A catalog of associations between rare coding variants and COVID-19 outcomes

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This research has been conducted using the UK Biobank Resource (Project 26041)

ABSTRACT

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes coronavirus disease-19 (COVID-19), a respiratory illness that can result in hospitalization or death. We investigated associations between rare genetic variants and seven COVID-19 outcomes in 543,213 individuals, including 8,248 with COVID-19. After accounting for multiple testing, we did not identify any clear associations with rare variants either exome-wide or when specifically focusing on (i) 14 interferon pathway genes in which rare deleterious variants have been reported in severe COVID-19 patients; (ii) 167 genes located in COVID-19 GWAS risk loci; or (iii) 32 additional genes of immunologic relevance and/or therapeutic potential. Our analyses indicate there are no significant associations with rare protein-coding variants with detectable effect sizes at our current sample sizes. Analyses will be updated as additional data become available, with results publicly browsable at https://rgc-covid19.regeneron.com.

MAIN TEXT

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1] causes coronavirus disease 2019 (COVID-19) [2]. COVID-19 ranges in clinical presentation from asymptomatic infection to flu-like illness with respiratory failure, hyperactive immune responses and death [3-5]. It is currently estimated that SARS-CoV-2 has infected >100 million individuals and has been attributed to >2 million recorded deaths worldwide. Known risk factors for severe disease include male sex, older age, ancestry, obesity and underlying cardiovascular, renal, and respiratory diseases [6-9], among others.

Since the start of the SARS-CoV-2 pandemic, host genetic analysis of common genetic variation among SARS-CoV-2 patients have identified at least nine genome-wide significant loci that modulate COVID-19 susceptibility and severity, including variants in/near *LZTFL1*, *IFNAR2*, *DPP9* and the *HLA* region [10-13]. However, to date, there has been no assessment of the contribution of rare genetic variation to COVID-19 disease susceptibility or severity through large population-based exome-wide association analyses.

To identify rare variants (RVs, minor allele frequency [MAF]<1%) associated with COVID-19 susceptibility and severity, we generated exome-wide sequencing data for 543,213 individuals from three studies (Geisinger Health System [GHS], Penn Medicine BioBank [PMBB] and UK Biobank [UKB]) and three ancestries (African, European and South Asian) (**Supplementary Table 1**). Of these, 8,248 had COVID-19, and among those 2,085 (25.28%) were hospitalized and 590 (7.15%) had severe disease (i.e. requiring ventilation or resulting in death; **Supplementary Table 2**). Using these data, we tested the association between RVs and seven COVID-19 outcomes: five related to disease susceptibility and two related to disease severity among COVID-19 cases (**Supplementary Table 3**). In a separate paper [13], we used these same phenotypes to validate the association with common risk variants reported in previous COVID-19 GWAS[10-12], thus demonstrating that our phenotypes are calibrated with those used in other studies.

For each phenotype, exome-wide association analyses were performed separately in each study and ancestry using REGENIE[14], testing single RVs (~7 million) and a burden of RVs in 18,886 protein-coding genes. The genomic inflation factor (λ_{GC}) for RVs was often <1 in individual studies, caused by a large proportion of variants having a minor allele count (MAC) of 0 in cases (**Supplementary Table 4**). In meta-analyses across studies and ancestries, we found no RV associations at a conservative $P<9.6\text{x}10^{-10}$, which corresponds to a Bonferroni correction for the number of variants and traits tested. The most significant associations with RVs are listed in **Table 1**, all observed with our COVID-19 hospitalization phenotype (2,085 hospitalized cases vs. 534,965 COVID-19 negative or unknown controls). Of these, we highlight an association with an RV in the promoter of *EEF2* (rs532051930:A, MAF=0.003%, OR=93.9, 95% CI 20.3-434.5, $P=6.2\text{x}10^{-9}$; **Supplementary Figure 1A**), a translation elongation factor which plays a key role in viral replication[15, 16].

Despite not reaching our threshold for genome-wide significance, we highlight the association with *EEF2* because: (i) it was supported by two independent studies (**Supplementary Figure 1B**); (ii) five additional RVs in the 89 bp promoter of *EEF2* (out of 50 tested) had an independent and directionally-consistent predisposing association with the same hospitalization phenotype ($P<0.05$; **Supplementary Table 5**); (iii) rs532051930 is predicted by DeepSEA [17] to be a regulatory variant and to disrupt binding of several transcription factors, including GABP, which has been linked to RV-induced aberrant gene expression [18]; (iv) rs532051930 is located at the peak of the transcription initiation region for *EEF2* (**Supplementary Figure 1C**) [19], suggesting that it might affect RNA polymerase II binding; and (v) among a subset of 1,988 individuals with available RNA-seq data from liver tissue, the only individual who was a carrier for rs532051930:A had the second highest expression of *EEF2* (**Supplementary Figure 1D**). These results raise the possibility that rs532051930 and potentially other promoter RVs increase *EEF2* transcription and, consequently, increase risk of hospitalization due to SARS-CoV-2 infection.

Given these supporting observations and the established role of *EEF2* in viral replication, we studied the genetic association with rs532051930 in greater detail, to understand if it was likely to be a true-positive association. First, we reviewed sequencing reads for all 26 carriers of this variant, to visually validate the heterozygote genotype call produced by the calling algorithm. Sequencing reads were consistent with a heterozygote call for all 26 individuals. Second, we determined if the association with this rare variant was robust to the association test used (**Supplementary Table 6**). A Firth test applied to a joint analysis of data across the two studies, adjusting for study specific covariates as an offset, resulted in $P=5.5\times10^{-8}$. Similar results were obtained by: (i) an approximation to this approach, which combines log-likelihood curves calculated at a grid of values with the Firth penalty, applied using approximate derivatives; (ii) a *P*-value-based meta-analysis, for which there is evidence of better type-I error control [20]; and (iii) the BinomiRare test [21], which uses a test statistic based on allele counts in cases only, adjusts for covariates and combines data across studies. We also applied tests without covariates and these uniformly led to less significant associations, but this is expected since the covariates explain variation in the phenotype. Third, we attempted to replicate this association by querying whether this variant was present in an additional 4,341 COVID-19 cases with exome- or whole-genome sequence data generated as part of the GenOMICC (n=2,969) [11], Columbia University COVID-19 Biobank (n=1,152) and Biobanque Quebec (n=220) [22] studies. We found no carriers for this variant in these additional COVID-19 cases (**Supplementary Table 7**). Given these findings, we conclude that it is not certain that there is a true association between rs532051930 and COVID-19 risk, illustrating the importance of replication.

Next, we addressed the possibility that associations with protein-coding RVs might help pinpoint target genes of common risk variants identified in GWAS of COVID-19. To this end, we focused on 167 genes located within 500 kb of the nine common variants associated with COVID-19 hospitalization in a separate analysis [13]. Of the 334 gene burden tests performed (167 genes x 2 burden tests), which considered both pLoF variants alone (M1 burden test) or pLoF plus deleterious missense variants (M3 burden test), 17 had a nominally significant association with the same COVID-19 hospitalization phenotype (**Supplementary Table 6**). Of these, burden tests for one gene – *CHAF1A* (OR=25 for the M1 burden test, 95% CI 4.9-128.5, P=1.0x10^{-4}) – remained borderline significant after correcting for the 334 tests performed (P<0.05/334=1.5x10^{-4}). *CHAF1A* is located 317 kb from the lead common variant at locus 19p13.3 [13], is highly expressed in EBV-transformed B-cells [23] and encodes a component of the chromatin assembling factor complex that affects cell differentiation, including the differentiation of pre-B cells into B-cells and macrophages [24].

We then examined the association with 14 genes in the interferon pathway, given recent reports that deleterious RVs in these genes may be implicated in severe clinical outcomes [25, 26]. Given the larger sample size in our studies, we examined whether there was any evidence for association between the COVID-19 hospitalization phenotype (2,085 cases vs. 534,965 controls) and the burden of rare (MAF<0.1%) pLoF variants (M1 burden test) or pLoF plus deleterious missense variants (M3 burden test) in these 14 genes, three of which are located within 500 kb of a COVID-19 GWAS risk variant (*IFNAR1*, *IFNAR2* and *TICAM1*). Of the 14 genes, only two genes had a nominal significant association: *STAT2* and *TLR7* (**Table 2**). However, neither remained significant after correcting for the 28 tests performed (both with P>0.05/28=0.0018). Further, these results were unchanged when testing COVID-19 severe cases (N=590), or when restricting the burden tests to include variants with a MAF<1% or singleton variants (**Supplementary Table 7**). Therefore, as recently reported by others [22], we found no evidence for an association between RVs in these 14 interferon signaling genes and risk of COVID-19.

Lastly, we performed the same analysis for an additional 32 genes that are involved in the etiology of SARS-CoV-2 infection (*ACE2, TMPRSS2*), encode therapeutic targets for COVID-19 obtained through ClinicalTrials.gov (*e.g. IL6R, JAK1*) or have been implicated in other immune or infectious diseases through GWAS (*e.g. IL33*). After correcting for multiple testing, there were also no significant associations with a burden of deleterious RVs for this group of COVID-19 therapeutic target genes (**Supplementary Table 8**).

In summary, we provide a catalog of RV associations with COVID-19 outcomes based on exome-sequence data, capturing genetic variation not assayed by array genotyping or imputation. We did not find any convincing associations with current sample sizes, but will continue to expand our analyses and update results periodically at https://rgc-covid19.regeneron.com.

METHODS

Participating Studies

Geisinger Health System (GHS). The GHS MyCode Community Health Initiative study has been described previously [27]. Briefly, the GHS study is a health system-based cohort from central and eastern Pennsylvania (USA) with ongoing recruitment since 2006. A subset of 144,182 MyCode participants sequenced as part of the GHS-Regeneron Genetics Center DiscovEHR partnership were included in this study. Information on COVID-19 outcomes were obtained through GHS's COVID-19 registry. Patients were identified as eligible for the registry based on relevant lab results and ICD-10 diagnosis codes; patient charts were then reviewed to confirm COVID-19 diagnoses. The registry contains data on outcomes, comorbidities, medications, supplemental oxygen use and ICU admissions.

Penn Medicine BioBank (PMBB) study. PMBB study participants are recruited through the University of Pennsylvania Health System, which enrolls participants during hospital or clinic visits. Participants donate blood or tissue and allow access to EHR information[28]. The PMBB COVID-19 registry consists of patients who have positive qPCR testing for SARS-COV-2. We then used electronic health records to classify COVID-19 patients into hospitalized and severe (ventilation or death) categories.

UK Biobank (UKB) study. We studied the host genetics of SARS-CoV-2 infection in participants of the UK Biobank study, which took place between 2006 and 2010 and includes approximately 500,000 adults aged 40-69 at recruitment. In collaboration with UK health authorities, the UK

Biobank has made available regular updates on COVID-19 status for all participants, including results from four main data types: qPCR test for SARS-CoV-2, anonymized electronic health records, primary care and death registry data. We report results based on the 12 September 2020 data refresh and excluded from the analysis 28,547 individuals with a death registry event prior to 2020.

COVID-19 phenotypes used for genetic association analyses

We grouped participants from each study into three broad COVID-19 disease categories (**Supplementary Table 2**): (i) positive – those with a positive qPCR or serology test for SARS-CoV-2, or a COVID-19-related ICD10 code (U07), hospitalization or death; (ii) negative – those with only negative qPCR or serology test results for SARS-CoV-2 and no COVID-19-related ICD10 code (U07), hospitalization or death; and (iii) unknown – those with no qPCR or serology test results and no COVID-19-related ICD10 code (U07), hospitalization or death. We then used these broad COVID-19 disease categories, in addition to hospitalization and disease severity information, to create seven COVID-19-related phenotypes for genetic association analyses, as detailed in **Supplementary Table 3**.

Array genotyping

Genotyping was performed on one of four SNP array types: Illumina OmniExpress Exome array (OMNI; 59345 samples from GHS), Illumina Global Screening Array (GSA; PMBB and 82,527 samples from GHS), Applied Biosystems UK BiLEVE Axiom Array (49,950 samples from UKB), or Applied Biosystems UK Biobank Axiom Array (438,427 samples from UKB). We retained variants with a minor allele frequency (MAF) >1%, <10% missingness, Hardy-Weinberg equilibrium test P-value>10^{-15}. Array data were then used: (i) to define ancestry subsets; and (ii) to generate a polygenic risk score (PRS) predictor, as part of the exome-wide association analyses carried out in REGENIE (see below).

Exome sequencing

Sample Preparation and Sequencing. Genomic DNA samples normalized to approximately 16 ng/ul were transferred to the Regeneron Genetics Center from the UK Biobank in 0.5ml 2D matrix tubes (Thermo Fisher Scientific) and stored in an automated sample biobank (LiCONiC Instruments) at -80°C prior to sample preparation. Exome capture was completed using a high-throughput, fully-automated approach developed at the Regeneron Genetics Center. Briefly, DNA libraries were created by enzymatically shearing 100ng of genomic DNA to a mean fragment size of 200 base pairs using a custom NEBNext Ultra II FS DNA library prep kit (New England Biolabs) and a common Y-shaped adapter (Integrated DNA Technologies [IDT]) was ligated to all DNA libraries. Unique, asymmetric 10 base pair barcodes were added to the DNA fragment during library amplification with KAPA HiFi polymerase (KAPA Biosystems) to facilitate multiplexed exome capture and sequencing. Equal amounts of sample were pooled prior to overnight exome capture, approximately 16 hours, with either (i) a slightly modified version of IDT's xGen probe library (for UKB, PMBB and 81,620 samples of GHS); or (ii) NimbleGen VCRome (58,856 samples of GHS). Captured fragments were bound to streptavidin-coupled Dynabeads (Thermo Fisher Scientific) and non-specific DNA fragments removed through a series of stringent washes using the xGen Hybridization and Wash kit according to the manufacturer's recommended protocol (Integrated DNA Technologies). The captured DNA was PCR amplified with KAPA HiFi and quantified by qPCR with a KAPA Library Quantification Kit (KAPA

Biosystems). The multiplexed samples were pooled and then sequenced using: (i) for UKB samples – 75 bp paired-end reads with two 10 base pair index reads on the Illumina NovaSeq 6000 platform using S2 or S4 flow cells; (ii) for GHS samples captured with VCRome – 75 bp paired-end reads with two 8 bp index reads on the Illumina HiSeq 2500; (iii) for GHS captured with IDT – two 8 bp index reads on the Illumina HiSeq 2500 or two 10 bp index reads on the Illumina NovaSeq 6000 on S4 flow cells; (iv) for UPENN-PMBB – two 10 bp index reads on the Illumina NovaSeq 6000 on S4 flow cells.

Variant calling and quality control. Sample read mapping and variant calling, aggregation and quality control were performed via the SPB protocol described in Van Hout et al. [29]. Briefly, for each sample, NovaSeq WES reads are mapped with BWA MEM to the hg38 reference genome. Small variants are identified with WeCall and reported as per-sample gVCFs. These gVCFs are aggregated with GLnexus into a joint-genotyped, multi-sample VCF (pVCF). SNV genotypes with read depth (DP) less than seven and indel genotypes with read depth less than ten are changed to no-call genotypes. After the application of the DP genotype filter, a variant-level allele balance filter is applied, retaining only variants that meet either of the following criteria: (i) at least one homozygous variant carrier or (ii) at least one heterozygous variant carrier with an allele balance (AB) greater than the cutoff ($AB \geq 0.15$ for SNVs and $AB \geq 0.20$ for indels).

Identification of low-quality variants from exome-sequencing using machine learning. Briefly, in each study, we defined a set of positive control and negative control variants based on: (i) concordance in genotype calls between array and exome sequencing data; (ii) Mendelian inconsistencies in the exome sequencing data; (iii) differences in allele frequencies between exome sequencing batches (UKB and GHS); (iv) variant loadings on 20 principal components derived from the analysis of variants with a MAF<1%; (v) transmitted singletons. The model was then trained on up to 30 available WeCall/GLnexus site quality metrics, including, for example, allele balance and depth of coverage. We split the data into training (80%) and test (20%) sets. We performed a grid search with 5-fold cross-validation on the training set to identify the hyperparameters that return the highest accuracy during cross-validation, which are then applied to the test set to confirm accuracy. This approach identified as low-quality a total of 7 million variants in the UKB study (86% in the buffer region), 7.2 million across the two GHS datasets (IDT and VCRome; 84% in the buffer region) and 1.1 million in the PMBB study (88% in the buffer region). These variants were removed from analysis in the respective studies.

Gene burden masks. Briefly, for each gene region as defined by Ensembl [30], genotype information from multiple rare coding variants was collapsed into a single burden genotype, such that individuals who were: (i) homozygous reference (Ref) for all variants in that gene were considered homozygous (RefRef); (ii) heterozygous for at least one variant in that gene were considered heterozygous (RefAlt); (iii) and only individuals that carried two copies of the alternative allele (Alt) of the same variant were considered homozygous for the alternative allele (AltAlt). We did not phase rare variants; compound heterozygotes, if present, were considered heterozygous (RefAlt). We did this separately for four classes of variants: (i) predicted loss of function (pLoF), which we refer to as an “M1” burden mask; (ii) pLoF or missense (“M2”); (iii) pLoF or missense variants predicted to be deleterious by 5/5 prediction algorithms (“M3”); (iv) pLoF or missense variants predicted to be deleterious by 1/5 prediction algorithms (“M4”). Variants were annotated using SnpEff 4.3[31] and the most severe consequence for each variant was chosen, considering complete protein-coding transcripts for each gene. The following variants were considered to be pLoF variants: frameshift-causing indels, variants affecting splice acceptor and donor sites, variants leading to stop gain, stop loss and start loss. The five missense deleterious algorithms used were SIFT [32], PolyPhen2 (HDIV), PolyPhen2 (HVAR) [33], LRT [34], and MutationTaster [35]. For each gene, and for each of these four groups, we considered five separate burden masks, based on the frequency of the alternative allele of the variants that were screened in that group: <1%, <0.1%, <0.01%, <0.001% and singletons only. Each burden mask was then tested for association with the same approach used for individual variants (see below).

Genetic association analyses

Association analyses in each study were performed using the genome-wide Firth logistic regression test implemented in REGENIE [14]. In this implementation, Firth's approach is applied when the p-value from standard logistic regression score test is below 0.05. As the Firth penalty (*i.e.* Jeffrey's invariant prior) corresponds to a data augmentation procedure where each observation is split into a case and a control with different weights, it can handle variants with no minor alleles among cases. With no covariates, this corresponds to adding 0.5 in every cell of a 2x2 table of allele counts versus case-control status.

