

Reproduction of the Control Group in REMDACTA Trial Using the Millennial Medical Record, an Electronic Health Record Database, in Japan

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Objective

- Reproducing a control group from a clinical trial using real world data (RWD) is desirable for particular analyses and ethically sound despite challenges pertaining to internal validity.
- To test the internal validity of this exercise, we attempt to reproduce a control group from a Randomized Controlled Trial (RCT) using Electronic Health Record (EHR) data and compared the outcomes of the original trial and that of the reproduced analysis.

Method

- We selected an RCT, REMDACTA trial, that was performed to evaluate the efficacy of tocilizumab plus remdesivir against placebo plus remdesivir in hospitalized patients with severe COVID-19 pneumonia.
- We reproduced the control group (patients with severe COVID-19 pneumonia taking only remdesivir), using Japanese EHR data, Millennial Medical Record, provided by Life Data Initiative.
- Target patients for the main analysis were hospitalized patients coded with ICD-10 code U07.1 (COVID-19) or with the diagnosed code for COVID-19 pneumonia. Only those with COVID-19 pneumonia were considered for sub analysis.
- Additional inclusion criteria were applied including undergoing image inspection identified by the procedure codes in Table 1, oxygen administration identified by the procedure code of J024, and those not taking any drug therapy for pneumonia before receiving the first remdesivir prescription.

Table 1 Procedure Codes for image inspection

Procedure Code	Description
E000-0	fluoroscopic examination
E001-0	picture diagnosis
E004-0	basic X-ray diagnosis
E200-0	Computed Tomography
E202-0	Magnetic Resonance Imaging
E203-0	computerized tomography

- We excluded patients having eGFR <30 mL/min and not having the procedure code of J038-0 (artificial kidney) before the first remdesivir prescription.
- We excluded patients having 5 times more than the standard value of ALT or AST before the first remdesivir prescription.
- The outcome of interest for comparison to the trial control group was median length of hospital stay.

Results

- The dataset had 787 patients having the admission dates in the inpatient data including the prescription of remdesivir.
- Chart 1 provides the distribution of days from the admission dates to the first remdesivir prescription dates. Following the REMDACTA trial which required all patients to be prescribed remdesivir on the admission dates, we excluded patients prescribed remdesivir more than 2 days after the admission dates which left 676 patients.
- REMDACTA included patients having both ICD-10 code U07.1 (COVID-19) and the diagnosed code for COVID-19 pneumonia. Among the 676 patients meeting the criteria, 110 patients were identified as COVID-19 pneumonia for sub analysis (Chart 2).

Chart 1 Distribution of Patients by number of days from the admission dates to the first remdesivir prescription dates

