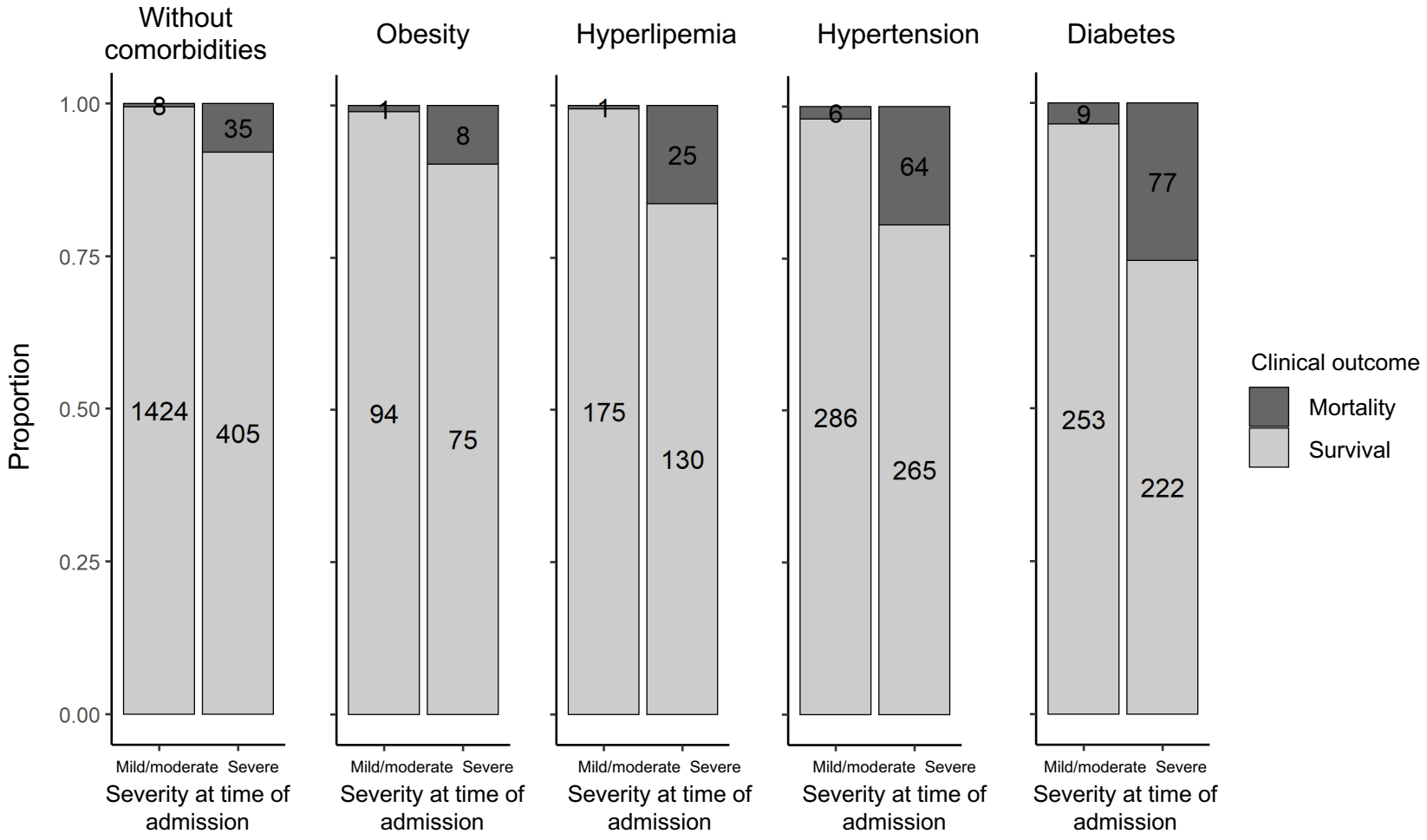
Mortality Factors



* Categorized in the same manner as in the previous slide

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Status of Drug Administration