We included in step 1 of REGENIE (*i.e.* prediction of individual trait values based on the genetic data) array variants with a minor allele frequency (MAF) >1%, <10% missingness, Hardy-Weinberg equilibrium test P-value>10^{-15} and linkage-disequilibrium (LD) pruning (1000 variant windows, 100 variant sliding windows and r^2<0.9). The exception was the GHS study, for which we used exome (not array) variants in step 1; we did this because two different exome capture technologies (IDT and VCRome) were used to sequence the GHS samples, and so it was important to capture in step 1 of REGENIE any differences in exome sequencing performance between IDT and VCRome. We excluded from step 1 any SNPs with high inter-chromosomal LD, in the major histo-compatibility (MHC) region, or in regions of low complexity.

The association model used in step 2 of REGENIE included as covariates (i) age, age^2, sex, age-by-sex and age^2-by-sex; (ii) 10 ancestry-informative principle components (PCs) derived from the analysis of a set of LD-pruned (50 variant windows, 5 variant sliding windows and r^2<0.5) common variants from the array (imputed for the GHS study) data; (iii) an indicator for exome sequencing batch (GHS: two IDT batches, one VCRome batch; UKB: six IDT batches); and (iv) 20 PCs derived from the analysis of exome variants with a MAF between $2.6x10^{-5}$ (roughly corresponding to a minor allele count [MAC] of 20) and 1%. We corrected for PCs built from rare variants because previous studies demonstrated PCs derived from common variants do not adequately correct for fine-scale population structure [36, 37].

Within each study, association analyses were performed separately for five different continental ancestries defined based on the array data: African (AFR), Admixed American (AMR), European (EUR) and South Asian (SAS). We determined continental ancestries by projecting each sample onto reference principle components calculated from the HapMap3 reference panel. Briefly, we merged our samples with HapMap3 samples and kept only SNPs in common between the two datasets. We further excluded SNPs with MAF<10%, genotype missingness >5% or Hardy-Weinberg Equilibrium test p-value < 10^{-5}. We calculated PCs for the HapMap3 samples and projected each of our samples onto those PCs. To assign a continental ancestry group to each non-HapMap3 sample, we trained a kernel density estimator (KDE) using the HapMap3 PCs and used the KDEs to calculate the likelihood of a given sample belonging to each of the five continental ancestry groups. When the likelihood for a given ancestry group was >0.3, the sample was assigned to that ancestry group. When two ancestry groups had a likelihood >0.3, we arbitrarily assigned AFR over EUR, AMR over EUR, AMR over EAS, SAS over EUR, and AMR over AFR. Samples were excluded from analysis if no ancestry likelihoods were >0.3, or if more than three ancestry likelihoods were > 0.3.

Results were subsequently meta-analyzed across studies and ancestries using an inverse variance-weighed fixed-effects meta-analysis.

Gene expression analysis in participants of the GHS study

For a subset of individuals from the GHS study (n=1,988, ascertained through the Geisinger Bariatric Surgery Clinic), RNA was extracted from liver biopsies conducted during bariatric surgery to evaluate liver disease. Individuals had class 3 obesity (BMI>40kg/m^2) or class 2 obesity (BMI 35-39 kg/m^2) with an obesity-related co-morbidity (e.g. type-2 diabetes, hypertension, sleep apnea, non-alcoholic fatty liver disease). RNA libraries were prepared using polyA-extraction and then sequenced with 75bp paired-end reads with two 10 bp index reads on the Illumina NovaSeq 6000 on S4 flow cells. RNA-seq data were then analyzed using the GTEx v8 workflow[38], using STAR [39] and RNASeqQC [40], except that GENCODE v32 was used in lieu of v26. Briefly: (i) raw expression counts were normalized with TMM (Trimmed Mean of M-values) as implemented in edgeR [40]; (ii) a rank-based inverse normal transformation was applied to the normalized expression values; (iii) principal components (PCs) analysis was performed on data from 25,078 genes with TPM >0.1 in >20% samples, to identify latent factors accounting for variation in gene expression; (iv) gene expression levels were adjusted for the top 100 PCs to improve power to identify cis-regulatory effects.

Frequency of *EEF2* rare promoter variant in COVID-19 cases from independent studies

To help understand if the association between COVID-19 risk and rs532051930 in *EEF2* was likely to be a true-positive association, we determine its frequency in 4,341 cases from three additional studies.

GenOMICC (n=2,969). Individuals with severe COVID-19 were ascertained as described previously[11]. DNA samples were then whole-genome sequenced on the Illumina NovaSeq 6000 platform, aligned to the human reference genome hg38 and variant called to GVCF stage on the DRAGEN pipeline (software v01.011.269.3.2.22, hardware v01.011.269) at Genomics England. rs532051930 +/-50bp was genotyped with the GATK GenotypeGVCFs tool v4.1.8.1 and filtered to minimum depth 8X. Ancestry for individuals with array genotyping was inferred using ADMIXTURE[41] populations defined in 1000 Genomes[42]. When one individual had a probability > 80% of pertaining to one ancestry, then the individual was assigned to this ancestry, otherwise the individual was considered to be of admixed ancestry, as performed in the Million veteran program [43]. Somalier v0.2.12[44] was used to estimate ancestry for samples with whole-genome sequencing data. Predictions from Somalier were compared against predictions from ADMIXTURE for 1833 samples with both array genotyping and whole-genome sequencing data. Of these, the ancestry assignment matched between the two approaches for 1832 samples. Somalier predictions were used for the remaining 927 samples, of which 813 could be confidently (≥95% probability) assigned to a population; the remaining 114 were assigned to admixed ancestry.

Columbia University COVID-19 biobank (n=1,152). This cohort has previously been described in detail[22]. Briefly, 1,152 COVID-19 patients that were treated for COVID-19 at the Columbia University Irving Medical Center were recruited to the Columbia University COVID-

19 Biobank between March and May 2020. All patients had PCR-confirmed SARS-CoV-2 infection and the vast majority had severe COVID-19 requiring hospitalization. For all cases, exomes were captured with the IDT xGen Exome Research Panel V1.0 and sequenced on Illumina's NovaSeq 6000 platform with 150 bp paired-end reads according to standard protocols. All cases were processed with the same bioinformatic pipeline for variant calling. In brief, reads were aligned to human reference GRCh37 using DRAGEN and duplicates were marked with Picard. Variants were called according to the Genome Analysis Toolkit (GATK) Best Practices recommendations v3.66[45]. Finally, variants were annotated with ClinEff[31] and the IGM's in-house tool ATAV[46]. A centralized database was used to store variant and per site coverage data for all samples enabling well controlled analyses without the need of generating jointly called VCF files (see Ren et al. 2020 for details[46]). For each patient, we performed ancestry classification into one of the six major ancestry groups (European, African, Latinx, East Asian, South Asian and Middle Eastern) using a neural network trained on a set of samples with known ancestry labels. We used a 50% probability cut-off to assign an ancestry label to each sample and labeled samples that did not reach 50% for any of the ancestral groups as "Admixed".

We only included samples that had at least 90% of the consensus coding sequence (CCDS release 20[47]) covered at ≥ 10x and ≤ 3% contamination levels according to VerifyBamID[48]. Additionally, we removed samples with a discordance between self-declared and sequence-derived gender and samples with an inferred relationship of second-degree or closer according to KING[49]. All cases had at least 10x coverage at the position of rs532051930.

Biobanque Québec Covid-19 (n=220). The Biobanque Québec COVID-19 (www.BQC19.ca) is a provincial biobank prospectively enrolling patients with suspected COVID-19, or COVID-19 confirmed through SARS-CoV-2 PCR testing and was previously described[22].

For this study, we used results from patients with available WGS data and who were recruited at the Jewish General Hospital (JGH) in Montreal. The JGH is a university affiliated hospital serving a large multi-ethnic adult population and the Québec government designated the JGH as the primary COVID-19 reference center early in the pandemic. In total, Biobanque Quebec contained 533 participants with WGS, including 62 cases of COVID-19 who required invasive ventilatory support (BiPAP, high flow oxygen, or endotracheal intubation) or died, 128 COVID-19 patients who were hospitalized but did not require invasive ventilatory support, 30 individuals with COVID-19 did not require hospitalization, and 313 SARS-CoV-2 PCR-negative participants. Using genetic PCAs derived from genome-wide genotyping, 76% of participants were of European ancestry, 9% were of African ancestry, 7% were of east Asian ancestry, and 5% were of south Asian ancestry.

We performed WGS at a mean depth of 30x on all individuals using Illumina's Novaseq 6000 platform (Illumina, San Diego, CA, USA). Sequencing results were analyzed using the McGill Genome Center bioinformatics pipelines[50], in accordance with Genome Analysis Toolkit (GATK) best practices recommendations[45]. Reads were aligned to the GRCh38 reference genome. Variant quality control was performed using the variantRecalibrator and applyVQSR functions from GATK.

Results availability

All genotype-phenotype association results reported in this study are available for browsing using the RGC's COVID-19 Results Browser (https://rgc-covid19.regeneron.com). Data access and use is limited to research purposes in accordance with the Terms of Use (https://rgc-covid19.regeneron.com/terms-of-use). The COVID-19 Results Browser provides a user-friendly interface to explore genetic association results, enabling users to query summary statistics across multiple cohorts and association studies using genes, variants or phenotypes of interest. Results are displayed in an interactive tabular view ordered by p-value – enabling filtering, sorting, grouping and viewing additional statistics – with link outs to individual GWAS reports, including interactive Manhattan and QQ plots. LocusZoom views of LD information surrounding variants of interest are also available, with LD calculated using the respective source genetic datasets.

The data resource supporting the COVID-19 Results Browser was built using a processed version of the raw association analysis outputs. Using the RGC's data engineering toolkit based in Apache Spark and Project Glow (https://projectglow.io/), association results were annotated, enriched and partitioned into a distributed, columnar data store using Apache Parquet. Processed Parquet files were registered with AWS Athena, which enables efficient, scalable queries on unfiltered association result datasets. Additionally, "filtered" views of associations significant at a threshold of p-value < 0.001 were stored in AWS RDS Aurora databases for low latency queries to service primary views of top associations. APIs into RDS and Athena are managed behind the scenes such that results with a p-value>0.001 are pulled from Athena as needed.

Competing interests

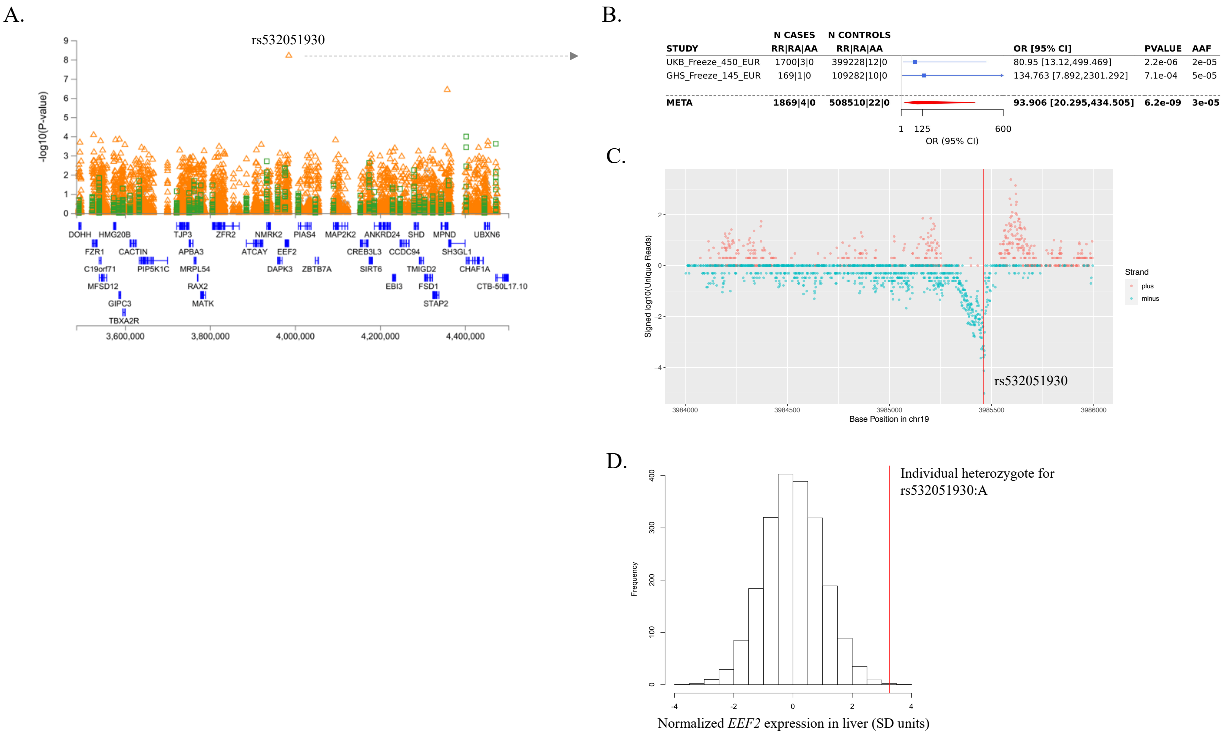
J.E.H., J.A.K., A.D., D.S., N.B, A.Y., A.M., R.L., E.M., X.B., D.S., F.S.P.K., J.D.B., C.O'D., A.J.M., D.A.T., A.H.L., J.M., K.W., L.G., S.E.M, H.M.K., L.D., E.S., M.J., S.B., K.S.M, W.J.S., A.R.S., A.E.L., J.M., J.O., L.H., M.N.C., J.G.R., A.B., G.R.A., and M.A.F. are current employees and/or stockholders of Regeneron Genetics Center or Regeneron Pharmaceuticals. X.Z., S.E., J.W.D. are employees of AbbVie and may hold stock in AbbVie. Financial support for this research was provided by AbbVie through the UKB Exome Sequencing Consortium. AbbVie participated in the interpretation of data, review, and approval of the publication. P.N. and M.M.P are employees and stockholders of Alnylam Pharmaceuticals. J.B.R. has served as an advisor to GlaxoSmithKline and Deerfield Capital and these agencies had no role in the design, implementation or interpretation of this study. S.S., E.W., A.C.P., and E.N.S. are employed by Takeda. S.S. holds shares in Takeda and Janssen. The other authors declare no competing interests.

Acknowledgements

This research has been conducted using the UK Biobank Resource (Project 26041). The Penn Medicine BioBank is funded by a gift from the Smilow family, the National Center for Advancing Translational Sciences of the National Institutes of Health under CTSA Award Number UL1TR001878, and the Perelman School of Medicine at the University of Pennsylvania. Whole genome sequencing of the Biobanque Québec Covid-19 cohort was funded by the CanCOGeN HostSeq project. The Richards research group is supported by the Canadian Institutes of Health Research (CIHR), the Lady Davis Institute of the Jewish General Hospital, the Canadian Foundation for Innovation, the NIH Foundation, Cancer Research UK and the Fonds de Recherche Québec Santé (FRQS). G.B.L. is supported by a joint research fellowship from Quebec's ministry of health and social services, and the FRQS. T.N. is supported by Research Fellowships of Japan Society for the Promotion of Science (JSPS) for Young Scientists and JSPS Overseas Challenge Program for Young Researchers. J.B.R. is supported by a FRQS Clinical Research Scholarship. The Columbia University Biobank was supported by Columbia University and the National Center for Advancing Translational Sciences, NIH, through Grant Number UL1TR001873. Columbia University COVID-19 Biobank members that additionally contributed to this work include Muredach P. Reilly, Wendy Chung, Eldad Hod, Soumitra Sengupta, Danielle Pendrick, Nitin Bhardwaj, Ning Shang, Atlas Khan, Chen Wang, Sheila M.

O'Byrne, Renu Nandakumar, Amritha Menon, Yat S. So, Richard Mayeux, Ali G. Gharavi, Iuliana Ionita-Laza, Andrea Califano, Christine K. Garcia, Peter Sims, and Anne-Catrin Uhlemann. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or Columbia University. GenOMICC was funded by Sepsis Research (the Fiona Elizabeth Agnew Trust), the Intensive Care Society, a Wellcome-Beit Prize award to J. K. Baillie (Wellcome Trust 103258/Z/13/A), a BBSRC Institute Program Support Grant to the Roslin Institute (BBS/E/D/20002172, BBS/E/D/10002070 and BBS/E/D/30002275), the Medical Research Council [grant MC_PC_19059]. Research performed at the Human Genetics Unit was funded by the MRC (MC_UU_00007/10, MC_UU_00007/15). Whole-genome sequencing was done in partnership with Genomics England and was funded by UK Department of Health and Social Care, UKRI and LifeArc. Genomics England and the 100,000 Genomes Project was funded by the National Institute for Health Research, the Wellcome Trust, the Medical Research Council, Cancer Research UK, the Department of Health and Social Care and NHS England. M Caulfield is an NIHR Senior Investigator. This work is part of the portfolio of translational research at the NIHR Biomedical Research Centre at Barts and Cambridge. LK was supported by an RCUK Innovation Fellowship from the National Productivity Investment Fund (MR/R026408/1). We acknowledge support from the MRC Human Genetics Unit programme grant, "Quantitative traits in health and disease" (U. MC_UU_00007/10). A. Tenesa acknowledges funding from MRC research grant MR/P015514/1, and HDR-UK award HDR-9004 and HDR-9003. Recruitment to GenOMICC was enabled by the National Institute of Healthcare Research Clinical Research Network (NIHR CRN) and the Chief Scientist Office (Scotland), who facilitate recruitment into research studies in NHS hospitals, and to the global ISARIC and InFACT consortia. We thank the patients and their loved ones who volunteered to contribute to this study at one of the most difficult times in their lives, and the research staff in every intensive care unit who recruited patients at personal risk during the most extreme conditions we have ever witnessed in UK hospitals.

Supplementary Figures



Supplementary Figure 1. Association between a rare promoter variant in EEF2 (rs532051930:A) and the COVID-19 hospitalization phenotype. (A) Regional association plot centered on rs532051930. Orange triangles: individual rare variants (MAF<0.5%). Green squares: burden tests. Grey circles: individual common variants (MAF>0.5%). **(B)** Forest plot showing association in the two individual datasets included in the meta-analysis of this variant. **(C)** Results from a population-scale PROcap (Precision Run-On 5' cap sequencing) study [19], which profiles transcription start sites of nascent RNAs attached to RNA polymerase. The variant rs532051930 (vertical red line) is located 2 bp away from the peak of transcription initiation. (**D**) Distribution of *EEF2* expression among 1,918 individuals from the GHS study with available RNA-seq data from liver tissue. Vertical red line indicates expression levels for the only individual who was heterozygote for the rare promoter variant rs532051930.

TABLES

Table 1. Top rare variant associations identified in this study ($P<10^{-8}$), all observed with the phenotype COVID-19 positive and hospitalized (cases) vs. COVID-19 negative or unknown (controls).

