

Supplemental Methods

SARS-CoV-2 Whole Genome Sequencing

Viral RNA Extraction

Viral RNA was extracted from clinical specimens utilizing the QIAamp 96 Virus QIAcube HT Kit (Qiagen, cat. no. 57731). Clinical testing for SARS-CoV-2 presence was performed by quantitative reverse transcription and PCR (qRT-PCR) with the CDC 2019-nCoV RT-PCR Diagnostic Panel utilizing the N1 probe in SARS-CoV-2 and RP probes for sample quality control as previously described (IDT, cat. no. 10006713). All specimens that failed to amplify the RP housekeeping gene were excluded from this study. All specimens with an N1 probe cycle threshold (Ct) less than or equal to 35 were considered positive and included in this study. RT-PCR was performed on all specimens to validate Ct values obtained by the clinical diagnostic laboratory. Ct values from the N1 probes were used in all subsequent analyses.

cDNA Synthesis and Viral Genome Amplification

cDNA synthesis was performed with SuperScript IV First Strand Synthesis Kit (ThermoFisher, cat. no. 18091050) using 11 µl of extracted viral nucleic acids and random hexamers according to manufacturer's specifications. Direct amplification of the viral genome cDNA was performed in multiplexed PCR reactions to generate ~400 bp amplicons tiled across the genome. The multiplex primer set, comprised of two non-overlapping primer pools, was created using Primal Scheme and provided by the Artic Network (version 3 and 4 releases). PCR amplification was carried out using Q5 Hot Start HF Taq Polymerase (NEB, cat. no. M0493L) with 5 µl of cDNA in a 25 µl reaction volume. A two-step PCR program was used with an initial step of 98 °C for 30 s, then 35 cycles of 98 °C for 15 s followed by five minutes at 64 °C. Separate reactions were carried out for each primer pool and validated by agarose gel electrophoresis alongside negative controls. Each reaction set included positive and negative amplification controls and was performed in a space physically separated for pre- and post-PCR processing steps to reduce contamination. Amplicon sets for each genome were pooled prior to sequencing library preparation.

Sequencing Library Preparation, Illumina Sequencing, and Genome Assembly

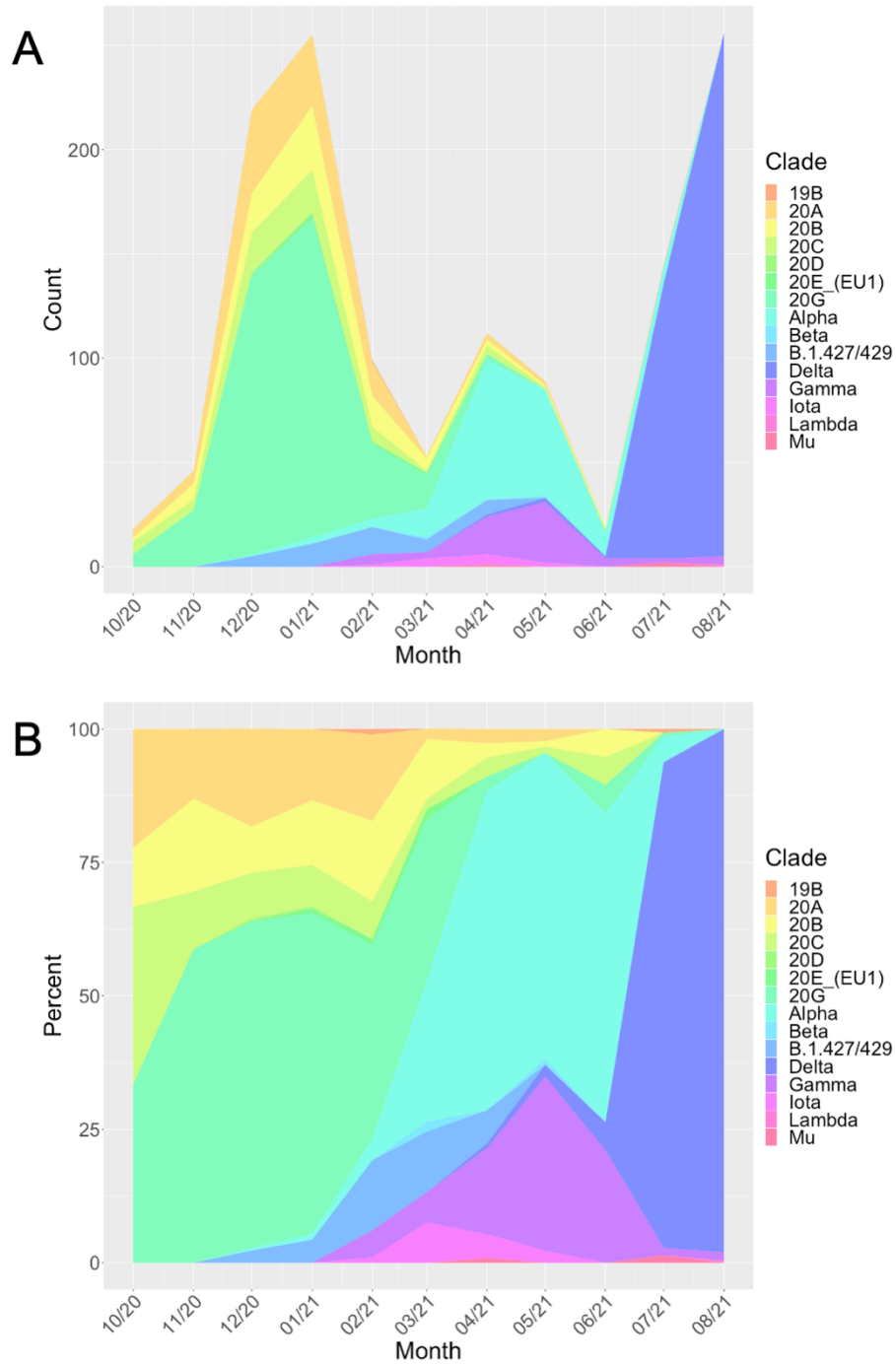
Sequencing library preparation of genome amplicon pools was performed using the SeqWell plexWell 384 kit per manufacturer's instructions. Pooled libraries of up to 96 genomes were sequenced on the Illumina MiSeq using the V2 500 cycle kit. Sequencing reads were trimmed to remove adapters and low-quality sequences using Trimmomatic v0.36. Trimmed reads were aligned to the reference genome sequence of SARS-CoV-2 (accession MN908947.3) using bwa v0.7.15. Pileups were generated from the alignment using samtools v1.9 and consensus sequence determined using iVar v1.2.2 with a minimum depth of 10, a minimum base quality score of 20, and a consensus frequency threshold of 0 (i.e. majority base as the consensus).¹ Consensus genome sequences were deposited in the GISAID public database (Table S1).