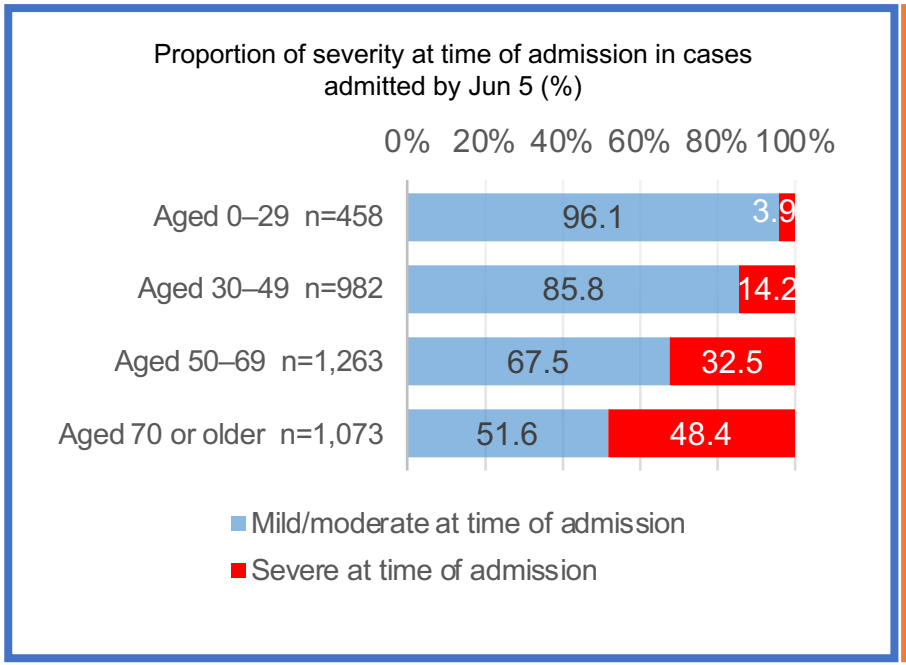
Total cases	Severity at time of admission × Timing of admission (admitted by or after Jun 5)					
	Mild/moderate			Severe		
	By 6/5/2020 (N=2,777)	From 6/6/2020 (N=2,119)	Total (N=4,896)	By 6/5/2020 (N=1,134)	From 6/6/2020 (N=237)	Total (N=1,371)
Steroids (excluding ciclesonide) * Excluding cases where steroids had been used prior to admission for purposes other than COVID-19	116 (4.3%)	132 (6.2%)	248 (5.1%)	257 (23.1%)	94 (39.7%)	351 (26.0%)
Anticoagulants	110 (4.0%)	58 (2.7%)	168 (3.4%)	257 (22.7%)	45 (19.0%)	302 (22.0%)

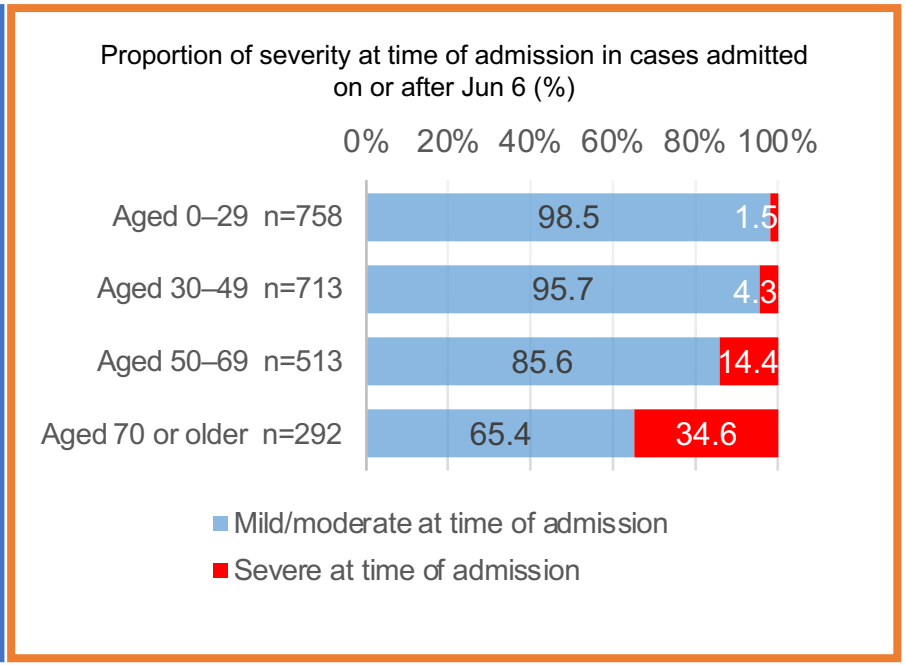
Cases to which drug was administered for COVID-19 treatment	Severity at time of admission × Timing of admission (admitted by or after Jun 5)					
	Mild/moderate			Severe		
	By 6/5/2020 (N=1,409)	From 6/6/2020 (N=646)	Total (N=2,055)	By 6/5/2020 (N=914)	From 6/6/2020 (N=177)	Total (N=1,091)
Favipiravir	848 (61.4%)	332 (51.5%)	1,180 (58.2%)	678 (75.4%)	101 (57.1%)	779 (72.4%)
Remdesivir	3 (0.2%)	45 (7.0%)	48 (2.4%)	8 (0.9%)	37 (21.0%)	45 (4.2%)
Ciclesonide	723 (52.9%)	336 (52.0%)	1,059 (52.6%)	403 (44.9%)	45 (25.4%)	448 (41.7%)
Nafamostat	87 (7.8%)	52 (8.1%)	139 (7.9%)	104 (13.2%)	24 (13.6%)	128 (13.3%)