Variant	Effect allele	Odds Ratio [95% CI]	P-value	N cases with 0|1|2 copies of effect allele	N controls with 0|1|2 copies of effect allele	Effect allele frequency	Gene	Variant effect
rs374698271	T	81.60 [18.71,355.81]	4.65E-09	1698|5|0	399222|18|0	0.00003	*RFX2*	Intronic
rs532051930	A	93.90 [20.29,434.50]	6.17E-09	1869|4|0	508510|22|0	0.00003	*EEF2*	5 prime UTR
rs751932982	A	22.68 [7.89,65.23]	6.92E-09	1869|2|2	508247|44|8	0.00006	*FAM9B*	Intronic

Table 2. Association between the phenotype COVID-19 positive and hospitalized (cases) vs COVID-19 negative or unknown (controls) and 14 genes related to interferon signaling that were recently reported to contain rare (MAF<0.1%), deleterious variants in patients with severe COVID-19 [14, 23].

Variants included in burden test	Gene	Odds Ratio (95% CI)	P-value	N cases with RR|RA|AA genotype*	N controls with RR|RA|AA genotype*	AAF
pLoF, MAF<0.1%	*IFNAR1*	0.805[0.146;4.438]	8.00E-01	2019|1|0	525406|359|0	0.00034
	IFNAR2	2.077[0.620;6.961]	2.40E-01	2082|3|0	534277|688|0	0.00064
	IKBKG	0.491[0.005;50.219]	7.60E-01	1873|0|0	508491|31|10	0.00005
	IRF3	0.956[0.251;3.643]	9.50E-01	2083|2|0	534559|406|0	0.00038
	IRF7	1.165[0.426;3.185]	7.70E-01	2082|3|0	534124|841|0	0.00079
	IRF9	0.371[0.003;53.766]	7.00E-01	1873|0|0	508479|53|0	0.00005
	STAT1	0.365[0.001;126.712]	7.40E-01	1873|0|0	508490|42|0	0.00004
	STAT2	0.355[0.028;4.438]	4.20E-01	1873|0|0	508405|127|0	0.00012
	TBK1	0.365[0.011;11.964]	5.70E-01	1873|0|0	508445|87|0	0.00009
	TICAM1	3.730[0.189;73.610]	3.90E-01	1872|1|0	508368|164|0	0.00016
	TLR3	1.128[0.144;8.834]	9.10E-01	2084|1|0	534674|291|0	0.00027
	TLR7	7.627[1.872;31.075]	4.60E-03	1872|0|1	508503|25|4	0.00003
	TRAF3	0.368[0.000;733.638]	8.00E-01	1873|0|0	508504|28|0	0.00003
	UNC93B1	1.302[0.272;6.238]	7.40E-01	1938|2|0	516861|409|0	0.0004
pLoF or missense predicted deleterious, MAF<0.1%	*IFNAR1*	0.756[0.234;2.444]	6.40E-01	2083|2|0	534219|746|0	0.0007
	IFNAR2	1.968[0.598;6.469]	2.70E-01	2082|3|0	534253|712|0	0.00067
	IKBKG	0.446[0.010;19.737]	6.80E-01	1873|0|0	508452|70|10	0.00009
	IRF3	0.786[0.238;2.592]	6.90E-01	2083|2|0	534413|552|0	0.00052
	IRF7	1.137[0.519;2.492]	7.50E-01	2080|5|0	533486|1479|0	0.00138
	IRF9	0.371[0.003;53.766]	7.00E-01	1873|0|0	508479|53|0	0.00005
	STAT1	0.365[0.038;3.488]	3.80E-01	2018|0|0	526009|218|0	0.00021
	STAT2	2.600[1.272;5.314]	8.80E-03	2073|12|0	533405|1559|1	0.00146
	TBK1	1.114[0.445;2.790]	8.20E-01	2081|4|0	533861|1103|1	0.00103
	TICAM1	3.657[0.188;71.218]	3.90E-01	1872|1|0	508365|167|0	0.00016
	TLR3	0.805[0.435;1.493]	4.90E-01	2077|8|0	532355|2609|1	0.00244
	TLR7	1.580[0.627;3.979]	3.30E-01	2001|3|1	525830|477|163	0.00076
	TRAF3	3.013[0.527;17.217]	2.10E-01	2019|1|0	525523|242|0	0.00023
	UNC93B1	1.665[0.774;3.582]	1.90E-01	2075|10|0	533331|1634|0	0.00153

* RR: individuals who have genotype Reference/Reference for all variants included in burden test. RA: individuals who have genotype Reference/Alternate for at least one variant. AA: individuals who have genotype Alternate/Alternate for at least one variant.

SUPPLEMENTARY TABLES

Supplementary Tables 1 to 10 are provided in a separate document.

Supplementary Table 1. Demographics and clinical characteristics of study participants.

Supplementary Table 2. Breakdown of COVID-19 status across the four studies included in the analysis.

Supplementary Table 3. Definitions used for the seven COVID-19 phenotypes analyzed.

Supplementary Table 4. Genomic inflation factor (λ_{GC}) observed in the analysis of exome sequence variants for each of the eight phenotypes tested.

Supplementary Table 5. Association between the COVID-19 hospitalization phenotype and 50 rare variants in the promoter of *EEF2*.

Supplementary Table 6. Evidence for association between the COVID-19 hospitalization phenotype and rs532051930 across different association tests.

Supplementary Table 7. No carriers of the rare variant rs532051930 in the promoter of EEF2 were observed in an additional 4,122 individuals with COVID-19.

Supplementary Table 8. Results from burden association tests for 167 genes located in eight loci described in Horowitz et al. [13].

Supplementary Table 9. Results from burden association tests for 14 genes related to interferon signaling and recently reported to contain rare (MAF<0.1%), deleterious variants in patients with severe COVID-19.

Supplementary Table 10. Results from burden association tests for an additional 32 genes that are involved in the etiology of SARS-CoV-2, encode therapeutic targets or have been implicated in other immune or infectious diseases through GWAS.

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SUPPLEMENTARY TEXT

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Immune, Respiratory, and Infectious Disease Therapeutic Area Genetics

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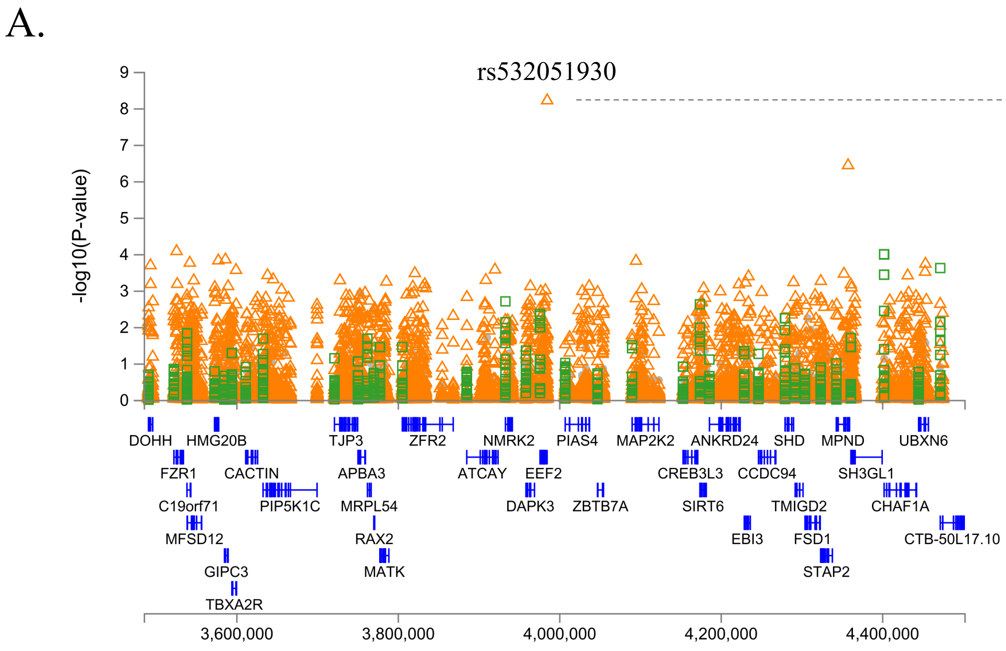
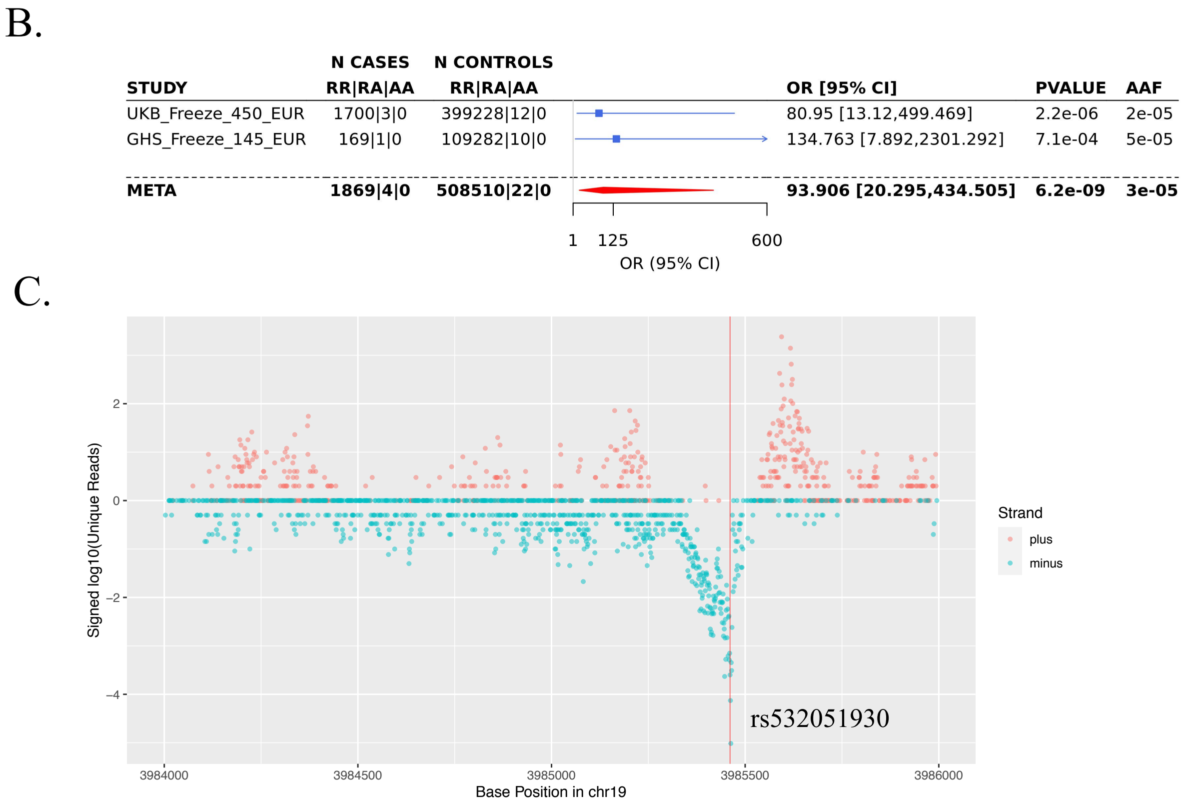
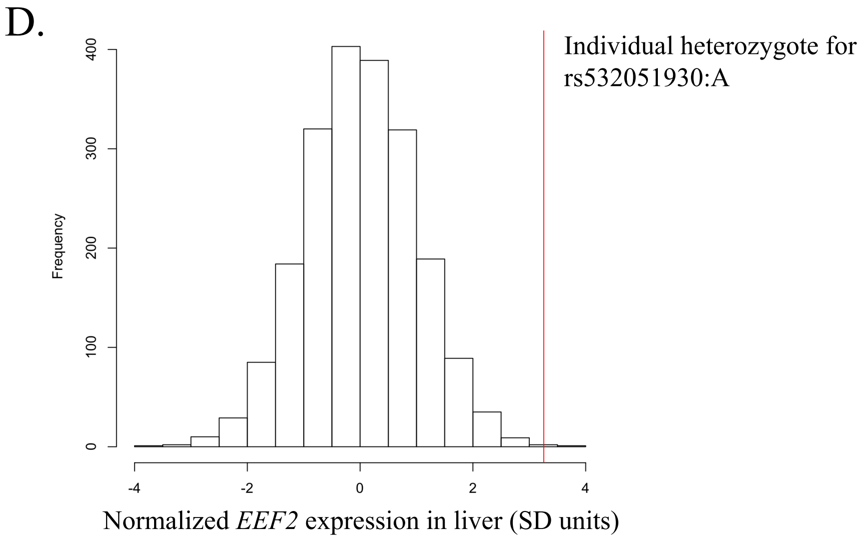
SUPPLEMENTARY FIGURES





STUDY	N CASES RR|RA|AA	N CONTROLS RR|RA|AA	OR [95% CI]	PVALUE	AAF
UKB_Freeze_450_EUR	1700|3|0	399228|12|0	80.95 [13.12,499.469]	2.2e-06	2e-05
GHS_Freeze_145_EUR	169|1|0	109282|10|0	134.763 [7.892,2301.292]	7.1e-04	5e-05
META	**1869|4|0**	**508510|22|0**	**93.906 [20.295,434.505]**	**6.2e-09**	**3e-05**



Supplementary Figure 1. Association between a rare promoter variant in *EEF2* (rs532051930:A) and the COVID-19 hospitalization phenotype. (A) Regional association plot centered on rs532051930. Orange triangles: individual rare variants (MAF<0.5%). Green squares: burden tests. Grey circles: individual common variants (MAF>0.5%). **(B)** Forest plot showing association in the two individual datasets included in the meta-analysis of this variant. **(C)** Results from a population-scale PROcap (Precision Run-On 5' cap sequencing) study [19], which profiles transcription start sites of nascent RNAs attached to RNA polymerase. The variant rs532051930 (vertical red line) is located 2 bp away from the peak of transcription initiation. **(D)** Distribution of *EEF2* expression among 1,918 individuals from the GHS study with available RNA-seq data from liver tissue. Vertical red line indicates expression levels for the only individual who was heterozygote for the rare promoter variant rs532051930.

SUPPLEMENTARY TABLES

Supplementary Table 1. Demographics and clinical characteristics of study participants.

Demographics	COVID-19 Positive		Covid-19 Negative or Unknown
	Hospitalized	Not Hospitalized	
UK Biobank			
Total N	1848	5400	416935
AFR ancestry, n (%)	80 (3.8)	134 (2.2)	8495 (1.8)
EUR ancestry, n (%)	1703 (81.9)	5030 (83.2)	399240 (85.7)
SAS ancestry, n (%)	65 (3.1)	236 (3.9)	9200 (1.9)
Average Age, y (% >60y)	59.7 (57)	52.6 (22)	56.2 (36)
Female, n (%)	737 (39.8)	2896 (53.6)	229572 (55.1)
Hypertension, n (%)	884 (47.8)	1214 (22.5)	96851 (23.2)
Cardiovascular Disease, n (%)	265 (14.3)	330 (6.1)	24859 (5.8)
Type 2 Diabetes, n (%)	342 (18.5)	378 (7)	25335 (6.1)
Chronic kidney disease, n (%)	134 (7.3)	112 (2.1)	8096 (1.9)
Asthma, n (%)	343 (18.5	886 (16.4)	59229 (14.2)
COPD, n (%)	208 (11.2)	164 (3)	10117 (2.4)
GHS			
Total N	170	664	109292
EUR ancestry, n (%)	170 (100)	664 (100)	109292 (100)
Average Age, y (% >60y)	67.81 (76.47)	54.74 (39.0)	55.75 (44.14)
Female, n (%)	90 (52.94)	435 (65.51)	68226 (62.42)
Hypertension, n (%)	138 (81.17)	343 (51.65)	53658 (49.09)
Cardiovascular Disease, n (%)	77 (45.29)	108 (16.26)	17269 (15.80)
Type 2 Diabetes, n (%)	73 (42.94)	158 (23.79)	23290 (21.30)
Chronic kidney disease, n (%)	64 (37.64)	94 (14.15)	14246 (13.03)
Asthma, n (%)	15 (8.82)	47 (7.07)	6975 (6.38)
COPD, n (%)	47(27.64)	67 (10.09)	10822 (9.90)
PMBB			
Total N	67	99	959
AFR ancestry, n (%)	67 (100)	99 (100)	959 (100)
Average Age, y (% >60y)	62.58 (61.19)	47.64 (19.19)	56.24 (43.27)
Female, n (%)	38 (56.7)	72 (72.7)	641 (66.8)
Hypertension, n (%)	59 (88.1)	52 (52.5)	704 (73.4)
Cardiovascular Disease, n (%)	40 (59.7)	17 (17.2)	359 (37.4)
Type 2 Diabetes, n (%)	50 (74.6)	31 (31.3)	440 (45.9)
Chronic kidney disease, n (%)	42 (62.7)	13 (13.1)	300 (31.3)
Asthma, n (%)	18 (26.9)	23 (23.2)	294 (30.7)
COPD, n (%)	20 (29.9)	8 (8.1)	145 (15.1)

Supplementary Table 2. Breakdown of COVID-19 status across the four studies included in the analysis.

COVID-19 status	Positive qPCR or serology for SARS-CoV-2	ICD10 U07 diagnosis or hospitalization	Severe COVID-19 (ventilation or death)	Negative qPCR or serology test for SARS-CoV-2				
					UK Biobank	GHS	PMBB	Total
Positive	Yes	Yes	Yes	Yes or No or NA	382	49	27	458
	Yes	Yes	No or NA	Yes or No or NA	1119	121	40	1,280
	Yes	No or NA	Yes	Yes or No or NA	0	0	0	0
	Yes	No or NA	No or NA	Yes or No or NA	5400	664	99	6,163
	No or NA	Yes	Yes	No or NA	122	0	0	122
	No or NA	Yes	No or NA	No or NA	77	0	0	77
	No or NA	No or NA	Yes	No or NA	0	0	0	0
	No or NA	Yes	Yes	Yes	37	0	0	37
	No or NA	Yes	No or NA	Yes	111	0	0	111
	No or NA	No or NA	Yes	Yes	0	0	0	0
					Total = 7248	Total = 834	Total = 166	Total = 8248
Negative	No or NA	No or NA	No or NA	Yes	32,867	15,574	959	49,400
Unknown	NA	No or NA	No or NA	NA	384,068	93,718	7,779	485,565
Total					424,183	110,126	8,904	543,213

Supplementary Table 3. Definitions used for the seven COVID-19 phenotypes analyzed.