Bioinformatics Analyses

Genome sequences were aligned using MAFFT v7.453 software and manually edited using MEGA v6.06. We used the Pango classification scheme (<https://cov-lineages.org/>; PangoLearn version 9/28/2021) to identify the lineages that subsequently were grouped in variants using scorpio (scorpio v0.3.12). To confirm the clustering of the sequences by lineage, we inferred a Maximum Likelihood phylogeny with IQ-Tree v2.0.5 using its ModelFinder function before each analysis to

estimate the nucleotide substitution model best-fitted for each dataset by means of Bayesian information criterion (BIC). We assessed the support of the clusters formed by the different lineages both with the Shimodaira–Hasegawa approximate likelihood-ratio test (SH-aLRT) and with ultrafast bootstrap (UFboot) with 1000 replicates each.

Supplemental Figure 1: Frequencies (A) and proportions (B) of lineages of SARS-CoV-2 identified in adult patients during 10-month study period (October 2020 – August 2021) in a Chicago partner hospital. Corresponding data for children in this study are shown in Figure 1; the variant proportions and chronology in adults generally resembled what was observed in children during the same period.



Supplemental Tables

eTable 1: GISAID Accession Numbers, Lineages, and Variant of Concern (VOC) Classification of 499 SARS-CoV-2 Sequences Included in Study

ID	GISAID Accession	Pango Lineage	NextClade Clade	Variant Classification
LC_200	EPI_ISL_1501823	B.1.349	20C	Non-VOC
LC_201	EPI_ISL_1501824	B.1.582	20C	Non-VOC
LC_202	EPI_ISL_1501825	B.1.2	20G	Non-VOC
LC_203	EPI_ISL_1501826	B.1.2	20G	Non-VOC
LC_204	EPI_ISL_1501827	B.1.2	20G	Non-VOC
LC_205	EPI_ISL_1501828	B.1.2	20G	Non-VOC
LC_206	EPI_ISL_1501829	B.1.509	20C	Non-VOC
LC_207	EPI_ISL_1501830	B.1.2	20G	Non-VOC
LC_208	EPI_ISL_1501831	B.1.576	20C	Non-VOC
LC_209	EPI_ISL_1501832	B.1.2	20G	Non-VOC
LC_210	EPI_ISL_1501833	B.1.2	20G	Non-VOC
LC_211	EPI_ISL_1501834	B.1.2	20G	Non-VOC
LC_212	EPI_ISL_1501835	B.1.240	20A	Non-VOC
LC_213	EPI_ISL_1501836	B.1.243	20A	Non-VOC
LC_214	EPI_ISL_1501837	B.1.509	20C	Non-VOC
LC_215	EPI_ISL_1501838	B.1.2	20G	Non-VOC
LC_216	EPI_ISL_1501839	B.1.2	20G	Non-VOC
LC_217	EPI_ISL_1501840	B.1.240	20A	Non-VOC
LC_218	EPI_ISL_1501841	B.1.1.222	20B	Non-VOC
LC_219	EPI_ISL_1501842	B.1.2	20G	Non-VOC
LC_220	EPI_ISL_1501843	B.1.1	20B	Non-VOC
LC_221	EPI_ISL_1501844	B.1.1.518	20B	Non-VOC
LC_222	EPI_ISL_1501845	B.1.36.10	20A	Non-VOC
LC_223	EPI_ISL_1501846	B.1.139	20A	Non-VOC
LC_224	EPI_ISL_1501847	B.1.240	20A	Non-VOC
LC_225	EPI_ISL_1501848	B.1.2	20G	Non-VOC
LC_226	EPI_ISL_1501849	B.1.110.3	20A	Non-VOC
LC_227	EPI_ISL_1501850	B.1.2	20G	Non-VOC
LC_228	EPI_ISL_1501851	B.1.2	20G	Non-VOC
LC_229	EPI_ISL_1501852	B.1.2	20G	Non-VOC
LC_230	EPI_ISL_1501853	B.1.2	20G	Non-VOC
LC_231	EPI_ISL_1501854	B.1.2	20G	Non-VOC
LC_232	EPI_ISL_1501855	B.1.565	20A	Non-VOC

LC_233	EPI ISL 1501856	B.1.1.434	20B	Non-VOC
LC_234	EPI ISL 1501857	B.1.2	20G	Non-VOC
LC_236	EPI ISL 1501858	B.1.1.518	20B	Non-VOC
LC_237	EPI ISL 1501859	B.1.2	20G	Non-VOC
LC_238	EPI ISL 1501860	B.1.2	20G	Non-VOC
LC_239	EPI ISL 1501861	B.1.2	20G	Non-VOC
LC_240	EPI ISL 1501862	B.1	20A	Non-VOC
LC_241	EPI ISL 1501863	B.1.2	20G	Non-VOC
LC_242	EPI ISL 1501864	B.1.2	20G	Non-VOC
LC_243	EPI ISL 1501865	B.1.2	20G	Non-VOC
LC_246	EPI ISL 1501866	B.1.2	20G	Non-VOC
LC_248	EPI ISL 1501867	B.1.2	20G	Non-VOC
LC_249	EPI ISL 1501868	B.1.2	20G	Non-VOC
LC_250	EPI ISL 1501869	B.1.2	20G	Non-VOC
LC_251	EPI ISL 1501870	B.1.2	20G	Non-VOC
LC_252	EPI ISL 1501871	C.31	20D	Non-VOC
LC_253	EPI ISL 1501872	B.1.2	20G	Non-VOC
LC_254	EPI ISL 1501873	B.1.2	20G	Non-VOC
LC_255	EPI ISL 1501874	B.1.324	20C	Non-VOC
LC_256	EPI ISL 1501875	B.1.2	20G	Non-VOC
LC_257	EPI ISL 1501876	B.1.2	20G	Non-VOC
LC_258	EPI ISL 1501877	B.1.2	20G	Non-VOC
LC_259	EPI ISL 1501878	B.1.2	20G	Non-VOC
LC_260	EPI ISL 1501879	B.1.2	20G	Non-VOC
LC_261	EPI ISL 1501880	B.1.2	20G	Non-VOC
LC_262	EPI ISL 1501881	B.1	20A	Non-VOC
LC_263	EPI ISL 1501882	B.1.2	20G	Non-VOC
LC_264	EPI ISL 1501883	B.1.2	20G	Non-VOC
LC_265	EPI ISL 1501884	B.1.1	20B	Non-VOC
LC_266	EPI ISL 1501885	B.1.2	20G	Non-VOC
LC_267	EPI ISL 1501886	B.1.2	20G	Non-VOC
LC_268	EPI ISL 1501887	B.1.2	20G	Non-VOC
LC_269	EPI ISL 1501888	B.1.2	20G	Non-VOC
LC_270	EPI ISL 1501889	B.1.565	20A	Non-VOC
LC_271	EPI ISL 1501890	B.1.2	20G	Non-VOC
LC_272	EPI ISL 1501891	B.1.2	20G	Non-VOC
LC_273	EPI ISL 1501892	B.1.2	20G	Non-VOC
LC_274	EPI ISL 1501893	B.1.234	20A	Non-VOC
LC_275	EPI ISL 1501894	B.1.2	20G	Non-VOC

