# Supplemental Digital Content 1. Methodology of whole genome sequencing of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) conducted in Niigata prefecture.

Viral RNA was extracted with the Quick-DNA/RNA Viral MagBead kit (Zymo Research) from a starting NPS specimen, or sputum samples diluted with PBS (-), volume of 150μL and final elution volume of 60μL. Whole-genome sequencing of SARS-CoV-2 were conducted according to the nCov-2019-sequencing-protocol-for-illumina of Itokawa K (https:[//www.protocols.io/view/ncov-2019-sequencing-protocol-for-illumina-](http://www.protocols.io/view/ncov-2019-sequencing-protocol-for-illumina-) eq2ly398mgx9/v). After reverse transcription of viral RNA, multiplex PCR was conducted with the two primer sets, pool 1 and pool 2 of Itokawa K primer set ver N5 (https://github.com/ItokawaK/Alt\_nCov2019\_primers/tree/master/Primers/ver\_N5). The

PCR products in pools 1 and 2 from the same clinical sample were pooled, purified, and subjected to Illumina library construction using a QIAseq FX DNA library kit (Qiagen). The iSeq 100 platform (Illumina) was used for sequencing the indexed libraries. The obtained sequence data were analyzed by SARS-CoV-2 Analysis Program (National Institute of Infectious Diseases, Center for Pathogenome Analysis and Research). Lineage was determined in accordance with PANGO lineage (https://cov-lineages.org/index.html).