Broad phenotype category	Phenotype	Case/control group	Definition			Sample size with genetic data			
			COVID-19 status	Hospitalized	Severe disease	UK Biobank	GHS	PMBB	Total
Risk of infection	COVID-19 positive vs. COVID-19 negative or unknown	Cases	Positive	Yes, No or NA	Yes, No or NA	7,248	834	166	8,248
		Controls	Negative or unknown	No or NA	No or NA	416,935	109,292	8,738	534,965
	COVID-19 positive vs. COVID-19 negative	Cases	Positive	Yes, No or NA	Yes, No or NA	7,248	834	166	8,248
		Controls	Negative	No or NA	No or NA	32,867	15,574	959	49,400
	COVID-19 positive and not hospitalized vs. COVID-19 negative or unknown	Cases	Positive	No	No	5,400	664	99	6,163
		Controls	Negative or unknown	No or NA	No or NA	416,935	109,292	8,738	534,965
	COVID-19 positive and hospitalized vs. COVID-19 negative or unknown	Cases	Positive	Yes (or death)	Yes, No or NA	1,848	170	67	2,085
		Controls	Negative or unknown	No or NA	No or NA	416,935	109,292	8,738	534,965
	COVID-19 positive and severe vs. COVID-19 negative or unknown	Cases	Positive	Yes, No or NA	Yes	541	49	NA	590
		Controls	Negative or unknown	No or NA	No or NA	416,935	109,292	NA	526,227
Risk of adverse outcomes amongst infected individuals	COVID-19 positive and hospitalized vs. COVID-19 positive and not hospitalized	Cases	Positive	Yes (or death)	Yes, No or NA	1,703	170	67	1,940
		Controls	Positive	No	No	5,030	664	99	5,793
	COVID-19 positive and severe vs. COVID-19 positive and not hospitalized	Cases	Positive	Yes, No or NA	Yes	523	49	NA	572
		Controls	Positive	No	No	5,164	664	NA	5,828

Supplementary Table 4. Genomic inflation factor (lambda GC) observed in the analysis of exome sequence variants for each of the seven phenotypes tested.

Phenotype	Study	Ancestry	N cases	N controls	Exome-sequencing variants with MAF<0.5% & MAC>=5			Exome-sequencing variants with MAF<0.5% & MAC>25			Exome-sequencing variants with MAF>0.5%		
					N variants	Proportion of variants with MAC=0 in cases	Lambda GC	N variants	Proportion of variants with MAC=0 in cases	Lambda GC	N variants	Proportion of variants with MAC=0 in cases	Lambda GC
COVID19_positive_hospitalized_vs_COVID19_negative_or_unknown_combined	UKB_Freeze_450	SAS	65	9200	798145	0.873	0.202	222553	0.719	0.774	227664	0.193	1.254
	UPENN-PMBB_Freeze_One	AFR	67	8738	890983	0.857	0.215	279379	0.708	0.748	486699	0.132	1.099
	UKB_Freeze_450	AFR	80	8495	812651	0.830	0.268	248412	0.653	0.803	380222	0.120	0.947
	GHS_Freeze_145_Exome	EUR	170	109292	2899753	0.933	0.042	889226	0.815	0.23	172227	0.046	0.997
	UKB_Freeze_450	EUR	1703	399240	6411484	0.849	0.126	2074846	0.622	0.555	166323	0.000	1.004
	Meta-analysis	ALL	2085	534965	8053662	0.832	0.126	2833904	0.599	0.554	352116	0.043	1.02
COVID19_positive_hospitalized_vs_COVID19_positive_not_hospitalized_combined	UPENN-PMBB_Freeze_One	AFR	67	99	NA	NA	NA	NA	NA	NA	330315	0.012	0.183
	GHS_Freeze_145_Exome	EUR	170	664	209299	0.549	0.866	NA	NA	NA	173449	0.035	1.079
	UKB_Freeze_450	EUR	1703	5030	424564	0.072	1.099	112045	0.000	1.043	166403	0.000	1.037
	Meta-analysis	ALL	1940	5793	462977	0.126	1.017	128932	0.000	1.021	398264	0.009	0.388
COVID19_positive_not_hospitalized_vs_COVID19_negative_or_unknown_combined	UPENN-PMBB_Freeze_One	AFR	99	8738	893407	0.796	0.338	280294	0.596	0.992	487296	0.076	0.961
	UKB_Freeze_450	AFR	134	8495	816964	0.736	0.48	250786	0.492	1.218	379423	0.050	0.998
	UKB_Freeze_450	SAS	236	9200	808557	0.652	0.622	226850	0.325	1.326	227147	0.016	1.016
	GHS_Freeze_145_Exome	EUR	664	109292	2907752	0.824	0.167	892254	0.559	0.731	172221	0.001	1.016
	UKB_Freeze_450	EUR	5030	399240	6440585	0.722	0.345	2086994	0.387	1.074	166350	0.000	1.019
	Meta-analysis	ALL	6163	534965	8091286	0.710	0.345	2849393	0.385	1.059	351738	0.020	0.982
COVID19_positive_severe_vs_COVID19_negative_or_unknown_combined	UKB_Freeze_450	SAS	18	9200	796240	0.961	0.04	222161	0.910	0.163	226990	0.496	0.749
	UKB_Freeze_450	AFR	33	8495	811241	0.919	0.132	248076	0.831	0.346	379346	0.302	0.821
	GHS_Freeze_145_Exome	EUR	49	109292	2895469	0.976	0.013	888545	0.932	0.08	172229	0.246	0.785
	UKB_Freeze_450	EUR	490	399240	6400400	0.931	0.034	2070233	0.812	0.176	166321	0.001	1.02
	Meta-analysis	ALL	590	526227	7876462	0.917	0.037	2721522	0.783	0.214	225588	0.090	0.889
COVID19_positive_severe_vs_COVID19_positive_not_hospitalized_combined	UKB_Freeze_450	AFR	33	134	NA	NA	NA	NA	NA	NA	235941	0.109	0.234
	GHS_Freeze_145_Exome	EUR	49	664	194798	0.818	0.273	NA	NA	NA	170209	0.228	1.141
	UKB_Freeze_450	EUR	490	5030	373269	0.327	1.078	87177	0.043	1.013	166184	0.001	0.998
	Meta-analysis	ALL	572	5828	410271	0.365	0.912	101899	0.035	0.968	301689	0.056	0.593
COVID19_positive_vs_COVID19_negative_combined	UPENN-PMBB_Freeze_One	AFR	166	959	195274	0.331	1.345	NA	NA	NA	484596	0.023	0.974
	UKB_Freeze_450	AFR	214	766	141313	0.206	1.071	NA	NA	NA	387132	0.013	0.938
	UKB_Freeze_450	SAS	301	844	149617	0.129	1.111	NA	NA	NA	228543	0.004	1.07
	GHS_Freeze_145_Exome	EUR	834	15574	896282	0.505	0.889	239671	0.091	1.024	172248	0.000	1.019
	UKB_Freeze_450	EUR	6733	31257	1361423	0.143	1.15	417941	0.001	1.015	166646	0.000	1
	Meta-analysis	ALL	8248	49400	1745716	0.203	1.023	575968	0.005	1.025	471978	0.006	0.984
COVID19_positive_vs_COVID19_negative_or_unknown_combined	UPENN-PMBB_Freeze_One	AFR	166	8738	897805	0.700	0.519	282679	0.434	1.219	486918	0.029	0.972
	UKB_Freeze_450	AFR	214	8495	821371	0.636	0.666	253263	0.335	1.356	379070	0.015	1.02
	UKB_Freeze_450	SAS	301	9200	812263	0.595	0.735	228572	0.246	1.267	226861	0.007	1.012
	GHS_Freeze_145_Exome	EUR	834	109292	2910461	0.799	0.205	893247	0.509	0.844	172192	0.001	1.026
	UKB_Freeze_450	EUR	6733	399240	6455895	0.675	0.446	2093385	0.315	1.175	166339	0.000	1.017
	Meta-analysis	ALL	8248	534965	8111082	0.663	0.443	2857926	0.315	1.161	351576	0.009	0.996

Supplementary Table 5. Association between the COVID-19 hospitalization phenotype and 50 rare variants in the promoter of EEF2.

rs ID	hg38	Effect allele	Odds Ratio	95% LCI	95% UCI	SE	P-value	Effect allele frequencty	N cases with 0|1|2 copies of effect allele	N controls with 0|1|2 copies of effect allele	Studies analyzed
rs532051930	19:3985461:G:A	A	93.9065	20.2954	434.505	0.7816	6.18E-09	2.55E-05	1869|4|0	508510|22|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs374797871	19:3985414:A:G	G	24.2157	1.84809	317.299	1.3127	0.0152	0.000547	146|1|0	17215|18|0	UKB_Freeze_450_AFR__UPENN-PMBB_Freeze_One_AFR__Meta
rs754033543	19:3985383:T:C	C	18.9215	1.73245	206.658	1.2198	0.0159	0.000027	1702|1|0	399219|21|0	UKB_Freeze_450_EUR__Meta
rs542049090	19:3985437:A:G	G	18.6529	1.72231	202.014	1.2155	0.0161	0.000026	1769|1|0	407947|20|0	UKB_Freeze_450_EUR__UPENN-PMBB_Freeze_One_AFR__Meta
rs897131413	19:3985457:G:C	C	17.7894	1.63807	193.191	1.2169	0.0180	0.000047	1872|1|0	508477|47|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs370100022	19:3985421:G:A	A	5.21063	1.10233	24.6302	0.7925	0.0373	0.000140	1936|2|0	517585|144|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__UKB_Freeze_450_SAS__Meta
rs546488032	19:3985433:G:A	A	6.19102	0.776398	49.3674	1.0593	0.0852	0.000057	1937|1|0	517671|56|1	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__UKB_Freeze_450_SAS__Meta
rs201347619	19:3985401:T:A	A	0.364401	0.0678296	1.95767	0.8578	0.2393	0.004028	147|0|0	17094|138|1	UKB_Freeze_450_AFR__UPENN-PMBB_Freeze_One_AFR__Meta
rs369523513	19:3985436:G:A	A	0.36233	0.0593301	2.21276	0.9232	0.2715	0.000116	2020|0|0	525596|120|1	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_AFR__UKB_Freeze_450_EUR__UPENN-PMBB_Freeze_One_AFR__Meta
rs373888946	19:3985451:G:T	T	0.363709	0.0429819	3.07768	1.0896	0.3533	0.000204	1873|0|0	508319|208|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs907273439	19:3985443:G:C	C	2.35632	0.354027	15.6831	0.9671	0.3755	0.000234	1871|2|0	508270|237|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs190787427	19:3985426:G:C	C	0.361534	0.0260517	5.0172	1.342	0.4484	0.000117	1938|0|0	517565|122|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__UKB_Freeze_450_SAS__Meta
rs377104055	19:3985429:T:C	C	0.361136	0.0234969	5.55049	1.3941	0.4650	0.000087	1850|0|0	416400|73|0	UKB_Freeze_450_AFR__UKB_Freeze_450_EUR__UPENN-PMBB_Freeze_One_AFR__Meta
rs200921166	19:3985402:C:T	T	0.360523	0.00840259	15.4686	1.9179	0.5948	0.000064	1703|0|0	399187|51|0	UKB_Freeze_450_EUR__Meta
rs774095261	19:3985425:C:A	A	0.352361	0.00521284	23.8177	2.1498	0.6275	0.000020	1850|0|0	416437|17|0	UKB_Freeze_450_AFR__UKB_Freeze_450_EUR__UPENN-PMBB_Freeze_One_AFR__Meta
rs529755390	19:3985441:T:C	C	0.361172	0.00447913	29.123	2.2398	0.6493	0.000049	1873|0|0	508368|50|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs777439048	19:3985423:A:C	C	0.377494	0.00480048	29.6849	2.227	0.6618	0.000062	1873|0|0	508457|63|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs1196793724	19:3985434:C:G	G	0.364183	0.00328972	40.3162	2.4015	0.6740	0.000044	1703|0|0	399202|35|0	UKB_Freeze_450_EUR__Meta
rs529755390	19:3985441:T:A	A	0.364438	0.0027381	48.5061	2.4955	0.6859	0.000047	1703|0|0	399119|38|0	UKB_Freeze_450_EUR__Meta
NA	985441:T:TGGCGGCGAC	CGGCGAC	0.364656	0.00182461	72.878	2.7029	0.7090	0.000044	1873|0|0	508368|45|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs190787427	19:3985426:G:A	A	0.365569	0.00170724	78.2788	2.7381	0.7132	0.000042	1703|0|0	399120|34|0	UKB_Freeze_450_EUR__Meta
rs1280637004	19:3985463:G:A	A	0.364255	0.000412394	321.736	3.4611	0.7704	0.000024	1703|0|0	399215|19|0	UKB_Freeze_450_EUR__Meta
rs563082396	19:3985435:C:A	A	0.364183	0.000353722	374.953	3.5393	0.7753	0.000034	1873|0|0	508468|35|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
NA	19:3985425:C:G	G	0.36411	0.000282174	469.838	3.6545	0.7822	0.000021	1703|0|0	399217|17|0	UKB_Freeze_450_EUR__Meta
rs374912847	19:3985392:G:A	A	0.362584	0.000204629	642.464	3.8163	0.7904	0.000014	1703|0|0	399229|11|0	UKB_Freeze_450_EUR__Meta
NA	19:3985455:G:A	A	0.363455	0.000175147	754.22	3.8969	0.7951	0.000016	1703|0|0	399227|13|0	UKB_Freeze_450_EUR__Meta
rs750678552	19:3985430:C:G	G	0.35912	0.000113616	1135.11	4.1116	0.8033	0.000432	65|0|0	9192|8|0	UKB_Freeze_450_SAS__Meta
rs776567094	19:3985428:G:A	A	0.365423	6.02E-05	2218.87	4.4447	0.8208	0.000019	1703|0|0	399218|15|0	UKB_Freeze_450_EUR__Meta
rs369523513	19:3985436:G:C	C	0.366851	5.09E-05	2645.82	4.5325	0.8249	0.000018	1873|0|0	508462|18|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
NA	19:3985417:G:C	C	0.363855	2.93E-05	4517.18	4.8096	0.8335	0.000014	1703|0|0	399224|11|0	UKB_Freeze_450_EUR__Meta
rs1027642860	19:3985460:A:C	C	0.36092	1.49E-05	8736.83	5.1503	0.8431	0.000009	1703|0|0	399229|7|0	UKB_Freeze_450_EUR__Meta
rs779559837	19:3985438:G:A	A	0.391097	3.10E-05	4928.25	4.8172	0.8455	0.000110	170|0|0	109251|24|0	GHS_Freeze_145_MegaFreeze_EUR__Meta
NA	19:3985444:C:T	T	0.382166	1.81E-05	8071.45	5.0807	0.8498	0.000022	1873|0|0	508485|22|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs776029459	19:3985405:C:G	G	0.374486	1.16E-05	12130.2	5.2989	0.8530	0.000017	1873|0|0	508513|17|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
NA	19:3985411:A:G	G	0.364948	5.36E-06	24871	5.6784	0.8591	0.000006	1703|0|0	399231|5|0	UKB_Freeze_450_EUR__Meta
rs995814367	19:3985458:G:A	A	0.365204	3.21E-06	41519	5.9395	0.8653	0.000012	1703|0|0	399229|10|0	UKB_Freeze_450_EUR__Meta
rs764194249	19:3985408:G:A	A	0.365204	2.04E-06	65358.2	6.171	0.8703	0.000006	1703|0|0	399234|5|0	UKB_Freeze_450_EUR__Meta
NA	19:3985442:G:A	A	0.366228	1.12E-06	119957	6.4794	0.8768	0.000009	1703|0|0	399223|7|0	UKB_Freeze_450_EUR__Meta
rs777439048	19:3985423:A:G	G	0.366667	6.02E-07	223245	6.7957	0.8826	0.000015	1703|0|0	399223|12|0	UKB_Freeze_450_EUR__Meta
rs886610889	19:3985452:A:ACGG	ACGG	0.383391	9.78E-07	150305	6.5711	0.8840	0.000046	170|0|0	109273|10|0	GHS_Freeze_145_MegaFreeze_EUR__Meta
rs748898673	19:3985399:A:C	C	0.366228	4.01E-07	334091	7.002	0.8859	0.000009	1703|0|0	399233|7|0	UKB_Freeze_450_EUR__Meta
rs560636284	19:3985439:G:A	A	0.92441	0.310456	2.75251	0.5567	0.8877	0.000897	1870|3|0	507593|913|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta
rs776567094	19:3985428:G:C	C	0.365825	2.96E-07	451572	7.1563	0.8882	0.000009	1703|0|0	399218|7|0	UKB_Freeze_450_EUR__Meta
rs1019385884	19:3985467:G:A	A	0.366008	2.35E-07	569136	7.2741	0.8901	0.000007	1703|0|0	399229|6|0	UKB_Freeze_450_EUR__Meta
rs1037024876	19:3985452:A:G	G	0.34294	5.19E-08	2.26E+06	8.0119	0.8937	0.000023	170|0|0	109273|5|0	GHS_Freeze_145_MegaFreeze_EUR__Meta
rs754780163	19:3985431:G:A	A	0.366888	1.38E-07	973791	7.5469	0.8943	0.000012	1703|0|0	399227|10|0	UKB_Freeze_450_EUR__Meta
NA	19:3985432:C:G	G	0.367034	7.63E-10	1.77E+08	10.2002	0.9217	0.000006	1703|0|0	399235|5|0	UKB_Freeze_450_EUR__Meta
NA	19:3985449:A:G	G	0.375987	7.77E-10	1.82E+08	10.2028	0.9236	0.000027	170|0|0	109282|6|0	GHS_Freeze_145_MegaFreeze_EUR__Meta
NA	19:3985446:G:A	A	0.367402	2.56E-13	5.28E+11	14.2826	0.9441	0.000006	1703|0|0	399232|5|0	UKB_Freeze_450_EUR__Meta
rs373344045	19:3985424:G:A	A	1.06354	0.140046	8.07673	1.0344	0.9525	0.000243	1872|1|0	508283|247|0	GHS_Freeze_145_MegaFreeze_EUR__UKB_Freeze_450_EUR__Meta

Supplementary Table 6. Evidence for association between the COVID-19 hospitalization phenotype and rs532051930 across different association tests.