LC_276	EPI ISL 1501895	B.1.543	20A	Non-VOC
LC_277	EPI ISL 1501896	B.1.2	20G	Non-VOC
LC_278	EPI ISL 1501897	B.1.2	20G	Non-VOC
LC_279	EPI ISL 1501898	B.1.1.222	20B	Non-VOC
LC_280	EPI ISL 1501899	B.1.2	20G	Non-VOC
LC_281	EPI ISL 1501900	B.1.2	20G	Non-VOC
LC_282	EPI ISL 1501901	B.1.565	20A	Non-VOC
LC_283	EPI ISL 1501902	B.1.2	20G	Non-VOC
LC_284	EPI ISL 1501903	B.1.2	20G	Non-VOC
LC_285	EPI ISL 1501904	B.1.1.222	20B	Non-VOC
LC_286	EPI ISL 1501905	B.1.2	20G	Non-VOC
LC_287	EPI ISL 1501906	B.1.2	20G	Non-VOC
LC_288	EPI ISL 1501907	B.1.1.432	20B	Non-VOC
LC_289	EPI ISL 1501908	B.1.2	20G	Non-VOC
LC_290	EPI ISL 1501909	B.1.1.222	20B	Non-VOC
LC_291	EPI ISL 1501910	B.1.2	20G	Non-VOC
LC_292	EPI ISL 1501911	B.1.243	20A	Non-VOC
LC_293	EPI ISL 1501912	B.1.596	20G	Non-VOC
LC_294	EPI ISL 1501913	B.1.2	20G	Non-VOC
LC_295	EPI ISL 1501914	B.1.2	20G	Non-VOC
LC_296	EPI ISL 1501915	B.1.2	20G	Non-VOC
LC_297	EPI ISL 1501916	B.1.1	20B	Non-VOC
LC_299	EPI ISL 1501918	B.1	20A	Non-VOC
LC_300	EPI ISL 1501919	B.1.1.434	20B	Non-VOC
LC_301	EPI ISL 1501920	B.1.576	20C	Non-VOC
LC_303	EPI ISL 1501921	B.1.139	20A	Non-VOC
LC_305	EPI ISL 1501922	B.1.2	20G	Non-VOC
LC_306	EPI ISL 1501923	B.1.2	20G	Non-VOC
LC_307	EPI ISL 1501924	B.1.2	20G	Non-VOC
LC_308	EPI ISL 1501925	B.1.2	20G	Non-VOC
LC_310	EPI ISL 1501927	B.1.305	20C	Non-VOC
LC_311	EPI ISL 1501928	B.1.1.518	20B	Non-VOC
LC_312	EPI ISL 1501929	B.1.396	20A	Non-VOC
LC_314	EPI ISL 1501930	C.31	20D	Non-VOC
LC_315	EPI ISL 1501931	B.1.2	20G	Non-VOC
LC_316	EPI ISL 1501932	B.1.576	20C	Non-VOC
LC_317	EPI ISL 1501933	B.1	20B	Non-VOC
LC_318	EPI ISL 1501934	B.1.2	20G	Non-VOC
LC_319	EPI ISL 1501935	B.1.2	20G	Non-VOC

LC_320	EPI ISL 1501936	B.1.2	20G	Non-VOC
LC_321	EPI ISL 1501937	B.1.2	20G	Non-VOC
LC_322	EPI ISL 1501938	B.1.2	20G	Non-VOC
LC_323	EPI ISL 1501939	B.1.1.518	20B	Non-VOC
LC_324	EPI ISL 1501940	B.1.1.416	20B	Non-VOC
LC_325	EPI ISL 1501941	B.1.595	20C	Non-VOC
LC_326	EPI ISL 1501942	B.1.2	20G	Non-VOC
LC_327	EPI ISL 1501943	B.1.578	20C	Non-VOC
LC_328	EPI ISL 1501944	B.1	20A	Non-VOC
LC_329	EPI ISL 1501945	B.1.2	20G	Non-VOC
LC_330	EPI ISL 1501946	B.1.2	20G	Non-VOC
LC_331	EPI ISL 1501947	B.1.2	20G	Non-VOC
LC_332	EPI ISL 1501948	B.1.2	20G	Non-VOC
LC_333	EPI ISL 1501949	B.1.2	20G	Non-VOC
LC_334	EPI ISL 1501950	B.1.565	20A	Non-VOC
LC_335	EPI ISL 1501951	B.1.509	20C	Non-VOC
LC_336	EPI ISL 1501952	B.1.2	20G	Non-VOC
LC_338	EPI ISL 1501953	B.1.1.317	20B	Non-VOC
LC_339	EPI ISL 1501954	B.1.2	20G	Non-VOC
LC_340	EPI ISL 1501955	B.1.2	20G	Non-VOC
LC_341	EPI ISL 1501956	B.1.427	20C	Non-VOC
LC_342	EPI ISL 1501957	B.1.232	20A	Non-VOC
LC_346	EPI ISL 1501959	B.1.2	20G	Non-VOC
LC_347	EPI ISL 1501960	B.1.1.192	20B	Non-VOC
LC_348	EPI ISL 1501961	B.1.2	20G	Non-VOC
LC_349	EPI ISL 1501962	B.1.2	20G	Non-VOC
LC_350	EPI ISL 1501963	B.1.240	20A	Non-VOC
LC_351	EPI ISL 1501964	A.2.5	19B	Non-VOC
LC_352	EPI ISL 1501965	B.1.2	20G	Non-VOC
LC_353	EPI ISL 1501966	B.1.2	20G	Non-VOC
LC_354	EPI ISL 1501967	B.1.232	20A	Non-VOC
LC_355	EPI ISL 1501968	B.1.139	20A	Non-VOC
LC_356	EPI ISL 1501969	B.1.576	20C	Non-VOC
LC_357	EPI ISL 1501970	B.1.2	20G	Non-VOC
LC_359	EPI ISL 1501972	B.1	20C	Non-VOC
LC_360	EPI ISL 1501973	B.1.2	20G	Non-VOC
LC_361	EPI ISL 1501974	B.1.2	20G	Non-VOC
LC_362	EPI ISL 1501975	B.1.429	20C	Non-VOC
LC_363	EPI ISL 1501976	B.1.2	20G	Non-VOC