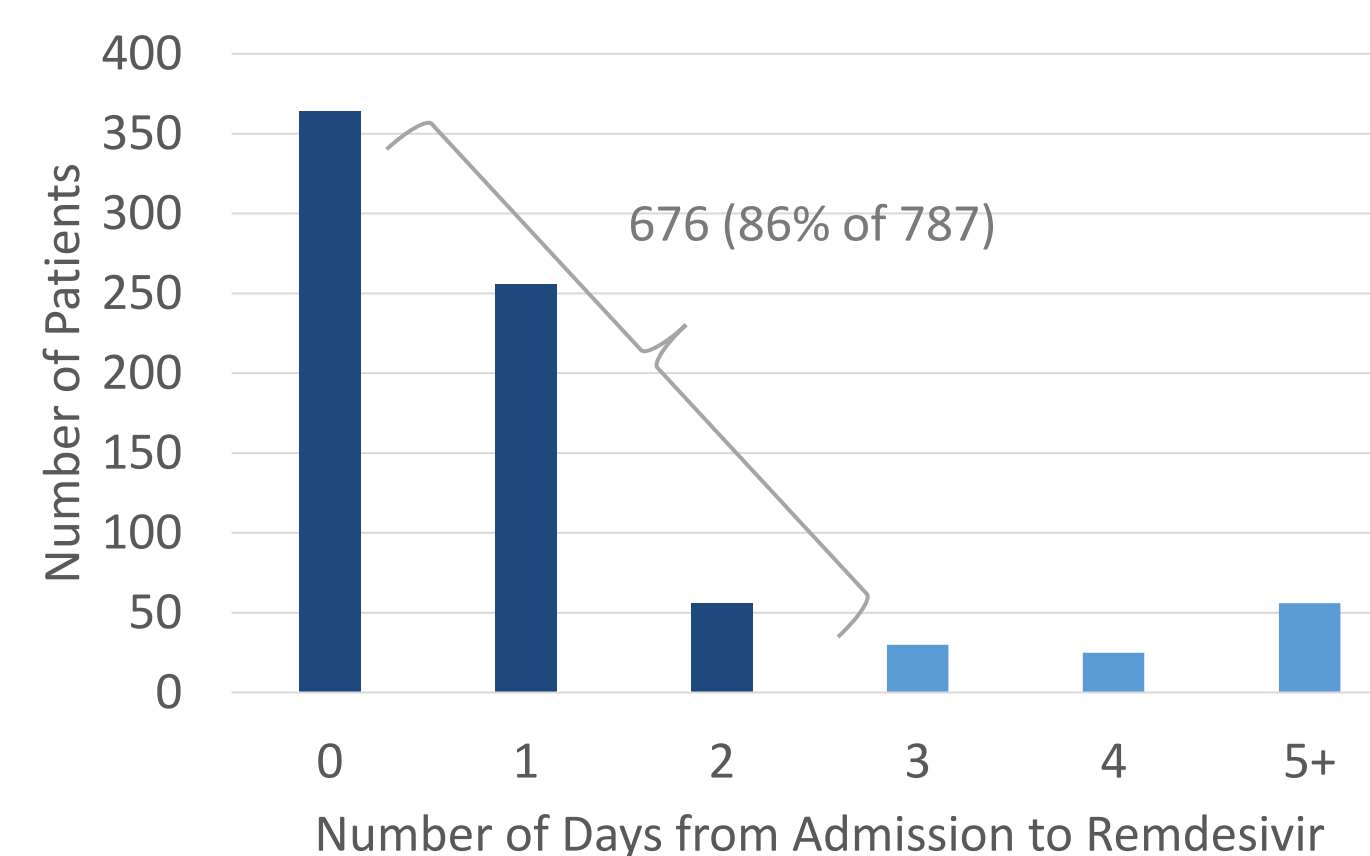
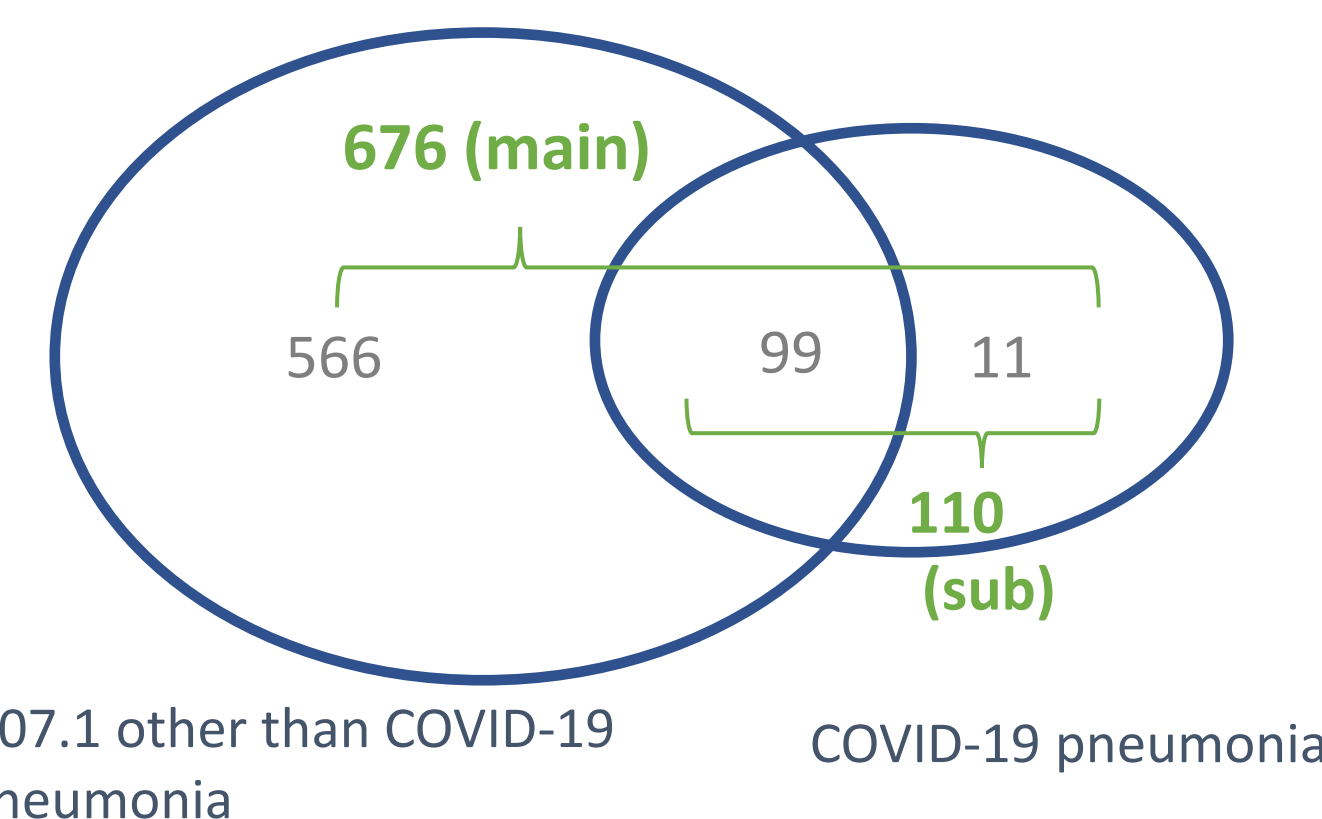
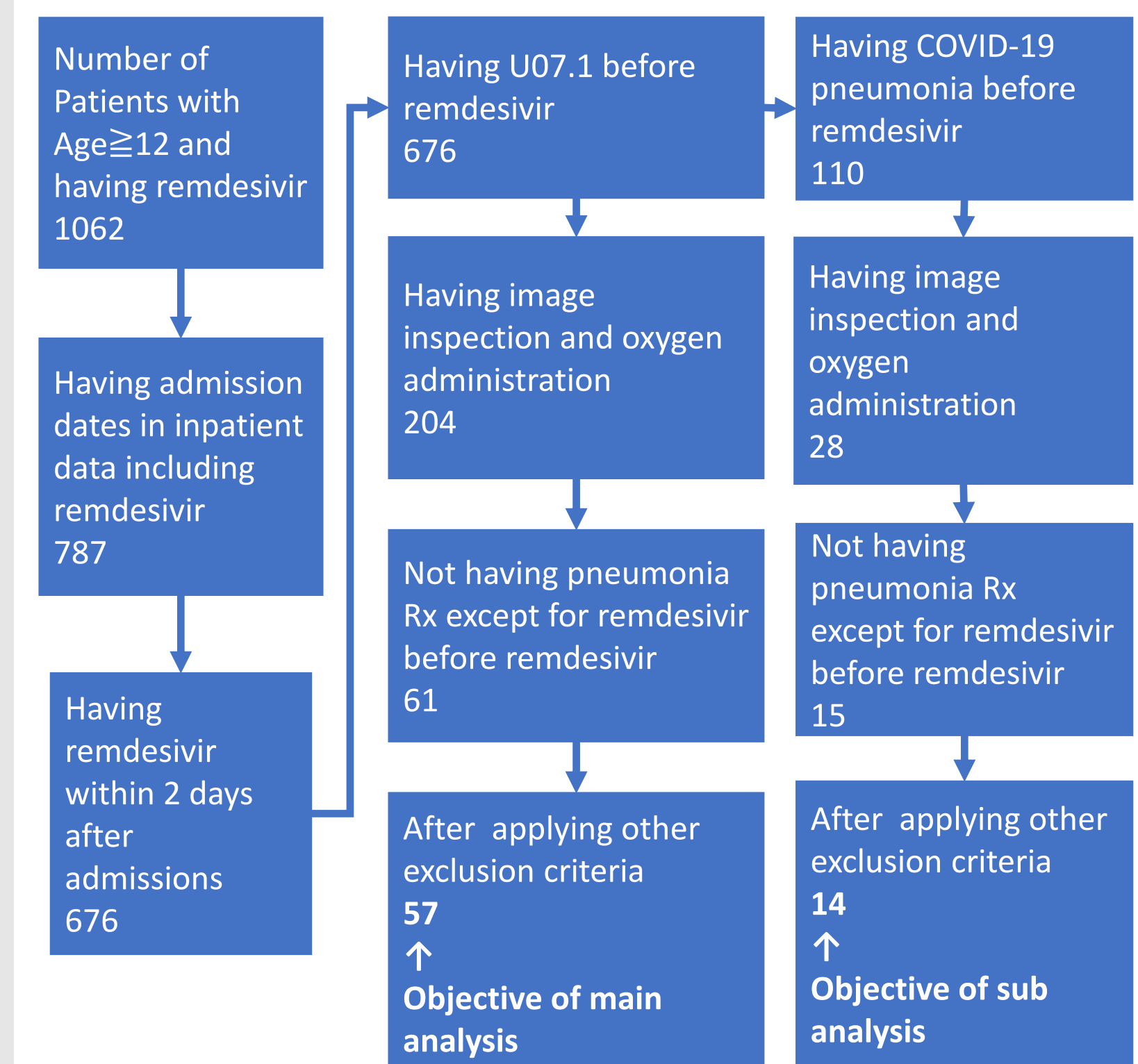


Chart 2 Venn diagram of Patients of main and sub analysis (before exclusions)



- All exclusion criteria were applied which left 57 and 14 patients matching the eligibility criteria for the main and sub analyses, respectively. The reduction in the number of patients was mainly attributed to the requirement of image inspection and oxygen administration (Chart 3).

Chart 3 Cascade chart of patients of main and sub analysis



- Median time of lengths of stay in the reproduced group were 13 and 11 days in the main and sub analyses, respectively [11.0–16.0, 95% CI of median time, in REMDACTA] (Table 2).

Table 2 Lengths of stay

	N	Length of Stay (Days)	
		Mean	Median
main analysis	57	14.1	13
sub analysis	14	13.0	11
REMDACTA	141		14 (11.0, 16.0)

Conclusion

- The median hospital length of stay for each group was successfully reproduced using EHR data.