Approach	Association test in individual studies	Approach used to combine results across studies	Association in UKB Europeans			Association in GHS Europeans			Association in UKB+GHS Europeans		
			OR (95% CI)	SE*	P-value	OR (95% CI)	SE*	P-value	OR (95% CI)	SE*	P-value
1 (default)	REGENIE Firth exact test, with covariates and LOCO	Inverse-variance fixed-effects meta-analysis	80.9 (13.1 - 499.5)	0.93	2.20E-06	134.8 (7.9 - 2301.3)	1.45	7.07E-04	93.9 (20.3 - 434.5)	0.78	6.17E-09
2		Sample size weighted meta-analysis							NA		3.14E-08
3		Meta-analysis of log-likelihood curves							85.6 (17.2 - 425.8)	0.82	5.51E-08
4	Firth exact test, no covariates	Inverse-variance fixed-effects meta-analysis	65.7 (16.9 - 195.3)	0.90	3.49E-06	92.1 (9.9 - 395.0)	1.4	0.00127	72.5 (16.4 - 321.0)	0.76	1.64E-08
5	Fisher's exact test (no covariates)		58.7 (10.6 - 218.5)	0.98	3.35E-05	64.6 (1.48 - 456.8)	1.75	0.017	60.1 (11.2 - 321.6)	0.86	1.70E-06
6	Logistic regression, with covariates		71.6 (15.6 - 241.7)	0.99	1.55E-05	106.5 (5.61 - 648.2)	1.74	0.00733	78.9 (14.6 - 425.0)	0.86	3.73E-07
7	Logistic regression, no covariates		58.7 (13.4 - 185.0)	0.96	2.37E-05	64.7 (3.51 - 340.4)	1.67	0.0123	60.2 (11.7 - 308.4)	0.83	9.00E-07
8	BinomiRare test, with covariates	Meta-analysis	NA		1.19E-05	NA		5.53E-05	NA		2.96E-07
9	Firth exact test, with covariates	Mega-analysis (UKB+GHS combined)	NA			NA			85.8 (17.2 - 427.2)	0.82	5.48E-08
10	Firth exact test, no covariates								54.4 (11.8 - 250.5)	0.78	2.91E-07
11	Fisher's exact test (no covariates)								49.4 (9.7 - 251.0)	0.83	2.53E-06
12	Logistic regression, with covariates								78.7 (14.6- 424.9)	0.86	3.88E-07
13	Logistic regression, no covariates								49.5 (9.9 - 246.2)	0.82	1.89E-06

*Re-calculated from the OR and p-value

Supplementary Table 7. No carriers of the rare variant rs532051930 in the promoter of EEF2 were observed in an additional 4,341 individuals with COVID-19.

		N COVID-19 cases				
Study	**Reference**	**Total**	**Hospitalized**	**Severe**	**Of European|African|Asian|Hispanic|other ancestry**	**Heterozygote for rs532051930:A**
GenOMICC	PMID 33307546	2969	2969	2969	2110 | 145 | 375 | NA | 339	0
Columbia University COVID-19 Biobank	https://www.medrxiv.org/content/10.1101/2020.12.18.20248226v2	1152	1082	479	67 | 463 | 33 | 506 | 83	0
Biobanque Québec Covid-19	https://www.medrxiv.org/content/10.1101/2020.12.18.20248226v2	220	128	62	154 | 30 | 29 | 7 | 0	0

Supplementary Table 8. Results from burden association tests for 167 genes located in eight loci described by Horowitz et al. (2021).

Trait	Gene	Burden test	MAF	Odds Ratio [95% CI]	P-value	N cases with RR|RA|AA genotype*	N controls with RR|RA|AA genotype*	AAF	GWAS SNP	Distance to GWAS SNP, bp	Distance to GWAS SNP, rank
COVID19 positive hospitalized vs COVID19 negative or unknown	*CHAF1A*	M1	<1%	25.216[4.947;128.539]	1.00E-04	1935|3|0	517687|45|0	0.00005	19:4719431:G:A	316669	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*CHAF1A*	M3	<1%	25.216[4.947;128.539]	1.00E-04	1935|3|0	517687|45|0	0.00005	19:4719431:G:A	316669	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*SLC22A31*	M1	<1%	5.583[1.807;17.256]	2.80E-03	1844|6|0	416071|402|0	0.00049	16:89117727	78271	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*SLC22A31*	M3	<1%	5.583[1.807;17.256]	2.80E-03	1844|6|0	416071|402|0	0.00049	16:89117727	78271	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*SARDH*	M1	<1%	2.367[1.315;4.259]	4.00E-03	2072|12|1	533477|1487|1	0.0014	9:133270015:A:C	393873	25
COVID19 positive hospitalized vs COVID19 negative or unknown	*SHD*	M1	<1%	5.283[1.619;17.242]	5.80E-03	1869|4|0	508290|242|0	0.00024	19:4719431:G:A	439368	22
COVID19 positive hospitalized vs COVID19 negative or unknown	*CTB-50L17.10*	M1	<1%	5.726[1.598;20.518]	7.40E-03	2017|3|0	525625|140|0	0.00014	19:4719431:G:A	247081	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*CTB-50L17.10*	M3	<1%	5.726[1.598;20.518]	7.40E-03	2017|3|0	525625|140|0	0.00014	19:4719431:G:A	247081	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*DBH*	M1	<1%	0.320[0.128;0.796]	1.40E-02	2083|2|0	532761|2204|0	0.00205	9:133270015:A:C	366356	22
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC14*	M1	<1%	6.544[1.434;29.868]	1.50E-02	1936|2|0	517625|95|12	0.00012	19:51739497	96143	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*OLIG2*	M1	<1%	12.046[1.255;115.574]	3.10E-02	1872|1|0	508456|76|0	0.00008	21:33252612:A:G	225750	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*OLIG2*	M3	<1%	12.046[1.255;115.574]	3.10E-02	1872|1|0	508456|76|0	0.00008	21:33252612:A:G	225750	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*PSORS1C2*	M1	<1%	5.176[1.151;23.275]	3.20E-02	1871|2|0	508350|182|0	0.00018	6:31153649:G:A	15699	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*PPP2R1A*	M3	<1%	5.429[1.129;26.105]	3.50E-02	1871|2|0	508337|195|0	0.00019	19:51739497	450599	33
COVID19 positive hospitalized vs COVID19 negative or unknown	*SH3GL1*	M1	<1%	10.804[1.173;99.499]	3.60E-02	1872|1|0	508459|73|0	0.00007	19:4719431:G:A	357832	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*MICB*	M1	<1%	2.106[1.007;4.401]	4.80E-02	2077|8|0	533921|1043|1	0.00098	6:31153649:G:A	344544	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*MICB*	M3	<1%	2.106[1.007;4.401]	4.80E-02	2077|8|0	533921|1043|1	0.00098	6:31153649:G:A	344544	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*ATP6V1G2*	M1	<1%	8.596[0.965;76.602]	5.40E-02	1872|1|0	508475|57|0	0.00006	6:31153649:G:A	391758	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*ATP6V1G2*	M3	<1%	8.596[0.965;76.602]	5.40E-02	1872|1|0	508475|57|0	0.00006	6:31153649:G:A	391758	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*SURF6*	M1	<1%	5.025[0.971;25.993]	5.40E-02	2016|2|0	525975|252|0	0.00024	9:133270015:A:C	61853	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*MYDGF*	M3	<1%	0.343[0.115;1.024]	5.50E-02	2085|0|0	534469|496|0	0.00046	19:4719431:G:A	61427	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*XCR1*	M1	<1%	3.068[0.967;9.733]	5.70E-02	2017|3|0	525432|333|0	0.00032	3:45859597:C:T	161348	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*C6orf15*	M3	<1%	3.003[0.965;9.351]	5.80E-02	2016|4|0	525465|299|1	0.00029	6:31153649:G:A	42269	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*LARS2*	M3	<1%	1.355[0.987;1.861]	6.00E-02	2036|48|1	524945|9982|38	0.00941	3:45859597:C:T	465144	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*PRRC2A*	M3	<1%	0.716[0.505;1.016]	6.10E-02	2063|22|0	524933|10025|7	0.00937	6:31153649:G:A	469140	34
COVID19 positive hospitalized vs COVID19 negative or unknown	*LIMD1*	M3	<1%	2.202[0.962;5.038]	6.20E-02	2079|6|0	534053|912|0	0.00085	3:45859597:C:T	264718	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*FPR1*	M1	<1%	9.521[0.887;102.209]	6.30E-02	2019|1|0	525731|34|0	0.00003	19:51739497	6444	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC14*	M3	<1%	3.535[0.936;13.349]	6.30E-02	2003|2|0	526273|179|18	0.00021	19:51739497	96143	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*CYBA*	M3	<1%	2.843[0.930;8.693]	6.70E-02	2080|5|0	534405|560|0	0.00053	16:89117727	474375	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*OLIG1*	M1	<1%	7.354[0.856;63.204]	6.90E-02	1872|1|0	508454|78|0	0.00008	21:33252612:A:G	182366	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*OLIG1*	M3	<1%	7.354[0.856;63.204]	6.90E-02	1872|1|0	508454|78|0	0.00008	21:33252612:A:G	182366	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF615*	M1	<1%	0.368[0.121;1.117]	7.80E-02	2085|0|0	534154|810|1	0.00076	19:51739497	253382	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF615*	M3	<1%	0.368[0.121;1.117]	7.80E-02	2085|0|0	534154|810|1	0.00076	19:51739497	253382	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*KDM4B*	M3	<1%	2.146[0.916;5.028]	7.90E-02	2077|8|0	533186|1778|1	0.00166	19:4719431:G:A	313459	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*CPNE7*	M1	<1%	2.509[0.871;7.222]	8.80E-02	2079|6|0	534223|742|0	0.0007	16:89117727	458170	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*DBH*	M3	<1%	0.824[0.657;1.033]	9.30E-02	2021|64|0	514043|20887|35	0.01957	9:133270015:A:C	366356	22
COVID19 positive hospitalized vs COVID19 negative or unknown	*SURF1*	M1	<1%	1.734[0.905;3.321]	9.70E-02	2075|10|0	533511|1454|0	0.00136	9:133270015:A:C	81897	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*CTU2*	M1	<1%	2.046[0.868;4.822]	1.00E-01	2076|9|0	533716|1247|2	0.00117	16:89117727	411197	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*FEM1A*	M1	<1%	3.778[0.670;21.285]	1.30E-01	2015|3|0	525914|313|0	0.0003	19:4719431:G:A	72423	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*FEM1A*	M3	<1%	3.778[0.670;21.285]	1.30E-01	2015|3|0	525914|313|0	0.0003	19:4719431:G:A	72423	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*LZTFL1*	M3	<1%	2.578[0.756;8.800]	1.30E-01	2082|3|0	534504|460|1	0.00043	3:45859597:C:T	33284	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*SURF2*	M3	<1%	0.471[0.176;1.262]	1.30E-01	2084|1|0	534038|927|0	0.00086	9:133270015:A:C	86577	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*ARRDC5*	M3	<1%	2.513[0.744;8.487]	1.40E-01	2080|5|0	534263|702|0	0.00066	19:4719431:G:A	171614	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*FLOT1*	M3	<1%	1.969[0.802;4.836]	1.40E-01	2077|8|0	533722|1242|1	0.00117	6:31153649:G:A	425534	26
COVID19 positive hospitalized vs COVID19 negative or unknown	*IGLON5*	M1	<1%	19.079[0.389;936.241]	1.40E-01	1872|1|0	508445|87|0	0.00009	19:51739497	427650	32
COVID19 positive hospitalized vs COVID19 negative or unknown	*SLC6A20*	M1	<1%	0.462[0.161;1.328]	1.50E-01	2085|0|0	534061|904|0	0.00084	3:45859597:C:T	101161	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*MAT2B*	M3	<1%	0.473[0.168;1.330]	1.60E-01	2084|1|0	534078|887|0	0.00083	5:163300447	202947	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*SARDH*	M3	<1%	1.293[0.905;1.848]	1.60E-01	2050|34|1	528071|6891|3	0.00645	9:133270015:A:C	393873	25
COVID19 positive hospitalized vs COVID19 negative or unknown	*TSC1*	M3	<1%	0.741[0.490;1.121]	1.60E-01	2069|16|0	528190|6768|7	0.00633	9:133270015:A:C	373781	23
COVID19 positive hospitalized vs COVID19 negative or unknown	*MUC21*	M1	<1%	0.367[0.086;1.555]	1.70E-01	2020|0|0	525263|501|1	0.00048	6:31153649:G:A	169691	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*MUC21*	M3	<1%	0.367[0.086;1.555]	1.70E-01	2020|0|0	525263|501|1	0.00048	6:31153649:G:A	169691	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*PLIN5*	M1	<1%	0.486[0.172;1.374]	1.70E-01	2084|1|0	534032|931|2	0.00087	19:4719431:G:A	195904	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*PLIN5*	M3	<1%	0.486[0.172;1.374]	1.70E-01	2084|1|0	534032|931|2	0.00087	19:4719431:G:A	195904	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*LIMD1*	M1	<1%	11.539[0.303;439.203]	1.90E-01	1872|1|0	508431|101|0	0.0001	3:45859597:C:T	264718	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*MVD*	M1	<1%	0.362[0.078;1.673]	1.90E-01	1938|0|0	517333|399|0	0.00038	16:89117727	465203	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*NCR3*	M3	<1%	0.373[0.086;1.608]	1.90E-01	2020|0|0	525351|414|0	0.00039	6:31153649:G:A	435417	30
COVID19 positive hospitalized vs COVID19 negative or unknown	*RNF166*	M3	<1%	2.052[0.696;6.046]	1.90E-01	2016|4|0	525167|598|0	0.00057	16:89117727	420160	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*SACM1L*	M1	<1%	3.293[0.554;19.585]	1.90E-01	1937|1|0	517584|148|0	0.00014	3:45859597:C:T	170132	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCDC94*	M1	<1%	3.763[0.497;28.456]	2.00E-01	2019|1|0	525606|159|0	0.00015	19:4719431:G:A	472285	23
COVID19 positive hospitalized vs COVID19 negative or unknown	*SACM1L*	M3	<1%	1.982[0.690;5.692]	2.00E-01	2080|5|0	534178|786|1	0.00074	3:45859597:C:T	170132	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*TRAPPC2L*	M1	<1%	0.759[0.498;1.158]	2.00E-01	2069|16|0	528171|6783|11	0.00635	16:89117727	260577	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF616*	M1	<1%	0.493[0.166;1.465]	2.00E-01	2004|1|0	525530|940|0	0.00089	19:51739497	375320	28
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF616*	M3	<1%	0.493[0.166;1.465]	2.00E-01	2004|1|0	525530|940|0	0.00089	19:51739497	375320	28
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF836*	M1	<1%	0.363[0.076;1.725]	2.00E-01	2085|0|0	534615|350|0	0.00033	19:51739497	415374	31
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF836*	M3	<1%	0.363[0.076;1.725]	2.00E-01	2085|0|0	534615|350|0	0.00033	19:51739497	415374	31
COVID19 positive hospitalized vs COVID19 negative or unknown	*CEACAM18*	M1	<1%	0.365[0.075;1.773]	2.10E-01	2005|0|0	526042|428|0	0.0004	19:51739497	260855	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*CEACAM18*	M3	<1%	0.365[0.075;1.773]	2.10E-01	2005|0|0	526042|428|0	0.0004	19:51739497	260855	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*DNAJC28*	M1	<1%	0.561[0.228;1.381]	2.10E-01	2083|2|0	533837|1128|0	0.00105	21:33252612:A:G	235614	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*APRT*	M3	<1%	0.502[0.168;1.501]	2.20E-01	2084|1|0	534131|834|0	0.00078	16:89117727	308030	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*BAG6*	M3	<1%	0.713[0.416;1.224]	2.20E-01	2076|9|0	531625|3337|3	0.00312	6:31153649:G:A	485481	36
COVID19 positive hospitalized vs COVID19 negative or unknown	*HMMR*	M3	<1%	0.688[0.377;1.254]	2.20E-01	2078|7|0	532229|2730|6	0.00256	5:163300447	160245	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*SLC6A20*	M3	<1%	0.721[0.428;1.216]	2.20E-01	2076|9|0	531236|3727|2	0.00348	3:45859597:C:T	101161	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*SPACA9*	M1	<1%	0.368[0.075;1.806]	2.20E-01	2085|0|0	534523|440|2	0.00041	9:133270015:A:C	386068	24
COVID19 positive hospitalized vs COVID19 negative or unknown	*VARS2*	M1	<1%	0.768[0.503;1.174]	2.20E-01	2069|16|0	529226|5729|10	0.00537	6:31153649:G:A	239238	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF841*	M1	<1%	0.562[0.225;1.399]	2.20E-01	2083|2|0	533694|1271|0	0.00119	19:51739497	325609	22
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF841*	M3	<1%	0.562[0.225;1.399]	2.20E-01	2083|2|0	533694|1271|0	0.00119	19:51739497	325609	22
COVID19 positive hospitalized vs COVID19 negative or unknown	*DDR1*	M1	<1%	0.365[0.071;1.871]	2.30E-01	1938|0|0	517314|418|0	0.0004	6:31153649:G:A	268430	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*FYCO1*	M3	<1%	1.270[0.862;1.871]	2.30E-01	2055|30|0	527455|7494|16	0.00703	3:45859597:C:T	62167	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNGR2*	M1	<1%	8.396[0.261;270.048]	2.30E-01	1872|1|0	508441|91|0	0.00009	21:33252612:A:G	150931	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*TCF19*	M3	<1%	0.506[0.167;1.534]	2.30E-01	2084|1|0	534099|865|1	0.00081	6:31153649:G:A	5820	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*VARS2*	M3	<1%	0.820[0.593;1.135]	2.30E-01	2055|30|0	525693|9261|11	0.00867	6:31153649:G:A	239238	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR2*	M1	<1%	2.077[0.620;6.961]	2.40E-01	2082|3|0	534277|688|0	0.00064	21:33252612:A:G	10690	1