LC_365	EPI ISL 1501977	B.1.2	20G	Non-VOC
LC_367	EPI ISL 1501978	B.1.2	20G	Non-VOC
LC_368	EPI ISL 1501979	B.1.2	20G	Non-VOC
LC_370	EPI ISL 1501980	B.1.2	20G	Non-VOC
LC_371	EPI ISL 1501981	B.1.427	20C	Non-VOC
LC_373	EPI ISL 1501983	B.1.1.7	20I/501Y.V1	Alpha
LC_374	EPI ISL 1501984	B.1.2	20G	Non-VOC
LC_375	EPI ISL 1501985	B.1.2	20G	Non-VOC
LC_376	EPI ISL 1501986	B.1.2	20G	Non-VOC
LC_377	EPI ISL 1501987	B.1.2	20G	Non-VOC
LC_378	EPI ISL 1501988	B.1.1.7	20I/501Y.V1	Alpha
LC_379	EPI ISL 1501989	B.1.1.518	20B	Non-VOC
LC_380	EPI ISL 1501990	B.1.2	20G	Non-VOC
LC_381	EPI ISL 1501991	B.1.232	20A	Non-VOC
LC_382	EPI ISL 1501992	B.1.596	20G	Non-VOC
LC_383	EPI ISL 1501993	B.1	20C	Non-VOC
LC_384	EPI ISL 1501994	B.1.429	20C	Non-VOC
LC_385	EPI ISL 1501995	B.1.239	20A	Non-VOC
LC_386	EPI ISL 1501996	B.1.1.519	20B	Non-VOC
LC_387	EPI ISL 1501997	B.1.427	20C	Non-VOC
LC_388	EPI ISL 1501998	B.1.1.222	20B	Non-VOC
LC_389	EPI ISL 1501999	B.1.2	20G	Non-VOC
LC_390	EPI ISL 1502000	B.1.243	20A	Non-VOC
LC_391	EPI ISL 1502001	B.1.2	20G	Non-VOC
LC_392	EPI ISL 1502002	B.1.2	20G	Non-VOC
LC_393	EPI ISL 1502003	B.1.2	20G	Non-VOC
LC_394	EPI ISL 1502004	B.1.609	20A	Non-VOC
LC_396	EPI ISL 1502005	B.1.427	20C	Non-VOC
LC_397	EPI ISL 1502006	B.1.427	20C	Non-VOC
LC_398	EPI ISL 1502007	B.1.429	20C	Non-VOC
LC_399	EPI ISL 1502008	B.1.1.7	20I/501Y.V1	Alpha
LC_400	EPI ISL 1502009	B.1.2	20G	Non-VOC
LC_401	EPI ISL 1502010	B.1.2	20G	Non-VOC
LC_403	EPI ISL 1502011	B.1.427	20C	Non-VOC
LC_404	EPI ISL 1502012	B.1.2	20G	Non-VOC
LC_405	EPI ISL 1502013	B.1.1.7	20I/501Y.V1	Alpha
LC_406	EPI ISL 1502014	B.1.2	20G	Non-VOC
LC_409	EPI ISL 1502015	B.1.2	20G	Non-VOC
LC_410	EPI ISL 1502016	B.1.2	20G	Non-VOC

LC_411	EPI ISL 1502017	B.1.2	20G	Non-VOC
LC_412	EPI ISL 1502018	B.1.243	20A	Non-VOC
LC_413	EPI ISL 1502019	B.1.2	20G	Non-VOC
LC_414	EPI ISL 1502020	B.1.400	20A	Non-VOC
LC_415	EPI ISL 1502021	P.1	20J/501Y.V3	Gamma
LC_416	EPI ISL 1502022	B.1.400	20A	Non-VOC
LC_417	EPI ISL 1502023	B.1.243	20A	Non-VOC
LC_418	EPI ISL 1502024	B.1.2	20G	Non-VOC
LC_420	EPI ISL 1502025	P.2	20B	Non-VOC
LC_421	EPI ISL 1502026	B.1.1.222	20B	Non-VOC
LC_422	EPI ISL 1502027	P.1	20J/501Y.V3	Gamma
LC_423	EPI ISL 1502028	B.1.239	20A	Non-VOC
LC_424	EPI ISL 1502029	B.1.1.519	20B	Non-VOC
LC_425	EPI ISL 1502030	B.1.1.7	20I/501Y.V1	Alpha
LC_426	EPI ISL 1502031	B.1.2	20G	Non-VOC
LC_427	EPI ISL 1502032	B.1.1.7	20I/501Y.V1	Alpha
LC_428	EPI ISL 1502033	B.1.2	20G	Non-VOC
LC_429	EPI ISL 1502034	P.2	20B	Non-VOC
LC_430	EPI ISL 1502035	B.1.2	20G	Non-VOC
LC_431	EPI ISL 1502036	B.1.1.7	20I/501Y.V1	Alpha
LC_432	EPI ISL 1502037	B.1.427	20C	Non-VOC
LC_433	EPI ISL 1502038	B.1.1.7	20I/501Y.V1	Alpha
LC_434	EPI ISL 1502039	B.1.2	20G	Non-VOC
LC_435	EPI ISL 1502040	P.1	20J/501Y.V3	Gamma
LC_436	EPI ISL 1502041	B.1.1.7	20I/501Y.V1	Alpha
LC_437	EPI ISL 1502042	B.1.1.7	20I/501Y.V1	Alpha
LC_438	EPI ISL 1502043	B.1.427	20C	Non-VOC
LC_439	EPI ISL 1502044	B.1.427	20C	Non-VOC
LC_440	EPI ISL 1502045	B.1.1.519	20B	Non-VOC
LC_441	EPI ISL 1502046	B.1.427	20C	Non-VOC
LC_442	EPI ISL 1502047	B.1.427	20C	Non-VOC
LC_443	EPI ISL 1704763	B.1.1.7	20I/501Y.V1	Alpha
LC_444	EPI ISL 1704764	B.1.1.7	20I/501Y.V1	Alpha
LC_445	EPI ISL 1704765	B.1.429	20C	Non-VOC
LC_446	EPI ISL 1704766	B.1.429	20C	Non-VOC
LC_447	EPI ISL 1704767	B.1.2	20G	Non-VOC
LC_448	EPI ISL 1704768	B.1.2	20G	Non-VOC
LC_449	EPI ISL 1704769	B.1.2	20G	Non-VOC
LC_450	EPI ISL 1704770	B.1.526	20C	Non-VOC

LC_451	EPI ISL 1704771	B.1.1.7	20I/501Y.V1	Alpha
LC_452	EPI ISL 1704772	P.1	20J/501Y.V3	Gamma
LC_453	EPI ISL 1704773	B.1.1.7	20I/501Y.V1	Alpha
LC_454	EPI ISL 1704715	B.1.2	20G	Non-VOC
LC_455	EPI ISL 1704716	B.1.429	20C	Non-VOC
LC_456	EPI ISL 1704717	B.1.427	20C	Non-VOC
LC_457	EPI ISL 1704718	B.1.427	20C	Non-VOC
LC_458	EPI ISL 1704719	B.1.427	20C	Non-VOC
LC_459	EPI ISL 1704720	B.1.1.519	20B	Non-VOC
LC_460	EPI ISL 1704721	B.1.1.519	20B	Non-VOC
LC_461	EPI ISL 1704722	R.1	20B	Non-VOC
LC_462	EPI ISL 1704723	B.1.1.7	20I/501Y.V1	Alpha
LC_463	EPI ISL 1704724	B.1.2	20G	Non-VOC
LC_464	EPI ISL 1704725	B.1.2	20G	Non-VOC
LC_465	EPI ISL 1704726	B.1.1.7	20I/501Y.V1	Alpha
LC_466	EPI ISL 1704727	B.1.429	20C	Non-VOC
LC_467	EPI ISL 1704728	B.1.1.7	20I/501Y.V1	Alpha
LC_468	EPI ISL 1704729	P.1	20J/501Y.V3	Gamma
LC_469	EPI ISL 1704730	B.1.1.7	20I/501Y.V1	Alpha
LC_470	EPI ISL 2009368	B.1.2	20G	Non-VOC
LC_471	EPI ISL 2009369	P.1	20J/501Y.V3	Gamma
LC_472	EPI ISL 2009370	Q.3	20I/501Y.V1	Alpha
LC_473	EPI ISL 2009371	P.1	20J/501Y.V3	Gamma
LC_474	EPI ISL 2009372	B.1.1.7	20I/501Y.V1	Alpha
LC_475	EPI ISL 2009373	B.1.1.7	20I/501Y.V1	Alpha
LC_476	EPI ISL 2009374	B.1.1.7	20I/501Y.V1	Alpha
LC_477	EPI ISL 2009375	B.1.1.7	20I/501Y.V1	Alpha
LC_478	EPI ISL 1704731	B.1.429	20C	Non-VOC
LC_479	EPI ISL 1704732	B.1.351	20H/501Y.V2	Beta
LC_480	EPI ISL 1704733	B.1.351	20H/501Y.V2	Beta
LC_481	EPI ISL 1704734	B.1.1.7	20I/501Y.V1	Alpha
LC_482	EPI ISL 1704735	B.1.596	20G	Non-VOC
LC_483	EPI ISL 1704736	B.1.1.7	20I/501Y.V1	Alpha
LC_484	EPI ISL 1704737	B.1.1.7	20I/501Y.V1	Alpha
LC_485	EPI ISL 1704738	P.1	20J/501Y.V3	Gamma
LC_486	EPI ISL 1704739	B.1.1.7	20I/501Y.V1	Alpha
LC_487	EPI ISL 1704740	B.1.526	20C	Non-VOC
LC_488	EPI ISL 1704741	P.1	20J/501Y.V3	Gamma
LC_489	EPI ISL 1704742	B.1.1.7	20I/501Y.V1	Alpha