* Categorized as severe at the time of admission when a case falls under any of the following at the time of admission: oxygen supply, treatment with an artificial respirator, an SpO_2 of 94% or lower, or a breathing rate of 24 per min. or more
* Missing values are excluded in the calculation of proportions (%)

Severity at Time of Admission

- As for severity at the time of admission, the proportion of severe cases*1 is high in the elderly.
- In cases admitted after Jun, the proportion of severe cases at the time of admission is low compared to cases admitted before Jun.





*1 **Categorized as severe at the time of admission when a case falls under any of the following at the time of admission: oxygen supply, treatment with an artificial respirator, an SpO_2 of 94% or lower, or a breathing rate of 24 per min. or more**

*2 **Note that <u>recent cases with a prolonged hospital stay are not included</u> because case data is registered after completion of discharge**

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Proportion of Deaths After Admission

- The proportion of deaths after admission is high in the elderly and severe cases at the time of admission.*1
- In cases admitted after Jun, the proportion of deaths after admission is low in any of the generations compared to cases admitted before Jun.

Proportion of Deaths After Admission
(by generation and severity at time of admission)

Mild/moderate cases at time of admission

	Admitted by Jun 5	Admitted on or after Jun 6	Aggregate
Aged 0–29	**0.0%** (0/440)	**0.0%** (0/747)	**0.0%** (0/1,187)
Aged 30–49	**0.2%** (2/842)	**0.0%** (0/682)	**0.1%** (2/1,524)
Aged 50–69	**1.1%** (9/852)	**0.0%** (0/439)	**0.7%** (9/1,291)
Aged 70 or older	**10.6%** (59/554)	**5.8%** (11/191)	**9.4%** (70/745)
Total	**2.6%** (70/2,688)	**0.5%** (11/2,059)	**1.7%** (81/4,747)

Severe at time of admission*2

	Admitted by Jun 5	Admitted on or after Jun 6	Aggregate
Aged 0–29	**5.6%** (1/18)	**0.0%** (0/11)	**3.4%** (1/29)
Aged 30–49	**2.2%** (3/139)	**0.0%** (0/31)	**1.8%** (3/170)
Aged 50–69	**10.9%** (45/411)	**1.4%** (1/74)	**9.5%** (46/485)
Aged 70 or older	**31.2%** (162/519)	**20.8%** (21/101)	**29.5%** (183/620)
Total	**19.4%** (211/1,087)	**10.1%** (22/217)	**17.9%** (233/1,304)

*1 Categorized as severe at the time of admission when a case falls under any of the following at the time of admission: oxygen supply, treatment with an artificial respirator, an SpO_2 of 94% or lower, or a breathing rate of 24 per min. or more

*2 Note that **recent cases with a prolonged hospital stay are not included** because case data is registered after completion of discharge

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Number of Days from Onset to Admission

○ **The number of days from the onset to admission is shorter in cases admitted on or after Jun 6 than in cases admitted before by Jun 5.**

No. of days from onset to admission

	Admitted by Jun 5 (N=3,336)	Admitted on or after Jun 6 (N=2,011)
Average	7.6 days	5.1 days
Medium time (Interquartile range)	7 days (4, 10)	5 days (3, 7)

* **Analysis was conducted for cases registered in the registry for which the onset date is recorded and in which the admission date came later than the onset date**

ACCEPTED MANUSCRIPT

Clinical epidemiology of hospitalized patients with COVID-19 in Japan: Report of the COVID-19 REGISTRY JAPAN

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The use of registry data in policy

1. Ministry of Health, Labour and Welfare

- Information on clinical picture, treatment status, length of hospital stay, selection of high-risk patients for prioritization of vaccination, information on cases of infection with mutated strains

2. Tokyo iCDC

- Provision of information on the clinical profile of patients in Tokyo
- Mainly used for risk communication

In Japan, COVIREGI is the only database that can provide detailed clinical information → used frequently

NCGM

The challenges of running a registry

1. Getting up and running

- Quick start-up requires advance preparation. However, in the past, Japan did not have this concept and it was not understood

2. Maintenance

- Began as a study by the Ministry of Health, Labour and Welfare
- No funding to continue
- It is necessary to consider how far the project can realistically be continued.