COVID19 positive hospitalized vs COVID19 negative or unknown	*SURF6*	M3	<1%	1.442[0.785;2.651]	2.40E-01	2071|14|0	532573|2388|4	0.00224	9:133270015:A:C	61853	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*AC074141.1*	M1	<1%	0.515[0.167;1.587]	2.50E-01	2084|1|0	534249|715|1	0.00067	19:51739497	133034	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*AC074141.1*	M3	<1%	0.515[0.167;1.587]	2.50E-01	2084|1|0	534249|715|1	0.00067	19:51739497	133034	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*MED22*	M1	<1%	2.725[0.493;15.068]	2.50E-01	1872|1|0	508339|193|0	0.00019	9:133270015:A:C	71489	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCNG1*	M3	<1%	2.100[0.575;7.670]	2.60E-01	2081|4|0	534370|595|0	0.00056	5:163300447	138809	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*MYDGF*	M1	<1%	0.315[0.042;2.346]	2.60E-01	2085|0|0	534773|192|0	0.00018	19:4719431:G:A	61427	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*NCR3*	M1	<1%	0.363[0.063;2.083]	2.60E-01	1873|0|0	508231|301|0	0.00029	6:31153649:G:A	435417	30
COVID19 positive hospitalized vs COVID19 negative or unknown	*SON*	M3	<1%	1.154[0.897;1.483]	2.60E-01	2014|70|1	518373|16570|22	0.01553	21:33252612:A:G	290480	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR2*	M3	<1%	1.968[0.598;6.469]	2.70E-01	2082|3|0	534253|712|0	0.00067	21:33252612:A:G	10690	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*SPG7*	M1	<1%	1.418[0.762;2.638]	2.70E-01	2075|10|0	532986|1978|1	0.00185	16:89117727	390690	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*GALNS*	M1	<1%	0.370[0.061;2.257]	2.80E-01	1953|0|0	516724|303|0	0.00029	16:89117727	303289	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*POU5F1*	M3	<1%	0.363[0.057;2.295]	2.80E-01	1873|0|0	508235|297|0	0.00029	6:31153649:G:A	10951	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC8*	M1	<1%	2.359[0.503;11.052]	2.80E-01	2017|3|0	525367|398|0	0.00038	19:51739497	287119	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF432*	M1	<1%	1.745[0.629;4.839]	2.80E-01	2078|7|0	533544|1421|0	0.00133	19:51739497	294222	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF432*	M3	<1%	1.745[0.629;4.839]	2.80E-01	2078|7|0	533544|1421|0	0.00133	19:51739497	294222	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*DONSON*	M3	<1%	1.265[0.809;1.979]	3.00E-01	2061|24|0	530103|4855|7	0.00456	21:33252612:A:G	325694	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*SURF2*	M1	<1%	0.532[0.161;1.757]	3.00E-01	2084|1|0	534311|654|0	0.00061	9:133270015:A:C	86577	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*SURF4*	M1	<1%	5.574[0.219;142.075]	3.00E-01	1937|1|0	517635|96|1	0.0001	9:133270015:A:C	93448	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*IGLON5*	M3	<1%	1.781[0.591;5.367]	3.10E-01	2080|5|0	534127|838|0	0.00078	19:51739497	427650	32
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC8*	M3	<1%	2.209[0.485;10.070]	3.10E-01	2082|3|0	534553|412|0	0.00039	19:51739497	287119	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*ADAMTSL2*	M3	<1%	0.674[0.308;1.477]	3.20E-01	2081|4|0	533538|1420|7	0.00134	9:133270015:A:C	264725	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*ARRDC5*	M1	<1%	4.900[0.209;114.787]	3.20E-01	1872|1|0	508406|126|0	0.00012	19:4719431:G:A	171614	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*GFI1B*	M3	<1%	0.761[0.444;1.304]	3.20E-01	2075|10|0	531725|3238|2	0.00303	9:133270015:A:C	283337	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*LIM2*	M3	<1%	1.580[0.643;3.881]	3.20E-01	2078|7|0	533775|1190|0	0.00111	19:51739497	359297	25
COVID19 positive hospitalized vs COVID19 negative or unknown	*OBP2B*	M1	<1%	1.214[0.828;1.778]	3.20E-01	2053|32|0	528194|6771|0	0.00633	9:133270015:A:C	64687	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*OBP2B*	M3	<1%	1.214[0.828;1.778]	3.20E-01	2053|32|0	528194|6771|0	0.00633	9:133270015:A:C	64687	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*PRRC2A*	M1	<1%	0.638[0.262;1.553]	3.20E-01	1870|3|0	505561|2971|0	0.00291	6:31153649:G:A	469140	34
COVID19 positive hospitalized vs COVID19 negative or unknown	*CDT1*	M1	<1%	2.121[0.474;9.487]	3.30E-01	2015|3|0	525792|435|0	0.00041	16:89117727	313896	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*RPL7A*	M3	<1%	0.364[0.048;2.778]	3.30E-01	1953|0|0	516804|223|0	0.00021	9:133270015:A:C	78228	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*TCF19*	M1	<1%	0.369[0.050;2.706]	3.30E-01	1938|0|0	517437|294|1	0.00028	6:31153649:G:A	5820	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*XCR1*	M3	<1%	1.753[0.566;5.428]	3.30E-01	2081|4|0	534290|675|0	0.00063	3:45859597:C:T	161348	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*CDSN*	M3	<1%	0.680[0.310;1.494]	3.40E-01	2074|11|0	531401|3563|1	0.00333	6:31153649:G:A	37625	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*CEL*	M1	<1%	0.802[0.513;1.256]	3.40E-01	2070|15|0	530001|4944|20	0.00465	9:133270015:A:C	208022	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCR9*	M1	<1%	0.354[0.041;3.080]	3.50E-01	1938|0|0	517545|187|0	0.00018	3:45859597:C:T	35336	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*CTU2*	M3	<1%	1.180[0.834;1.670]	3.50E-01	2047|38|0	526415|8544|6	0.008	16:89117727	411197	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*SPACA9*	M3	<1%	0.689[0.317;1.498]	3.50E-01	2081|4|0	533295|1668|2	0.00156	9:133270015:A:C	386068	24
COVID19 positive hospitalized vs COVID19 negative or unknown	*CEL*	M3	<1%	0.832[0.564;1.229]	3.60E-01	2064|21|0	528589|6355|21	0.00598	9:133270015:A:C	208022	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*CRYZL1*	M1	<1%	0.363[0.042;3.132]	3.60E-01	1938|0|0	517520|212|0	0.0002	21:33252612:A:G	337178	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*FAM163B*	M3	<1%	1.436[0.647;3.191]	3.70E-01	2066|19|0	530396|4569|0	0.00427	9:133270015:A:C	309006	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*MPND*	M1	<1%	0.376[0.044;3.228]	3.70E-01	2020|0|0	525540|224|1	0.00021	19:4719431:G:A	375838	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*C21orf62*	M1	<1%	0.362[0.038;3.417]	3.80E-01	1938|0|0	517567|165|0	0.00016	21:33252612:A:G	458851	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*C21orf62*	M3	<1%	0.362[0.038;3.417]	3.80E-01	1938|0|0	517567|165|0	0.00016	21:33252612:A:G	458851	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*PIEZO1*	M1	<1%	0.722[0.350;1.488]	3.80E-01	2080|5|0	533243|1722|0	0.00161	16:89117727	402123	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*ACSF3*	M3	<1%	0.874[0.642;1.189]	3.90E-01	2048|37|0	524213|10735|17	0.01006	16:89117727	17046	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*HMMR*	M1	<1%	0.722[0.342;1.522]	3.90E-01	2080|5|0	533239|1721|5	0.00162	5:163300447	160245	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*SHD*	M3	<1%	1.511[0.585;3.902]	3.90E-01	2079|6|0	533918|1045|2	0.00098	19:4719431:G:A	439368	22
COVID19 positive hospitalized vs COVID19 negative or unknown	*TICAM1*	M1	<1%	3.730[0.189;73.610]	3.90E-01	1872|1|0	508368|164|0	0.00016	19:4719431:G:A	96807	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*TICAM1*	M3	<1%	3.657[0.188;71.218]	3.90E-01	1872|1|0	508365|167|0	0.00016	19:4719431:G:A	96807	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*SURF1*	M3	<1%	1.308[0.702;2.439]	4.00E-01	2072|13|0	532627|2338|0	0.00219	9:133270015:A:C	81897	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*CXCR6*	M1	<1%	0.364[0.034;3.941]	4.10E-01	1940|0|0	517072|198|0	0.00019	3:45859597:C:T	86884	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*DDX39B*	M3	<1%	0.367[0.034;3.973]	4.10E-01	1873|0|0	508265|267|0	0.00026	6:31153649:G:A	376784	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*IL17C*	M3	<1%	1.666[0.496;5.595]	4.10E-01	2081|4|0	534261|704|0	0.00066	16:89117727	479086	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*UBXN6*	M1	<1%	0.368[0.034;3.984]	4.10E-01	2020|0|0	525583|182|0	0.00017	19:4719431:G:A	273934	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*PPP1R18*	M1	<1%	0.365[0.031;4.278]	4.20E-01	1873|0|0	508356|176|0	0.00017	6:31153649:G:A	476381	35
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF614*	M1	<1%	2.130[0.339;13.393]	4.20E-01	2083|2|0	534709|256|0	0.00024	19:51739497	273639	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF614*	M3	<1%	2.130[0.339;13.393]	4.20E-01	2083|2|0	534709|256|0	0.00024	19:51739497	273639	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*ETFB*	M3	<1%	1.329[0.655;2.696]	4.30E-01	2077|8|0	533213|1751|1	0.00164	19:51739497	394287	29
COVID19 positive hospitalized vs COVID19 negative or unknown	*ACSF3*	M1	<1%	0.683[0.258;1.808]	4.40E-01	2082|3|0	534093|872|0	0.00081	16:89117727	17046	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*ANKRD11*	M3	<1%	1.168[0.788;1.733]	4.40E-01	2056|29|0	528339|6623|3	0.0062	16:89117727	150750	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*DNAJC28*	M3	<1%	0.762[0.384;1.512]	4.40E-01	2079|6|0	533031|1934|0	0.00181	21:33252612:A:G	235614	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*FYCO1*	M1	<1%	1.425[0.575;3.534]	4.40E-01	2080|5|0	533865|1098|2	0.00103	3:45859597:C:T	62167	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*GALNS*	M3	<1%	0.747[0.357;1.563]	4.40E-01	2080|5|0	533141|1823|1	0.0017	16:89117727	303289	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNGR2*	M3	<1%	3.072[0.176;53.618]	4.40E-01	1872|1|0	508406|126|0	0.00012	21:33252612:A:G	150931	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*PLIN3*	M3	<1%	0.591[0.154;2.274]	4.40E-01	2084|1|0	534513|451|1	0.00042	19:4719431:G:A	119760	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*PLIN4*	M3	<1%	1.203[0.756;1.912]	4.40E-01	2064|21|0	530811|4133|21	0.00391	19:4719431:G:A	214973	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*TRAPPC2L*	M3	<1%	0.856[0.575;1.273]	4.40E-01	2064|21|0	527447|7504|14	0.00703	16:89117727	260577	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*ADAMTSL2*	M1	<1%	0.727[0.317;1.669]	4.50E-01	2081|4|0	533744|1214|7	0.00115	9:133270015:A:C	264725	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*GART*	M1	<1%	1.393[0.591;3.285]	4.50E-01	2078|7|0	533417|1548|0	0.00145	21:33252612:A:G	251511	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*IL10RB*	M1	<1%	2.965[0.174;50.555]	4.50E-01	1937|1|0	517584|148|0	0.00014	21:33252612:A:G	13853	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*SLC2A6*	M1	<1%	0.377[0.030;4.670]	4.50E-01	2085|0|0	534801|163|1	0.00015	9:133270015:A:C	202005	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF649*	M1	<1%	0.367[0.027;4.993]	4.50E-01	1873|0|0	508363|169|0	0.00017	19:51739497	151120	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF649*	M3	<1%	0.367[0.027;4.993]	4.50E-01	1873|0|0	508363|169|0	0.00017	19:51739497	151120	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*AIF1*	M1	<1%	0.364[0.025;5.368]	4.60E-01	1938|0|0	517587|145|0	0.00014	6:31153649:G:A	461680	32
COVID19 positive hospitalized vs COVID19 negative or unknown	*SEMA6B*	M1	<1%	0.359[0.023;5.521]	4.60E-01	1873|0|0	508407|125|0	0.00012	19:4719431:G:A	176518	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*SEMA6B*	M3	<1%	0.359[0.023;5.521]	4.60E-01	1873|0|0	508407|125|0	0.00012	19:4719431:G:A	176518	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*EBI3*	M1	<1%	0.366[0.023;5.774]	4.70E-01	1873|0|0	508388|144|0	0.00014	19:4719431:G:A	489881	24
COVID19 positive hospitalized vs COVID19 negative or unknown	*FLOT1*	M1	<1%	0.365[0.023;5.722]	4.70E-01	1873|0|0	508397|135|0	0.00013	6:31153649:G:A	425534	26
COVID19 positive hospitalized vs COVID19 negative or unknown	*MED22*	M3	<1%	0.600[0.150;2.401]	4.70E-01	2084|1|0	534484|481|0	0.00045	9:133270015:A:C	71489	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*NKG7*	M3	<1%	1.921[0.322;11.460]	4.70E-01	1871|2|0	508207|325|0	0.00032	19:51739497	367721	26
COVID19 positive hospitalized vs COVID19 negative or unknown	*SLC2A6*	M3	<1%	1.403[0.555;3.542]	4.70E-01	2079|6|0	533752|1212|1	0.00114	9:133270015:A:C	202005	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*C19orf84*	M1	<1%	0.363[0.021;6.289]	4.90E-01	1770|0|0	407837|141|0	0.00017	19:51739497	350514	24
COVID19 positive hospitalized vs COVID19 negative or unknown	*C19orf84*	M3	<1%	0.363[0.021;6.289]	4.90E-01	1770|0|0	407837|141|0	0.00017	19:51739497	350514	24
COVID19 positive hospitalized vs COVID19 negative or unknown	*LZTFL1*	M1	<1%	0.368[0.022;6.171]	4.90E-01	1873|0|0	508386|146|0	0.00014	3:45859597:C:T	33284	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*TMIGD2*	M1	<1%	1.872[0.319;11.005]	4.90E-01	2016|2|0	525931|295|1	0.00028	19:4719431:G:A	426833	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*TMIGD2*	M3	<1%	1.872[0.319;11.005]	4.90E-01	2016|2|0	525931|295|1	0.00028	19:4719431:G:A	426833	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*GART*	M3	<1%	1.178[0.728;1.903]	5.00E-01	2065|20|0	530814|4149|2	0.00389	21:33252612:A:G	251511	9