LC_490	EPI ISL 1704743	B.1.1.7	20I/501Y.V1	Alpha
LC_491	EPI ISL 1704744	P.1	20J/501Y.V3	Gamma
LC_492	EPI ISL 1704745	B.1.1.7	20I/501Y.V1	Alpha
LC_493	EPI ISL 1704746	B.1.1.7	20I/501Y.V1	Alpha
LC_494	EPI ISL 1704747	B.1.1.7	20I/501Y.V1	Alpha
LC_495	EPI ISL 1704748	B.1.1.7	20I/501Y.V1	Alpha
LC_496	EPI ISL 1704749	B.1.1.7	20I/501Y.V1	Alpha
LC_497	EPI ISL 1704750	B.1.2	20G	Non-VOC
LC_498	EPI ISL 1704751	P.1	20J/501Y.V3	Gamma
LC_499	EPI ISL 1704752	B.1.427	20C	Non-VOC
LC_500	EPI ISL 1704753	B.1.427	20C	Non-VOC
LC_501	EPI ISL 1704754	B.1.1.7	20I/501Y.V1	Alpha
LC_502	EPI ISL 1704755	B.1.1.7	20I/501Y.V1	Alpha
LC_503	EPI ISL 1704756	P.1.12	20J/501Y.V3	Gamma
LC_504	EPI ISL 1704757	B.1.1.7	20I/501Y.V1	Alpha
LC_505	EPI ISL 1704758	B.1.427	20C	Non-VOC
LC_506	EPI ISL 1704759	B.1.429	20C	Non-VOC
LC_507	EPI ISL 1704760	R.1	20B	Non-VOC
LC_508	EPI ISL 1704761	R.1	20B	Non-VOC
LC_509	EPI ISL 1704762	B.1.1.7	20I/501Y.V1	Alpha
LC_510	EPI ISL 2009376	B.1.1.7	20I/501Y.V1	Alpha
LC_512	EPI ISL 2009377	B.1.1.7	20I/501Y.V1	Alpha
LC_513	EPI ISL 2009378	P.2	20B	Non-VOC
LC_515	EPI ISL 2009380	B.1.1.7	20I/501Y.V1	Alpha
LC_516	EPI ISL 2009381	B.1.637	20C	Non-VOC
LC_517	EPI ISL 2009382	B.1.1.7	20I/501Y.V1	Alpha
LC_519	EPI ISL 2009383	B.1.1.7	20I/501Y.V1	Alpha
LC_520	EPI ISL 2009384	B.1.1.7	20I/501Y.V1	Alpha
LC_521	EPI ISL 2009385	B.1.1.7	20I/501Y.V1	Alpha
LC_523	EPI ISL 2009386	B.1.429	20C	Non-VOC
LC_524	EPI ISL 2009387	B.1.1.7	20I/501Y.V1	Alpha
LC_525	EPI ISL 2009388	B.1.1.7	20I/501Y.V1	Alpha
LC_526	EPI ISL 2009389	P.1	20J/501Y.V3	Gamma
LC_527	EPI ISL 2009390	B.1.1.7	20I/501Y.V1	Alpha
LC_528	EPI ISL 2009391	B.1.1.7	20I/501Y.V1	Alpha
LC_529	EPI ISL 2009392	B.1.351	20H/501Y.V2	Beta
LC_531	EPI ISL 2009394	P.1	20J/501Y.V3	Gamma
LC_532	EPI ISL 2009395	P.1	20J/501Y.V3	Gamma
LC_578	EPI ISL 2373051	B.1.1.7	20I/501Y.V1	Alpha

LC_580	EPI ISL 2373052	B.1.1.519	20B	Non-VOC
LC_581	EPI ISL 2373053	B.1.1.7	20I/501Y.V1	Alpha
LC_582	EPI ISL 2373054	B.1.1.7	20I/501Y.V1	Alpha
LC_583	EPI ISL 2373055	P.1	20J/501Y.V3	Gamma
LC_584	EPI ISL 2373056	B.1.1.7	20I/501Y.V1	Alpha
LC_586	EPI ISL 2373057	P.1	20J/501Y.V3	Gamma
LC_587	EPI ISL 2373058	Q.3	20I/501Y.V1	Alpha
LC_590	EPI ISL 2373059	B.1.1.7	20I/501Y.V1	Alpha
LC_591	EPI ISL 2373060	B.1.1.7	20I/501Y.V1	Alpha
LC_592	EPI ISL 2373061	P.1	20J/501Y.V3	Gamma
LC_593	EPI ISL 2373062	P.1	20J/501Y.V3	Gamma
LC_594	EPI ISL 2373063	B.1.637	20C	Non-VOC
LC_595	EPI ISL 2373064	P.1	20J/501Y.V3	Gamma
LC_596	EPI ISL 2373065	B.1.1.7	20I/501Y.V1	Alpha
LC_597	EPI ISL 2373066	B.1.1.7	20I/501Y.V1	Alpha
LC_598	EPI ISL 2373067	B.1.1.7	20I/501Y.V1	Alpha
LC_599	EPI ISL 2373068	B.1.1.519	20B	Non-VOC
LC_600	EPI ISL 2373069	P.1	20J/501Y.V3	Gamma
LC_601	EPI ISL 2373070	P.1	20J/501Y.V3	Gamma
LC_604	EPI ISL 2373071	None	20I/501Y.V1	Alpha
LC_605	EPI ISL 2373072	B.1.1.7	20I/501Y.V1	Alpha
LC_606	EPI ISL 2373073	B.1.1.7	20I/501Y.V1	Alpha
LC_607	EPI ISL 2373074	B.1.1.7	20I/501Y.V1	Alpha
LC_608	EPI ISL 2373075	B.1.1.7	20I/501Y.V1	Alpha
LC_609	EPI ISL 2373076	P.1	20J/501Y.V3	Gamma
LC_610	EPI ISL 2373077	B.1.1.222	20B	Non-VOC
LC_611	EPI ISL 2373078	B.1.1.7	20I/501Y.V1	Alpha
LC_612	EPI ISL 2373079	P.1	20J/501Y.V3	Gamma
LC_613	EPI ISL 2373080	B.1.1.7	20I/501Y.V1	Alpha
LC_614	EPI ISL 2373081	P.1	20J/501Y.V3	Gamma
LC_615	EPI ISL 2373082	B.1.1.7	20I/501Y.V1	Alpha
LC_616	EPI ISL 2373083	B.1.1.7	20I/501Y.V1	Alpha
LC_617	EPI ISL 2373084	B.1.1.7	20I/501Y.V1	Alpha
LC_618	EPI ISL 2373085	B.1.1.7	20I/501Y.V1	Alpha
LC_619	EPI ISL 2373086	B.1.525	20A	Non-VOC
LC_620	EPI ISL 2373087	B.1.1.7	20I/501Y.V1	Alpha
LC_621	EPI ISL 2373088	B.1.1.7	20I/501Y.V1	Alpha
LC_622	EPI ISL 2373089	B.1.1.7	20I/501Y.V1	Alpha
LC_623	EPI ISL 2373090	B.1.1.7	20I/501Y.V1	Alpha