The challenges of running a registry

3. On-site support

- Data entry needs to be done manually, so data entry support is needed
- It is not possible to input data from existing data such as EMR
- Existing databases cannot be used as linkage is not advanced at all in Japan
- Heavy burden on analysis team
- Development of a system for the use of data: there is pressure to make free use of data, but the discussion goes on without the researchers who have invested the effort to obtain the data

NCGM

Future Prospects

Accumulation of further findings as epidemiological research

- ✓ Further analysis of factors leading to severe cases and mortality-related factors, the efficacy of drugs, involvement of lifestyles, etc.
- ✓ Application to various cross-sectional and longitudinal studies as well as registries for evaluation of long-term prognoses

Utilization for development of pharmaceuticals and medical devices

- ✓ Data based on the state of actual cases that contributes to development of pharmaceuticals and medical devices

Collaboration with specimen banks

- ✓ Further study development through the integration of laboratory information and specimen information

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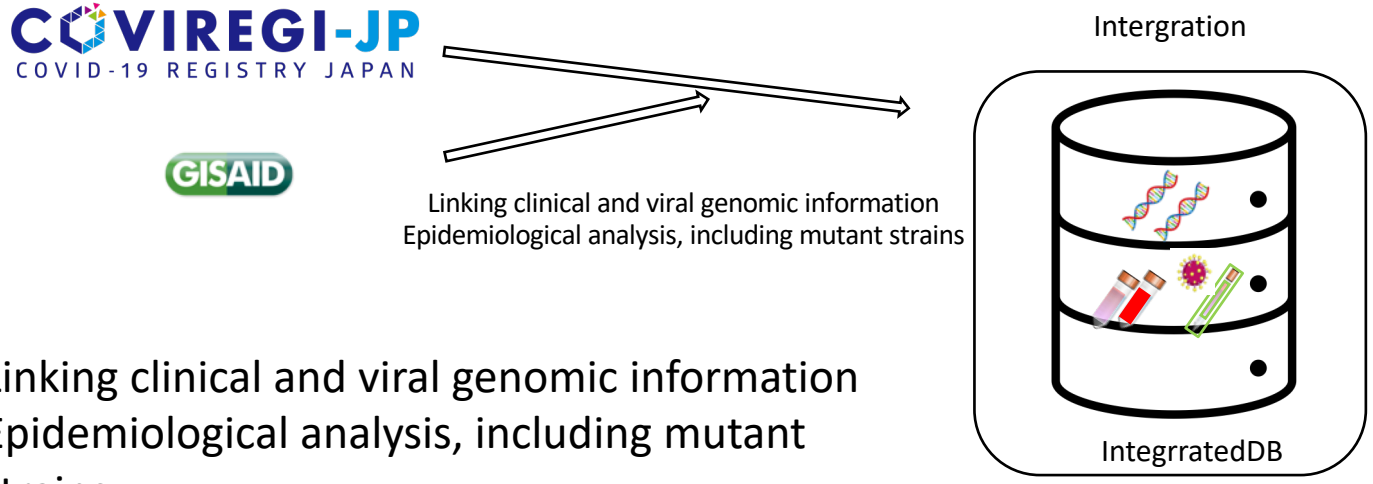
From COVIREGI-Jp to REBIND

(REpository of data and Biospecimen of INfectious Disease)

- COVIREGI-JP has been established as a case registry and already contains detailed clinical information on more than 36,000 cases.
- The analysis of mutant strains is an urgent issue, and the system will be modified to enable the collation of clinical information with viral genome data.
- While using the existing framework, the system will be merged with the system to be established in the data bank project, and eventually integrated.



Linking clinical and viral genomic information
Epidemiological analysis, including mutant strains

REBIND

(REpository of data and Biospecimen of INfectious Disease)