COVID19 positive hospitalized vs COVID19 negative or unknown	*LTB*	M3	<1%	0.359[0.018;7.128]	5.00E-01	1873|0|0	508445|87|0	0.00009	6:31153649:G:A	427059	27
COVID19 positive hospitalized vs COVID19 negative or unknown	*NUDCD2*	M3	<1%	0.607[0.142;2.598]	5.00E-01	2084|1|0	534582|383|0	0.00036	5:163300447	153519	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*SURF4*	M3	<1%	0.612[0.149;2.513]	5.00E-01	2084|1|0	534492|472|1	0.00044	9:133270015:A:C	93448	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*C6orf15*	M1	<1%	0.370[0.019;7.362]	5.10E-01	1873|0|0	508407|124|1	0.00012	6:31153649:G:A	42269	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*CDT1*	M3	<1%	0.840[0.500;1.412]	5.10E-01	2073|12|0	532038|2920|7	0.00274	16:89117727	313896	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*FPR2*	M1	<1%	0.365[0.019;7.103]	5.10E-01	1953|0|0	516947|80|0	0.00008	19:51739497	29161	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*FPR2*	M3	<1%	0.365[0.019;7.103]	5.10E-01	1953|0|0	516947|80|0	0.00008	19:51739497	29161	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*MPND*	M3	<1%	1.146[0.765;1.717]	5.10E-01	2059|25|1	528772|6178|15	0.0058	19:4719431:G:A	375838	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*GTF3C5*	M3	<1%	1.236[0.644;2.372]	5.20E-01	2074|11|0	532496|2469|0	0.00231	9:133270015:A:C	239004	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*MVD*	M3	<1%	0.778[0.361;1.676]	5.20E-01	2080|5|0	533277|1687|1	0.00158	16:89117727	465203	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*CBFA2T3*	M1	<1%	2.336[0.164;33.240]	5.30E-01	1872|1|0	508348|183|1	0.00018	16:89117727	240752	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCNG1*	M1	<1%	0.370[0.017;7.948]	5.30E-01	2020|0|0	525664|101|0	0.0001	5:163300447	138809	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*IL17C*	M1	<1%	0.364[0.016;8.237]	5.30E-01	1873|0|0	508415|117|0	0.00011	16:89117727	479086	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*AC018755.18*	M3	<1%	1.134[0.757;1.697]	5.40E-01	2058|27|0	528870|6077|18	0.00572	19:51739497	127267	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*HAS1*	M3	<1%	1.169[0.709;1.925]	5.40E-01	2067|18|0	530804|4159|2	0.00389	19:51739497	26071	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*PLIN3*	M1	<1%	0.640[0.151;2.712]	5.40E-01	2084|1|0	534575|389|1	0.00036	19:4719431:G:A	119760	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*APRT*	M1	<1%	0.637[0.147;2.755]	5.50E-01	1939|1|0	516800|470|0	0.00045	16:89117727	308030	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*FPR3*	M3	<1%	0.379[0.016;9.247]	5.50E-01	1940|0|0	517201|69|0	0.00007	19:51739497	84251	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF577*	M1	<1%	0.710[0.232;2.175]	5.50E-01	2083|2|0	534235|729|1	0.00068	19:51739497	133034	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF577*	M3	<1%	0.710[0.232;2.175]	5.50E-01	2083|2|0	534235|729|1	0.00068	19:51739497	133034	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCR3*	M3	<1%	0.839[0.467;1.509]	5.60E-01	2076|9|0	532705|2252|8	0.00212	3:45859597:C:T	404806	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*REXO4*	M1	<1%	1.410[0.440;4.521]	5.60E-01	2081|4|0	534520|442|3	0.00042	9:133270015:A:C	136937	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*ABO*	M1	<1%	1.163[0.694;1.949]	5.70E-01	2068|17|0	531205|3752|8	0.00352	9:133270015:A:C	14414	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*ABO*	M3	<1%	1.163[0.694;1.949]	5.70E-01	2068|17|0	531205|3752|8	0.00352	9:133270015:A:C	14414	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*CRYZL1*	M3	<1%	0.755[0.288;1.982]	5.70E-01	2082|3|0	533923|1041|1	0.00097	21:33252612:A:G	337178	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*DPP9*	M1	<1%	0.364[0.011;12.326]	5.70E-01	1938|0|0	517629|103|0	0.0001	19:4719431:G:A	42868	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*GTF2H4*	M1	<1%	0.648[0.147;2.863]	5.70E-01	1872|1|0	508061|471|0	0.00046	6:31153649:G:A	244613	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*GTF2H4*	M3	<1%	0.648[0.147;2.863]	5.70E-01	1872|1|0	508061|471|0	0.00046	6:31153649:G:A	244613	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*NFKBIL1*	M1	<1%	0.362[0.010;12.546]	5.70E-01	1938|0|0	517626|106|0	0.0001	6:31153649:G:A	394045	22
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAP2*	M1	<1%	0.647[0.146;2.879]	5.70E-01	2084|1|0	534556|408|1	0.00038	19:4719431:G:A	395299	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAP2*	M3	<1%	0.647[0.146;2.879]	5.70E-01	2084|1|0	534556|408|1	0.00038	19:4719431:G:A	395299	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*AC018755.18*	M1	<1%	1.121[0.745;1.688]	5.80E-01	2059|26|0	529089|5858|18	0.00551	19:51739497	127267	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*DDR1*	M3	<1%	0.897[0.612;1.314]	5.80E-01	2061|24|0	528177|6786|2	0.00634	6:31153649:G:A	268430	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*GTF3C5*	M1	<1%	1.613[0.302;8.614]	5.80E-01	2018|2|0	525364|401|0	0.00038	9:133270015:A:C	239004	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*IER3*	M3	<1%	0.366[0.011;12.404]	5.80E-01	1940|0|0	517178|92|0	0.00009	6:31153649:G:A	409714	23
COVID19 positive hospitalized vs COVID19 negative or unknown	*RPL13*	M1	<1%	0.386[0.014;11.051]	5.80E-01	2020|0|0	525710|55|0	0.00005	16:89117727	443232	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*RPL13*	M3	<1%	0.386[0.014;11.051]	5.80E-01	2020|0|0	525710|55|0	0.00005	16:89117727	443232	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*CXCR6*	M3	<1%	1.374[0.439;4.303]	5.90E-01	2082|3|0	533961|1004|0	0.00094	3:45859597:C:T	86884	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*DDX39B*	M1	<1%	0.369[0.010;13.799]	5.90E-01	1873|0|0	508388|144|0	0.00014	6:31153649:G:A	376784	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*EBI3*	M3	<1%	0.659[0.147;2.957]	5.90E-01	2084|1|0	534577|387|1	0.00036	19:4719431:G:A	489881	24
COVID19 positive hospitalized vs COVID19 negative or unknown	*HLA-C*	M1	<1%	0.819[0.399;1.682]	5.90E-01	1932|6|0	515869|1859|4	0.0018	6:31153649:G:A	115519	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*HLA-C*	M3	<1%	0.819[0.399;1.682]	5.90E-01	1932|6|0	515869|1859|4	0.0018	6:31153649:G:A	115519	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*SNAI3*	M1	<1%	2.035[0.154;26.820]	5.90E-01	1937|1|0	517625|104|3	0.00011	16:89117727	439280	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*CYBA*	M1	<1%	0.365[0.009;15.232]	6.00E-01	1873|0|0	508439|93|0	0.00009	16:89117727	474375	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*LTA*	M3	<1%	0.370[0.009;15.194]	6.00E-01	1873|0|0	508450|82|0	0.00008	6:31153649:G:A	419093	24
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC10*	M3	<1%	1.257[0.533;2.964]	6.00E-01	2080|5|0	532691|2274|0	0.00212	19:51739497	328399	23
COVID19 positive hospitalized vs COVID19 negative or unknown	*ETFB*	M1	<1%	0.382[0.010;15.023]	6.10E-01	2018|0|0	526137|90|0	0.00009	19:51739497	394287	29
COVID19 positive hospitalized vs COVID19 negative or unknown	*IER3*	M1	<1%	0.365[0.008;17.529]	6.10E-01	1873|0|0	508462|70|0	0.00007	6:31153649:G:A	409714	23
COVID19 positive hospitalized vs COVID19 negative or unknown	*MAT2B*	M1	<1%	0.365[0.008;17.788]	6.10E-01	1873|0|0	508463|69|0	0.00007	5:163300447	202947	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*RPL7A*	M1	<1%	0.364[0.007;18.601]	6.10E-01	1873|0|0	508464|68|0	0.00007	9:133270015:A:C	78228	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*TMEM50B*	M3	<1%	1.489[0.318;6.964]	6.10E-01	2004|1|0	526117|353|0	0.00033	21:33252612:A:G	198205	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCR9*	M3	<1%	0.845[0.435;1.640]	6.20E-01	2075|10|0	531749|3216|0	0.003	3:45859597:C:T	35336	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*PIEZO1*	M3	<1%	0.954[0.793;1.149]	6.20E-01	1973|111|1	504609|30275|81	0.02844	16:89117727	402123	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLECL1*	M1	<1%	1.211[0.569;2.576]	6.20E-01	2010|8|0	524449|1772|6	0.0017	19:51739497	475425	34
COVID19 positive hospitalized vs COVID19 negative or unknown	*TMEM8C*	M1	<1%	0.366[0.007;19.640]	6.20E-01	1873|0|0	508459|73|0	0.00007	9:133270015:A:C	244620	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*ANKRD11*	M1	<1%	0.370[0.006;21.174]	6.30E-01	1873|0|0	508426|106|0	0.0001	16:89117727	150750	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*HLA-B*	M1	<1%	0.370[0.006;21.195]	6.30E-01	1873|0|0	508450|82|0	0.00008	6:31153649:G:A	200833	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*HLA-B*	M3	<1%	0.370[0.006;21.195]	6.30E-01	1873|0|0	508450|82|0	0.00008	6:31153649:G:A	200833	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*LTB*	M1	<1%	0.364[0.006;22.319]	6.30E-01	1873|0|0	508475|57|0	0.00006	6:31153649:G:A	427059	27
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLECL1*	M3	<1%	1.204[0.567;2.557]	6.30E-01	2077|8|0	533180|1779|6	0.00167	19:51739497	475425	34
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR1*	M3	<1%	0.756[0.234;2.444]	6.40E-01	2083|2|0	534219|746|0	0.0007	21:33252612:A:G	72443	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*NRM*	M1	<1%	1.796[0.152;21.204]	6.40E-01	1952|1|0	516825|202|0	0.0002	6:31153649:G:A	464989	33
COVID19 positive hospitalized vs COVID19 negative or unknown	*GFI1B*	M1	<1%	0.367[0.004;30.523]	6.60E-01	1873|0|0	508466|66|0	0.00006	9:133270015:A:C	283337	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*PLIN4*	M1	<1%	1.140[0.639;2.033]	6.60E-01	2072|13|0	532007|2949|9	0.00277	19:4719431:G:A	214973	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*SON*	M1	<1%	0.364[0.004;34.635]	6.60E-01	1940|0|0	517207|63|0	0.00006	21:33252612:A:G	290480	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*HAS1*	M1	<1%	1.189[0.532;2.654]	6.70E-01	2078|7|0	533219|1745|1	0.00163	19:51739497	26071	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*LRG1*	M3	<1%	1.270[0.427;3.778]	6.70E-01	2083|2|0	534605|360|0	0.00034	19:4719431:G:A	181492	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC6*	M1	<1%	0.708[0.143;3.510]	6.70E-01	1872|1|0	507687|845|0	0.00083	19:51739497	219416	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC6*	M3	<1%	0.708[0.143;3.510]	6.70E-01	1872|1|0	507687|845|0	0.00083	19:51739497	219416	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*TNF*	M3	<1%	1.319[0.364;4.770]	6.70E-01	1950|3|0	516388|639|0	0.00062	6:31153649:G:A	422092	25
COVID19 positive hospitalized vs COVID19 negative or unknown	*LST1*	M1	<1%	0.366[0.003;43.447]	6.80E-01	1873|0|0	508483|49|0	0.00005	6:31153649:G:A	433650	29
COVID19 positive hospitalized vs COVID19 negative or unknown	*LST1*	M3	<1%	0.366[0.003;43.447]	6.80E-01	1873|0|0	508483|49|0	0.00005	6:31153649:G:A	433650	29
COVID19 positive hospitalized vs COVID19 negative or unknown	*MCCD1*	M1	<1%	1.676[0.149;18.821]	6.80E-01	1872|1|0	508364|168|0	0.00017	6:31153649:G:A	375365	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*MCCD1*	M3	<1%	1.676[0.149;18.821]	6.80E-01	1872|1|0	508364|168|0	0.00017	6:31153649:G:A	375365	19
COVID19 positive hospitalized vs COVID19 negative or unknown	*TNFAIP8L1*	M1	<1%	0.367[0.003;43.093]	6.80E-01	1873|0|0	508485|47|0	0.00005	19:4719431:G:A	67562	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCR1*	M1	<1%	0.364[0.002;56.469]	6.90E-01	1873|0|0	508498|34|0	0.00003	3:45859597:C:T	343648	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*LIM2*	M1	<1%	0.370[0.003;49.414]	6.90E-01	1940|0|0	517211|59|0	0.00006	19:51739497	359297	25
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF613*	M3	<1%	1.380[0.280;6.797]	6.90E-01	2083|2|0	534542|423|0	0.0004	19:51739497	196723	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*MICA*	M1	<1%	1.113[0.628;1.974]	7.10E-01	2072|13|0	531757|3199|9	0.00301	6:31153649:G:A	249983	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*MICA*	M3	<1%	1.113[0.628;1.974]	7.10E-01	2072|13|0	531757|3199|9	0.00301	6:31153649:G:A	249983	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF778*	M1	<1%	0.826[0.298;2.288]	7.10E-01	2082|3|0	533989|974|2	0.00091	16:89117727	103400	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF778*	M3	<1%	0.826[0.298;2.288]	7.10E-01	2082|3|0	533989|974|2	0.00091	16:89117727	103400	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*FPR1*	M3	<1%	0.796[0.234;2.707]	7.20E-01	2083|2|0	534362|603|0	0.00056	19:51739497	6444	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*PSORS1C2*	M3	<1%	1.214[0.419;3.516]	7.20E-01	2016|4|0	524628|1136|1	0.00108	6:31153649:G:A	15699	4
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF613*	M1	<1%	0.741[0.144;3.824]	7.20E-01	2084|1|0	534564|401|0	0.00037	19:51739497	196723	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*DONSON*	M1	<1%	1.206[0.418;3.480]	7.30E-01	2081|4|0	534292|671|2	0.00063	21:33252612:A:G	325694	11

COVID19 positive hospitalized vs COVID19 negative or unknown	*FSD1*	M1	<1%	0.369[0.001;117.744]	7.30E-01	1873|0|0	508494|38|0	0.00004	19:4719431:G:A	414685	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*GBGT1*	M3	<1%	1.049[0.804;1.368]	7.30E-01	2027|57|1	521986|12948|31	0.01217	9:133270015:A:C	116439	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC12*	M1	<1%	1.182[0.460;3.036]	7.30E-01	2080|5|0	533981|982|2	0.00092	19:51739497	247857	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC12*	M3	<1%	1.179[0.459;3.029]	7.30E-01	2080|5|0	533980|983|2	0.00092	19:51739497	247857	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*CDH15*	M1	<1%	1.304[0.277;6.149]	7.40E-01	2083|2|0	534534|431|0	0.0004	16:89117727	54104	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*POU5F1*	M1	<1%	0.357[0.001;166.756]	7.40E-01	1873|0|0	508507|25|0	0.00002	6:31153649:G:A	10951	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*FAM163B*	M1	<1%	0.369[0.001;163.914]	7.50E-01	1873|0|0	508499|33|0	0.00003	9:133270015:A:C	309006	21
COVID19 positive hospitalized vs COVID19 negative or unknown	*STKLD1*	M1	<1%	1.166[0.455;2.987]	7.50E-01	2080|5|0	533984|980|1	0.00092	9:133270015:A:C	106458	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*TMEM50B*	M1	<1%	0.368[0.001;185.287]	7.50E-01	1873|0|0	508494|38|0	0.00004	21:33252612:A:G	198205	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF350*	M1	<1%	0.761[0.144;4.027]	7.50E-01	2084|1|0	534690|274|1	0.00026	19:51739497	225356	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF350*	M3	<1%	0.761[0.144;4.027]	7.50E-01	2084|1|0	534690|274|1	0.00026	19:51739497	225356	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCDC94*	M3	<1%	1.203[0.364;3.973]	7.60E-01	2083|2|0	534347|617|1	0.00058	19:4719431:G:A	472285	23
COVID19 positive hospitalized vs COVID19 negative or unknown	*DPCR1*	M1	<1%	0.823[0.237;2.860]	7.60E-01	2083|2|0	534233|731|1	0.00068	6:31153649:G:A	219027	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*DPCR1*	M3	<1%	0.823[0.237;2.860]	7.60E-01	2083|2|0	534233|731|1	0.00068	6:31153649:G:A	219027	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*DPP9*	M3	<1%	1.064[0.709;1.598]	7.60E-01	2060|25|0	528522|6430|13	0.00603	19:4719431:G:A	42868	1
COVID19 positive hospitalized vs COVID19 negative or unknown	*FPR3*	M1	<1%	0.369[0.001;215.142]	7.60E-01	1873|0|0	508510|22|0	0.00002	19:51739497	84251	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*PSORS1C1*	M1	<1%	0.898[0.453;1.780]	7.60E-01	2079|6|0	533000|1964|1	0.00184	6:31153649:G:A	24017	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*PSORS1C1*	M3	<1%	0.898[0.453;1.780]	7.60E-01	2079|6|0	533000|1964|1	0.00184	6:31153649:G:A	24017	5
COVID19 positive hospitalized vs COVID19 negative or unknown	*RNF166*	M1	<1%	1.273[0.270;6.009]	7.60E-01	2018|2|0	525477|288|0	0.00027	16:89117727	420160	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCR3*	M1	<1%	0.856[0.309;2.372]	7.70E-01	2017|3|0	525195|568|2	0.00054	3:45859597:C:T	404806	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF175*	M1	<1%	0.888[0.400;1.975]	7.70E-01	2081|4|0	533617|1345|3	0.00126	19:51739497	166168	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*ZNF175*	M3	<1%	0.888[0.400;1.975]	7.70E-01	2081|4|0	533617|1345|3	0.00126	19:51739497	166168	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*PABPN1L*	M1	<1%	0.834[0.238;2.922]	7.80E-01	2083|2|0	534369|595|1	0.00056	16:89117727	253991	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*RALGDS*	M1	<1%	1.232[0.274;5.532]	7.90E-01	2083|2|0	534634|331|0	0.00031	9:133270015:A:C	171429	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*TMEM8C*	M3	<1%	0.844[0.235;3.029]	7.90E-01	2083|2|0	534301|664|0	0.00062	9:133270015:A:C	244620	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*UBXN6*	M3	<1%	0.924[0.509;1.677]	7.90E-01	2076|8|1	532445|2517|3	0.00236	19:4719431:G:A	273934	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR1*	M1	<1%	0.805[0.146;4.438]	8.00E-01	2019|1|0	525406|359|0	0.00034	21:33252612:A:G	72443	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*NRM*	M3	<1%	0.850[0.238;3.033]	8.00E-01	2083|2|0	534283|682|0	0.00064	6:31153649:G:A	464989	33
COVID19 positive hospitalized vs COVID19 negative or unknown	*REXO4*	M3	<1%	1.097[0.527;2.285]	8.00E-01	2077|8|0	533569|1392|4	0.00131	9:133270015:A:C	136937	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*CACFD1*	M3	<1%	0.919[0.453;1.861]	8.10E-01	2080|5|0	533381|1583|1	0.00148	9:133270015:A:C	190051	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*LARS2*	M1	<1%	0.808[0.140;4.671]	8.10E-01	2004|1|0	526142|328|0	0.00031	3:45859597:C:T	465144	11
COVID19 positive hospitalized vs COVID19 negative or unknown	*PPP1R18*	M3	<1%	0.909[0.427;1.937]	8.10E-01	2079|6|0	534061|896|8	0.00085	6:31153649:G:A	476381	35
COVID19 positive hospitalized vs COVID19 negative or unknown	*PPP2R1A*	M1	<1%	0.366[0.000;1508.610]	8.10E-01	1873|0|0	508508|24|0	0.00002	19:51739497	450599	33
COVID19 positive hospitalized vs COVID19 negative or unknown	*UHRF1*	M1	<1%	0.368[0.000;1325.460]	8.10E-01	1873|0|0	508517|15|0	0.00001	19:4719431:G:A	190042	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*UHRF1*	M3	<1%	0.368[0.000;1325.460]	8.10E-01	1873|0|0	508517|15|0	0.00001	19:4719431:G:A	190042	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*CDH15*	M3	<1%	1.069[0.605;1.891]	8.20E-01	2072|13|0	532726|2233|6	0.0021	16:89117727	54104	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*MUC22*	M1	<1%	0.871[0.247;3.070]	8.30E-01	1913|2|0	425252|412|9	0.00051	6:31153649:G:A	142943	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*MUC22*	M3	<1%	0.871[0.247;3.070]	8.30E-01	1913|2|0	425252|412|9	0.00051	6:31153649:G:A	142943	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC10*	M1	<1%	1.119[0.395;3.165]	8.30E-01	1934|4|0	515732|2000|0	0.00193	19:51739497	328399	23
COVID19 positive hospitalized vs COVID19 negative or unknown	*CPNE7*	M3	<1%	1.048[0.644;1.708]	8.50E-01	2067|18|0	530935|4030|0	0.00377	16:89117727	458170	18
COVID19 positive hospitalized vs COVID19 negative or unknown	*LTA*	M1	<1%	0.367[0.000;12959.200]	8.50E-01	1873|0|0	508522|10|0	0.00001	6:31153649:G:A	419093	24
COVID19 positive hospitalized vs COVID19 negative or unknown	*RALGDS*	M3	<1%	0.954[0.589;1.545]	8.50E-01	2069|16|0	530761|4198|6	0.00393	9:133270015:A:C	171429	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*AIF1*	M3	<1%	0.852[0.143;5.082]	8.60E-01	2084|1|0	534686|279|0	0.00026	6:31153649:G:A	461680	32
COVID19 positive hospitalized vs COVID19 negative or unknown	*PABPN1L*	M3	<1%	0.916[0.358;2.345]	8.60E-01	2081|4|0	533859|1105|1	0.00103	16:89117727	253991	7
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC5*	M3	<1%	1.036[0.692;1.549]	8.60E-01	2060|25|0	528848|6101|16	0.00573	19:51739497	127267	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*TNF*	M1	<1%	0.368[0.000;22777.100]	8.60E-01	1873|0|0	508514|18|0	0.00002	6:31153649:G:A	422092	25
COVID19 positive hospitalized vs COVID19 negative or unknown	*CACFD1*	M1	<1%	1.191[0.145;9.818]	8.70E-01	2019|1|0	525594|171|0	0.00016	9:133270015:A:C	190051	14
COVID19 positive hospitalized vs COVID19 negative or unknown	*CLDND2*	M3	<1%	0.894[0.241;3.316]	8.70E-01	2083|2|0	534613|350|2	0.00033	19:51739497	372356	27
COVID19 positive hospitalized vs COVID19 negative or unknown	*SH3GL1*	M3	<1%	0.895[0.240;3.344]	8.70E-01	2083|2|0	534346|619|0	0.00058	19:4719431:G:A	357832	17
COVID19 positive hospitalized vs COVID19 negative or unknown	*TNFAIP8L1*	M3	<1%	1.190[0.143;9.890]	8.70E-01	2019|1|0	525556|209|0	0.0002	19:4719431:G:A	67562	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*TSC1*	M1	<1%	0.912[0.307;2.703]	8.70E-01	2082|3|0	534222|743|0	0.00069	9:133270015:A:C	373781	23
COVID19 positive hospitalized vs COVID19 negative or unknown	*SFTA2*	M1	<1%	0.373[0.000;129089.000]	8.80E-01	170|0|0	109274|18|0	0.00008	6:31153649:G:A	222162	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*SFTA2*	M3	<1%	0.373[0.000;129089.000]	8.80E-01	170|0|0	109274|18|0	0.00008	6:31153649:G:A	222162	13
COVID19 positive hospitalized vs COVID19 negative or unknown	*MDC1*	M3	<1%	0.914[0.244;3.430]	8.90E-01	2083|2|0	534403|562|0	0.00053	6:31153649:G:A	453185	31
COVID19 positive hospitalized vs COVID19 negative or unknown	*VSIG10L*	M1	<1%	0.959[0.522;1.761]	8.90E-01	2078|7|0	532727|2236|2	0.00209	19:51739497	406887	30
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCHCR1*	M3	<1%	0.971[0.605;1.557]	9.00E-01	2068|17|0	530623|4332|10	0.00407	6:31153649:G:A	11058	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*GBGT1*	M1	<1%	0.968[0.588;1.596]	9.00E-01	2071|13|1	531599|3355|11	0.00316	9:133270015:A:C	116439	10
COVID19 positive hospitalized vs COVID19 negative or unknown	*TUBB*	M1	<1%	0.381[0.000;1930640.000]	9.00E-01	1873|0|0	508521|11|0	0.00001	6:31153649:G:A	433143	28
COVID19 positive hospitalized vs COVID19 negative or unknown	*TUBB*	M3	<1%	0.381[0.000;1930640.000]	9.00E-01	1873|0|0	508521|11|0	0.00001	6:31153649:G:A	433143	28
COVID19 positive hospitalized vs COVID19 negative or unknown	*MDC1*	M1	<1%	0.927[0.245;3.513]	9.10E-01	2083|2|0	534414|551|0	0.00051	6:31153649:G:A	453185	31
COVID19 positive hospitalized vs COVID19 negative or unknown	*NFKBIL1*	M3	<1%	1.132[0.140;9.129]	9.10E-01	2084|1|0	534693|272|0	0.00025	6:31153649:G:A	394045	22
COVID19 positive hospitalized vs COVID19 negative or unknown	*ADAMTS13*	M1	<1%	1.076[0.256;4.523]	9.20E-01	2083|2|0	534440|525|0	0.00049	9:133270015:A:C	152428	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*ADAMTS13*	M3	<1%	1.076[0.256;4.523]	9.20E-01	2083|2|0	534440|525|0	0.00049	9:133270015:A:C	152428	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*CBFA2T3*	M3	<1%	1.028[0.613;1.725]	9.20E-01	2070|15|0	530741|4223|1	0.00395	16:89117727	240752	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*FSD1*	M3	<1%	0.945[0.314;2.841]	9.20E-01	2082|3|0	534131|834|0	0.00078	19:4719431:G:A	414685	20
COVID19 positive hospitalized vs COVID19 negative or unknown	*SIGLEC5*	M1	<1%	1.022[0.680;1.537]	9.20E-01	2061|24|0	529067|5882|16	0.00553	19:51739497	127267	8
COVID19 positive hospitalized vs COVID19 negative or unknown	*CLDND2*	M1	<1%	1.105[0.137;8.938]	9.30E-01	1937|1|0	517548|183|1	0.00018	19:51739497	372356	27
COVID19 positive hospitalized vs COVID19 negative or unknown	*IL10RB*	M3	<1%	0.923[0.141;6.047]	9.30E-01	2017|1|0	525901|326|0	0.00031	21:33252612:A:G	13853	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*BAG6*	M1	<1%	1.057[0.137;8.174]	9.60E-01	2004|1|0	526193|274|3	0.00027	6:31153649:G:A	485481	36
COVID19 positive hospitalized vs COVID19 negative or unknown	*STKLD1*	M3	<1%	1.016[0.526;1.960]	9.60E-01	2076|9|0	533250|1713|2	0.00161	9:133270015:A:C	106458	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCHCR1*	M1	<1%	0.991[0.597;1.647]	9.70E-01	2070|15|0	531208|3748|9	0.00352	6:31153649:G:A	11058	3
COVID19 positive hospitalized vs COVID19 negative or unknown	*NUDCD2*	M1	<1%	1.039[0.135;8.008]	9.70E-01	2084|1|0	534749|216|0	0.0002	5:163300447	153519	2
COVID19 positive hospitalized vs COVID19 negative or unknown	*SPG7*	M3	<1%	1.004[0.786;1.283]	9.70E-01	2025|60|0	519685|15227|53	0.01433	16:89117727	390690	12
COVID19 positive hospitalized vs COVID19 negative or unknown	*CDSN*	M1	<1%	0.986[0.235;4.140]	9.80E-01	2076|9|0	532683|2282|0	0.00213	6:31153649:G:A	37625	6
COVID19 positive hospitalized vs COVID19 negative or unknown	*KDM4B*	M1	<1%	0.972[0.142;6.666]	9.80E-01	1939|1|0	516645|625|0	0.0006	19:4719431:G:A	313459	15
COVID19 positive hospitalized vs COVID19 negative or unknown	*NKG7*	M1	<1%	0.977[0.140;6.842]	9.80E-01	1872|1|0	508276|256|0	0.00025	19:51739497	367721	26
COVID19 positive hospitalized vs COVID19 negative or unknown	*SNAI3*	M3	<1%	1.005[0.682;1.480]	9.80E-01	2062|23|0	528564|6389|12	0.00599	16:89117727	439280	16
COVID19 positive hospitalized vs COVID19 negative or unknown	*VSIG10L*	M3	<1%	1.004[0.723;1.393]	9.80E-01	2047|38|0	524592|10351|22	0.00971	19:51739497	406887	30
COVID19 positive hospitalized vs COVID19 negative or unknown	*LRG1*	M1	<1%	0.989[0.143;6.860]	9.90E-01	2019|1|0	525547|218|0	0.00021	19:4719431:G:A	181492	9
COVID19 positive hospitalized vs COVID19 negative or unknown	*CCR1*	M3	<1%	1.001[0.234;4.283]	1.00E+00	2084|1|0	534421|543|1	0.00051	3:45859597:C:T	343648	9