LC_624	EPI ISL 2373091	B.1.1.7	20I/501Y.V1	Alpha
LC_625	EPI ISL 2373092	B.1.1.7	20I/501Y.V1	Alpha
LC_626	EPI ISL 2373093	B.1.1.7	20I/501Y.V1	Alpha
LC_627	EPI ISL 2373094	P.1	20J/501Y.V3	Gamma
LC_628	EPI ISL 2373095	B.1.1.7	20I/501Y.V1	Alpha
LC_629	EPI ISL 2373096	B.1.1.7	20I/501Y.V1	Alpha
LC_630	EPI ISL 2373097	B.1.1.7	20I/501Y.V1	Alpha
LC_631	EPI ISL 2373098	B.1.1.7	20I/501Y.V1	Alpha
LC_632	EPI ISL 2373099	B.1.1.7	20I/501Y.V1	Alpha
LC_633	EPI ISL 2373100	P.1	20J/501Y.V3	Gamma
LC_634	EPI ISL 2373101	B.1.1.7	20I/501Y.V1	Alpha
LC_635	EPI ISL 2373102	B.1.1.7	20I/501Y.V1	Alpha
LC_636	EPI ISL 2373103	P.1	20J/501Y.V3	Gamma
LC_637	EPI ISL 2373104	P.1	20J/501Y.V3	Gamma
LC_638	EPI ISL 2373105	B.1.1.7	20I/501Y.V1	Alpha
LC_639	EPI ISL 2373106	B.1.1.7	20I/501Y.V1	Alpha
LC_640	EPI ISL 2373107	P.1	20J/501Y.V3	Gamma
LC_641	EPI ISL 2842585	P.1	20J (Gamma, V3)	Gamma
LC_642	EPI ISL 2842586	None	20I (Alpha, V1)	Alpha
LC_643	EPI ISL 2842587	P.1	20J (Gamma, V3)	Gamma
LC_644	EPI ISL 2842588	B.1.1.7	20I (Alpha, V1)	Alpha
LC_645	EPI ISL 2842589	P.1	20J (Gamma, V3)	Gamma
LC_646	EPI ISL 2842590	B.1.1.7	20I (Alpha, V1)	Alpha
LC_647	EPI ISL 2842591	B.1.1.7	20I (Alpha, V1)	Alpha
LC_648	EPI ISL 2842592	B.1.1.7	20I (Alpha, V1)	Alpha
LC_649	EPI ISL 2842593	B.1.1.7	20I (Alpha, V1)	Alpha
LC_650	EPI ISL 2842594	P.1	20J (Gamma, V3)	Gamma
LC_651	EPI ISL 2842595	B.1.1.7	20I (Alpha, V1)	Alpha
LC_654	EPI ISL 2842580	AY.5	21A (Delta)	Delta
LC_655	EPI ISL 2842581	P.1	20J (Gamma, V3)	Gamma
LC_657	EPI ISL 2842582	P.1	20J (Gamma, V3)	Gamma
LC_658	EPI ISL 2842583	P.1	20J (Gamma, V3)	Gamma

LC_659	EPI ISL 2842584	B.1.1.7	20I (Alpha, V1)	Alpha
LC_660	EPI ISL 3304311	AY.4	21A (Delta)	Delta
LC_661	EPI ISL 3304312	B.1.1.7	20I (Alpha, V1)	Alpha
LC_662	EPI ISL 3304313	B.1.617.2	21A (Delta)	Delta
LC_663	EPI ISL 3185847	P.1	20J (Gamma, V3)	Gamma
LC_664	EPI ISL 3185848	AY.3	21A (Delta)	Delta
LC_665	EPI ISL 3185849	AY.3	21A (Delta)	Delta
LC_666	EPI ISL 3185850	AY.25	21A (Delta)	Delta
LC_667	EPI ISL 3185851	AY.4	21A (Delta)	Delta
LC_671	EPI ISL 3304314	AY.23	21A (Delta)	Delta
LC_672	EPI ISL 3304315	AY.4	21A (Delta)	Delta
LC_673	EPI ISL 3304316	B.1.617.2	21A (Delta)	Delta
LC_674	EPI ISL 3304317	AY.5	21A (Delta)	Delta
LC_675	EPI ISL 3304318	AY.25	21A (Delta)	Delta
LC_677	EPI ISL 3304319	B.1.617.2	21A (Delta)	Delta
LC_679	EPI ISL 3304320	AY.4	21A (Delta)	Delta
LC_680	EPI ISL 3304321	AY.4	21A (Delta)	Delta
LC_681	EPI ISL 3304322	AY.25	21A (Delta)	Delta
LC_682	EPI ISL 3304323	AY.4	21A (Delta)	Delta
LC_683	EPI ISL 3304324	B.1.617.2	21A (Delta)	Delta
LC_684	EPI ISL 3304325	B.1.617.2	21A (Delta)	Delta
LC_685	EPI ISL 3304326	AY.4	21A (Delta)	Delta
LC_686	EPI ISL 3304327	B.1.1.7	20I (Alpha, V1)	Alpha
LC_687	EPI ISL 3304328	AY.20	21A (Delta)	Delta
LC_688	EPI ISL 3304329	B.1.617.2	21A (Delta)	Delta
LC_689	EPI ISL 3304330	B.1.617.2	21A (Delta)	Delta
LC_690	EPI ISL 3304331	AY.3	21A (Delta)	Delta
LC_691	EPI ISL 3304332	AY.26	21A (Delta)	Delta
LC_692	EPI ISL 3304333	B.1.617.2	21A (Delta)	Delta
LC_693	EPI ISL 3304334	B.1.617.2	21A (Delta)	Delta
LC_694	EPI ISL 3304335	AY.4	21A (Delta)	Delta
LC_695	EPI ISL 3304336	AY.3	21A (Delta)	Delta
LC_697	EPI ISL 3304338	B.1.617.2	21A (Delta)	Delta
LC_698	EPI ISL 3304339	AY.10	21A (Delta)	Delta
LC_700	EPI ISL 3304340	AY.4	21A (Delta)	Delta
LC_701	EPI ISL 3304341	AY.3	21A (Delta)	Delta
LC_702	EPI ISL 3304342	B.1.617.2	21A (Delta)	Delta

LC_703	EPI ISL 3304343	B.1.617.2	21A (Delta)	Delta
LC_704	EPI ISL 3304344	B.1.617.2	21A (Delta)	Delta
LC_705	EPI ISL 4026596	B.1.617.2	21A (Delta)	Delta
LC_706	EPI ISL 4026597	AY.3	21A (Delta)	Delta
LC_707	EPI ISL 4026598	AY.3	21A (Delta)	Delta
LC_708	EPI ISL 4026599	B.1.617.2	21A (Delta)	Delta
LC_709	EPI ISL 4026600	B.1.617.2	21A (Delta)	Delta
LC_710	EPI ISL 4026601	AY.26	21A (Delta)	Delta
LC_711	EPI ISL 4026602	AY.25	21A (Delta)	Delta
LC_712	EPI ISL 4026603	AY.3	21A (Delta)	Delta
LC_713	EPI ISL 4026604	B.1.617.2	21A (Delta)	Delta
LC_714	EPI ISL 4026605	B.1.617.2	21A (Delta)	Delta
LC_715	EPI ISL 4026606	AY.25	21A (Delta)	Delta
LC_716	EPI ISL 4026607	B.1.617.2	21A (Delta)	Delta
LC_717	EPI ISL 4026608	AY.3.1	21A (Delta)	Delta
LC_718	EPI ISL 4026609	AY.3	21A (Delta)	Delta
LC_719	EPI ISL 4026610	AY.25	21A (Delta)	Delta
LC_720	EPI ISL 4026611	AY.25	21A (Delta)	Delta
LC_721	EPI ISL 4026612	AY.3	21A (Delta)	Delta
LC_722	EPI ISL 4026613	B.1.617.2	21A (Delta)	Delta
LC_723	EPI ISL 4026614	AY.25	21A (Delta)	Delta
LC_724	EPI ISL 4026615	AY.14	21A (Delta)	Delta
LC_725	EPI ISL 4026616	AY.25	21A (Delta)	Delta
LC_727	EPI ISL 4026618	B.1.617.2	21A (Delta)	Delta
LC_728	EPI ISL 4026619	B.1.617.2	21A (Delta)	Delta
LC_730	EPI ISL 4026620	AY.3	21A (Delta)	Delta
LC_731	EPI ISL 4026621	AY.3	21A (Delta)	Delta
LC_732	EPI ISL 4026622	B.1.617.2	21A (Delta)	Delta
LC_733	EPI ISL 4026623	AY.3	21A (Delta)	Delta
LC_735	EPI ISL 4026624	B.1.617.2	21A (Delta)	Delta
LC_736	EPI ISL 4026625	AY.26	21A (Delta)	Delta
LC_737	EPI ISL 4026626	AY.25	21A (Delta)	Delta
LC_739	EPI ISL 4026627	AY.25	21A (Delta)	Delta
LC_740	EPI ISL 4026628	B.1.617.2	21A (Delta)	Delta
LC_741	EPI ISL 4026629	B.1.617.2	21A (Delta)	Delta
LC_742	EPI ISL 4026630	AY.3	21A (Delta)	Delta
LC_743	EPI ISL 4026631	B.1.617.2	21A (Delta)	Delta
LC_744	EPI ISL 5258008	B.1.617.2	21A (Delta)	Delta
LC_745	EPI ISL 5258009	B.1.617.2	21A (Delta)	Delta

LC_746	EPI ISL 5258010	AY.25	21A (Delta)	Delta
LC_747	EPI ISL 5258011	B.1.617.2	21A (Delta)	Delta
LC_748	EPI ISL 5258012	AY.26	21A (Delta)	Delta
LC_749	EPI ISL 5258013	AY.20	21A (Delta)	Delta
LC_750	EPI ISL 5258014	B.1.617.2	21A (Delta)	Delta
LC_751	EPI ISL 5258015	B.1.617.2	21A (Delta)	Delta
LC_752	EPI ISL 5258016	B.1.617.2	21A (Delta)	Delta
LC_753	EPI ISL 5258017	B.1.617.2	21A (Delta)	Delta
LC_754	EPI ISL 5258018	AY.25	21A (Delta)	Delta
LC_755	EPI ISL 5258019	AY.26	21A (Delta)	Delta
LC_756	EPI ISL 5258020	AY.26	21A (Delta)	Delta
LC_757	EPI ISL 5258021	AY.3	21A (Delta)	Delta
LC_758	EPI ISL 5258026	AY.3	21A (Delta)	Delta
LC_759	EPI ISL 5258027	B.1.617.2	21A (Delta)	Delta
LC_760	EPI ISL 5258028	AY.25	21A (Delta)	Delta
LC_761	EPI ISL 5258029	AY.34	21A (Delta)	Delta
LC_762	EPI ISL 5258030	B.1.617.2	21A (Delta)	Delta
LC_763	EPI ISL 5258031	AY.3	21A (Delta)	Delta
LC_764	EPI ISL 5258032	B.1.617.2	21A (Delta)	Delta
LC_765	EPI ISL 5258033	B.1.617.2	21A (Delta)	Delta
LC_766	EPI ISL 5258034	AY.3	21A (Delta)	Delta
LC_767	EPI ISL 5258035	B.1.617.2	21A (Delta)	Delta
LC_768	EPI ISL 5258036	AY.25	21A (Delta)	Delta
LC_769	EPI ISL 5258037	AY.20	21A (Delta)	Delta
LC_770	EPI ISL 5258038	B.1.617.2	21A (Delta)	Delta
LC_771	EPI ISL 5258039	AY.3	21A (Delta)	Delta
LC_773	EPI ISL 5258041	AY.25	21A (Delta)	Delta
LC_774	EPI ISL 5258042	B.1.617.2	21A (Delta)	Delta
LC_775	EPI ISL 5258043	B.1.617.2	21A (Delta)	Delta
LC_776	EPI ISL 5258044	AY.26	21A (Delta)	Delta
LC_777	EPI ISL 5258045	B.1.617.2	21A (Delta)	Delta
LC_778	EPI ISL 5258046	AY.3	21A (Delta)	Delta
LC_779	EPI ISL 5258047	B.1.617.2	21A (Delta)	Delta
LC_780	EPI ISL 5258048	B.1.617.2	21A (Delta)	Delta
LC_781	EPI ISL 5258049	B.1.617.2	21A (Delta)	Delta
LC_782	EPI ISL 5258050	B.1.617.2	21A (Delta)	Delta
LC_783	EPI ISL 5258051	AY.3	21A (Delta)	Delta
LC_784	EPI ISL 5258052	B.1.617.2	21A (Delta)	Delta
LC_785	EPI ISL 5258053	B.1.617.2	21A (Delta)	Delta

LC_786	EPI ISL 5258054	AY.25	21A (Delta)	Delta
LC_787	EPI ISL 5258055	B.1.617.2	21A (Delta)	Delta
LC_788	EPI ISL 5258056	B.1.617.2	21A (Delta)	Delta
LC_789	EPI ISL 5258057	AY.3	21A (Delta)	Delta
LC_791	EPI ISL 5258059	B.1.617.2	21A (Delta)	Delta
LC_792	EPI ISL 5258060	B.1.617.2	21A (Delta)	Delta
LC_793	EPI ISL 5258061	B.1.617.2	21A (Delta)	Delta

Based on the lineage of SARS-CoV-2 identified by WGS, children were grouped based on whether their COVID-19 infection was caused by a VOC, as well as the specific VOC lineage, using CDC definitions as of August 19th, 2021.²

eTable 2: Medical conditions with high-risk of COVID-19 complications

Medical Condition	Highest Level of Evidence
Bronchiectasis	Meta-Analysis and/or systematic review
Bronchopulmonary dysplasia	
Pulmonary hypertension and pulmonary embolism	
Cancer	
Cerebrovascular disease	
Chronic kidney disease	
Chronic liver disease	
COPD	
Diabetes mellitus, type 1	
Diabetes mellitus, type 2	
Heart conditions	
Interstitial lung disease	
Smoking, current and former	
Tuberculosis	
Obesity*	
Pregnancy and Recent Pregnancy	
Mental health disorders	Observational study
Down syndrome	
HIV	
Neurologic conditions	
Overweight*	
Sickle cell disease	
Solid organ or blood stem cell transplantation	
Substance use disorders	
Use of corticosteroids or other immunosuppressive medications	

Children in this study were classified as high risk for COVID-19 complications if they had an underlying condition for which there are high-quality and reproducible data (i.e., meta-analysis, systematic review, or observational study; excluding small studies, case reports/series, or conflicting evidence) based on CDC classification as of August 31st, 2021.³

*Obesity identified as body mass index (BMI) ≥ 30 kg/m² (or $\geq 95^{\text{th}}$ ile), and overweight defined as BMI 25-30 (or 85-95thile). If height was unknown and BMI was undetermined, patient was identified as high risk if weight > 95thile.

eTable 3: COVID-19 World Health Organization Clinical Progression Scale⁴

Patient State	Descriptor	Score
Uninfected	Uninfected; no viral RNA detected	0
Ambulatory mild disease	Asymptomatic; viral RNA detected	1
	Symptomatic; independent	2
	Symptomatic; assistance needed	3
Hospitalized: moderate disease	Hospitalized; no oxygen therapy*	4
	Hospitalized; oxygen by mask or nasal cannula	5
Hospitalized: severe disease	Hospitalized; oxygen by non-invasive ventilation or high-flow nasal cannula	6
	Intubation and mechanical ventilation, $pO_2/FiO_2 \geq 150$ or $SpO_2/FiO_2 \geq 200$	7
	Mechanical ventilation $pO_2/FiO_2 < 150$ ($SpO_2/FiO_2 < 200$) or vasopressors	8
	Mechanical ventilation pO_2/FiO_2 and vasopressors, dialysis, or extracorporeal membrane oxygenation	9
Dead	Dead	10

pO_2 : partial pressure of oxygen. FiO_2 : fraction of inspired oxygen. SpO_2 : oxygen saturation.

*If hospitalized for reasons other than COVID-19, status recorded as for ambulatory patient.

eTable 4: Sensitivity analysis[^] assessing association between COVID-19 severity and SARS-CoV-2 variants of concern correcting for potential impact of COVID-19 vaccine and monoclonal antibodies

	Marker of COVID-19 Severity: Odds Ratio (95% Confidence Interval; <i>p</i> Value)				
	Hospitalized for COVID-19	COVID-19 Pharmacologic Treatment	Respiratory Support	Intensive Care Unit Admission	WHO Clinical Progression Scale Score ≥ 6
Age	1.02 (0.96-1.09; 0.5)	1.2 (1.1-1.4; <0.001)*	1.2 (1.1-1.3; 0.003)*	1.2 (1.1-1.3; 0.003)*	1.2 (1.1-1.4; 0.003)*
Race (Black)	1.03 (0.36-2.7; >0.9)	0.60 (0.15-2.1; 0.4)	0.53 (0.11-2.1; 0.4)	0.61 (0.12-2.4; 0.5)	0.7 (0.12-2.8; 0.6)
Ethnicity (Hispanic)	1.3 (0.56-2.8; 0.6)	0.43 (0.12-1.3; 0.2)	0.44 (0.11-1.5; 0.2)	0.45 (0.11-1.6; 0.2)	0.43 (0.08-1.7; 0.3)
High-risk condition for COVID-19 complications	5.1 (2.4-12.0, <0.001)*	-	-	-	-
Pediatric COVID-19 community incidence	1.0 (1.0-1.0; 0.6)	1.0 (1.0-1.0; 0.2)	1.0 (1.0-1.0; 0.8)	1.0 (1.0-1.0; 0.2)	1.0 (1.0-1.0; 0.7)
SARS-CoV-2 lineage					
<i>Non-VOC</i>	ref	ref	ref	Ref	Ref
<i>Alpha VOC</i>	2.8 (0.95-8.4; 0.06)	2.1 (0.5-9.4; 0.3)	2.1 (0.34-12.9; 0.4)	2.2 (0.43-11.9; 0.3)	2.8 (0.4-24.3; 0.3)
<i>Gamma VOC</i>	6.5 (1.9-22.7; 0.003)*	4.7 (0.97-23.2; 0.05)	10.6 (2.2-65.0; 0.005)*	4.3 (0.72-26.1; 0.1)	11.2 (1.8-98.1; 0.013)*
<i>Delta VOC</i>	2.5 (0.80-8.1; 0.12)	2.3 (0.53-10.8; 0.3)	3.1 (0.57-19.9; 0.2)	2.2 (0.43-12.7; 0.3)	3.3 (0.46-31.0; 0.2)

VOC- variant of concern. y- years. m- month. ref- reference group for VOC odds ratio calculations. N/A- not applicable. High-risk conditions were excluded from the model for some outcomes because having a high-risk condition was mutually inclusive with the outcome of interest.

[^]A small number of patients were fully vaccinated (n=2; one each in the gamma and delta VOC groups) at time of their breakthrough infection or had received SARS-CoV-2 monoclonal antibodies (n=3; all in the alpha VOC group) as an outpatient early in infection to prevent subsequent morbidity. A sensitivity analysis was performed whereby we repeated the models reported in Table 1, presuming that these five patients would have experienced each severity marker had they not received these therapies. *Bolted values indicate statistical significance ($p < 0.05$).

Supplemental References

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2. Centers for Disease Control and Prevention; SARS-CoV-2 Variant Classifications and Definitions. Accessed August 31st, 2021, <https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-info.html>
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4. WHO Working Group on the Clinical Characterisation and Management of COVID-19 infection; A minimal common outcome measure set for COVID-19 clinical research. *Lancet Infect Dis*. Aug 2020;20(8):e192-e197. doi:10.1016/s1473-3099(20)30483-7