* RR: individuals who have genotype Reference/Reference for all variants included in burden test. RA: individuals who have genotype Reference/Alternate for at least one variant. AA: individuals who have genotype Alternate/Alternate for at least one variant.

Supplementary Table 9. Results from burden association tests for 14 genes related to interferon signaling.

Trait	*Gene*	Burden test	MAF	Odds Ratio [95% CI]	P-value	N cases with RR|RA|AA genotype*	N controls with RR|RA|AA genotype*	AAF
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR1*	M1	<0.1%	0.8 (0.15, 4.44)	0.8033	2019|1|0	525406|359|0	3.41E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR2*	M1	<0.1%	2.08 (0.62, 6.96)	0.2361	2082|3|0	534277|688|0	6.43E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IKBKG*	M1	<0.1%	0.49 (0.0, 50.22)	0.7634	1873|0|0	508491|31|10	5.00E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF3*	M1	<0.1%	0.96 (0.25, 3.64)	0.9476	2083|2|0	534559|406|0	3.80E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF7*	M1	<0.1%	1.16 (0.43, 3.18)	0.766	2082|3|0	534124|841|0	7.86E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF9*	M1	<0.1%	0.37 (0.0, 53.77)	0.696	1873|0|0	508479|53|0	5.19E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT1*	M1	<0.1%	0.37 (0.0, 126.71)	0.7357	1873|0|0	508490|42|0	4.11E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT2*	M1	<0.1%	0.35 (0.03, 4.44)	0.4215	1873|0|0	508405|127|0	1.24E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TBK1*	M1	<0.1%	0.37 (0.01, 11.96)	0.5714	1873|0|0	508445|87|0	8.52E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TICAM1*	M1	<0.1%	3.73 (0.19, 73.61)	0.387	1872|1|0	508368|164|0	1.62E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR3*	M1	<0.1%	1.13 (0.14, 8.83)	0.909	2084|1|0	534674|291|0	2.72E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR7*	M1	<0.1%	7.63 (1.87, 31.08)	0.004584	1872|0|1	508503|25|4	3.43E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TRAF3*	M1	<0.1%	0.37 (0.0, 733.64)	0.7966	1873|0|0	508504|28|0	2.74E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*UNC93B1*	M1	<0.1%	1.3 (0.27, 6.24)	0.741	1938|2|0	516861|409|0	3.96E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR1*	M1	<1%	0.8 (0.15, 4.44)	0.8033	2019|1|0	525406|359|0	3.41E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR2*	M1	<1%	2.08 (0.62, 6.96)	0.2361	2082|3|0	534277|688|0	6.43E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IKBKG*	M1	<1%	0.49 (0.0, 50.22)	0.7634	1873|0|0	508491|31|10	5.00E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF3*	M1	<1%	1.82 (0.54, 6.13)	0.3334	2082|2|1	534509|455|1	4.29E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF7*	M1	<1%	1.16 (0.43, 3.18)	0.766	2082|3|0	534124|841|0	7.86E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF9*	M1	<1%	0.37 (0.0, 53.77)	0.696	1873|0|0	508479|53|0	5.19E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT1*	M1	<1%	0.37 (0.0, 126.71)	0.7357	1873|0|0	508490|42|0	4.11E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT2*	M1	<1%	0.35 (0.03, 4.44)	0.4215	1873|0|0	508405|127|0	1.24E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TBK1*	M1	<1%	0.37 (0.01, 11.96)	0.5714	1873|0|0	508445|87|0	8.52E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TICAM1*	M1	<1%	3.73 (0.19, 73.61)	0.387	1872|1|0	508368|164|0	1.62E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR3*	M1	<1%	1.13 (0.14, 8.83)	0.909	2084|1|0	534674|291|0	2.72E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR7*	M1	<1%	7.63 (1.87, 31.08)	0.004584	1872|0|1	508503|25|4	3.43E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TRAF3*	M1	<1%	0.37 (0.0, 733.64)	0.7966	1873|0|0	508504|28|0	2.74E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*UNC93B1*	M1	<1%	1.3 (0.27, 6.24)	0.741	1938|2|0	516861|409|0	3.96E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR1*	M1	singleton	0.37 (0.0, 44.0)	0.6857	1873|0|0	508477|55|0	5.39E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR2*	M1	singleton	0.36 (0.0, 179.42)	0.7463	1873|0|0	508500|32|0	3.13E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IKBKG*	M1	singleton	0.55 (0.0, 2706.13)	0.8906	1873|0|0	508523|7|2	1.08E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF3*	M1	singleton	0.37 (0.0, 113.18)	0.7313	1873|0|0	508495|37|0	3.62E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF7*	M1	singleton	0.37 (0.0, 64.55)	0.7071	1873|0|0	508481|51|0	5.00E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF9*	M1	singleton	0.37 (0.0, 249.69)	0.7666	1873|0|0	508505|27|0	2.64E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT1*	M1	singleton	0.37 (0.0, 301.54)	0.7688	1873|0|0	508502|30|0	2.94E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT2*	M1	singleton	0.37 (0.0, 37.61)	0.6705	1873|0|0	508487|45|0	4.41E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TBK1*	M1	singleton	0.36 (0.0, 86.69)	0.7179	1873|0|0	508501|31|0	3.04E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TICAM1*	M1	singleton	18.3 (1.71, 196.34)	0.01636	1872|1|0	508489|43|0	4.31E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR3*	M1	singleton	15.34 (1.46, 161.33)	0.02294	1939|1|0	517242|28|0	2.79E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR7*	M1	singleton	12.49 (2.71, 57.56)	0.001198	1872|0|1	508520|10|2	1.57E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TRAF3*	M1	singleton	0.37 (0.0, 8930.06)	0.8463	1873|0|0	508514|18|0	1.76E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*UNC93B1*	M1	singleton	0.37 (0.0, 186.54)	0.7539	1873|0|0	508489|43|0	4.21E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR1*	M3	<0.1%	0.76 (0.23, 2.44)	0.64	2083|2|0	534219|746|0	6.96E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR2*	M3	<0.1%	1.97 (0.6, 6.47)	0.2651	2082|3|0	534253|712|0	6.66E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IKBKG*	M3	<0.1%	0.45 (0.01, 19.74)	0.6761	1873|0|0	508452|70|10	8.82E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF3*	M3	<0.1%	0.79 (0.24, 2.59)	0.692	2083|2|0	534413|552|0	5.16E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF7*	M3	<0.1%	1.14 (0.52, 2.49)	0.7481	2080|5|0	533486|1479|0	1.38E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF9*	M3	<0.1%	0.37 (0.0, 53.77)	0.696	1873|0|0	508479|53|0	5.19E-05

COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT1*	M3	<0.1%	0.37 (0.04, 3.49)	0.3816	2018|0|0	526009|218|0	2.06E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT2*	M3	<0.1%	2.6 (1.27, 5.31)	0.008795	2073|12|0	533405|1559|1	1.46E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*TBK1*	M3	<0.1%	1.11 (0.45, 2.79)	0.8171	2081|4|0	533861|1103|1	1.03E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*TICAM1*	M3	<0.1%	3.66 (0.19, 71.22)	0.392	1872|1|0	508365|167|0	1.65E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR3*	M3	<0.1%	0.81 (0.43, 1.49)	0.4921	2077|8|0	532355|2609|1	2.44E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR7*	M3	<0.1%	1.58 (0.63, 3.98)	0.3321	2001|3|1	525830|477|163	7.64E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TRAF3*	M3	<0.1%	3.01 (0.53, 17.22)	0.2148	2019|1|0	525523|242|0	2.30E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*UNC93B1*	M3	<0.1%	1.66 (0.77, 3.58)	0.1922	2075|10|0	533331|1634|0	1.53E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR1*	M3	<1%	0.76 (0.23, 2.44)	0.64	2083|2|0	534219|746|0	6.96E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR2*	M3	<1%	1.97 (0.6, 6.47)	0.2651	2082|3|0	534253|712|0	6.66E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IKBKG*	M3	<1%	1.04 (0.54, 2.01)	0.9101	1935|0|3	516444|949|339	1.57E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF3*	M3	<1%	1.38 (0.46, 4.15)	0.5704	2082|2|1	534363|601|1	5.65E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF7*	M3	<1%	1.14 (0.52, 2.49)	0.7481	2080|5|0	533486|1479|0	1.38E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF9*	M3	<1%	0.37 (0.0, 53.77)	0.696	1873|0|0	508479|53|0	5.19E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT1*	M3	<1%	0.37 (0.04, 3.49)	0.3816	2018|0|0	526009|218|0	2.06E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT2*	M3	<1%	2.6 (1.27, 5.31)	0.008795	2073|12|0	533405|1559|1	1.46E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*TBK1*	M3	<1%	1.11 (0.45, 2.79)	0.8171	2081|4|0	533861|1103|1	1.03E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*TICAM1*	M3	<1%	3.66 (0.19, 71.22)	0.392	1872|1|0	508365|167|0	1.65E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR3*	M3	<1%	0.83 (0.52, 1.32)	0.4285	2070|15|0	530068|4895|2	4.57E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR7*	M3	<1%	1.58 (0.63, 3.98)	0.3321	2001|3|1	525830|477|163	7.64E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TRAF3*	M3	<1%	0.89 (0.48, 1.65)	0.711	2076|9|0	532255|2706|4	2.54E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*UNC93B1*	M3	<1%	1.66 (0.77, 3.58)	0.1922	2075|10|0	533331|1634|0	1.53E-03
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR1*	M3	singleton	0.37 (0.01, 20.63)	0.6273	1873|0|0	508465|67|0	6.56E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IFNAR2*	M3	singleton	0.36 (0.0, 138.92)	0.7352	1873|0|0	508498|34|0	3.33E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IKBKG*	M3	singleton	0.55 (0.0, 2553.85)	0.889	1873|0|0	508522|8|2	1.18E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF3*	M3	singleton	0.37 (0.0, 46.47)	0.687	1940|0|0	517212|58|0	5.59E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF7*	M3	singleton	2.94 (0.17, 51.0)	0.4591	2004|1|0	526371|99|0	9.46E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*IRF9*	M3	singleton	0.37 (0.0, 249.69)	0.7666	1873|0|0	508505|27|0	2.64E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT1*	M3	singleton	0.37 (0.01, 19.67)	0.6207	1873|0|0	508458|74|0	7.25E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*STAT2*	M3	singleton	35.11 (4.02, 306.33)	0.001283	2018|2|0	525651|114|0	1.10E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TBK1*	M3	singleton	0.37 (0.02, 8.91)	0.5401	2005|0|0	526361|109|0	1.03E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TICAM1*	M3	singleton	17.91 (1.68, 190.85)	0.01686	1872|1|0	508486|46|0	4.60E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR3*	M3	singleton	0.93 (0.14, 6.19)	0.943	2084|1|0	534786|178|1	1.69E-04
COVID19 positive hospitalized vs COVID19 negative or unknown	*TLR7*	M3	singleton	4.02 (1.16, 13.91)	0.02818	1939|0|1	517197|55|18	8.96E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*TRAF3*	M3	singleton	0.37 (0.01, 21.93)	0.6308	1873|0|0	508461|71|0	6.96E-05
COVID19 positive hospitalized vs COVID19 negative or unknown	*UNC93B1*	M3	singleton	0.38 (0.01, 12.45)	0.5832	1953|0|0	516939|88|0	8.48E-05
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR1*	M1	<0.1%	2.62 (0.18, 38.8)	0.4837	571|1|0	516685|342|0	3.31E-04
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR2*	M1	<0.1%	1.97 (0.17, 22.68)	0.5855	589|1|0	525553|674|0	6.41E-04
COVID19 positive severe vs COVID19 negative or unknown	*IKBKG*	M1	<0.1%	14.74 (1.12, 193.22)	0.04042	539|0|0	508491|31|10	5.01E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF3*	M1	<0.1%	3.02 (0.6, 15.18)	0.1793	589|1|0	525854|373|0	3.55E-04
COVID19 positive severe vs COVID19 negative or unknown	*IRF7*	M1	<0.1%	2.68 (0.39, 18.58)	0.3189	588|2|0	525395|832|0	7.92E-04
COVID19 positive severe vs COVID19 negative or unknown	*IRF9*	M1	<0.1%	0.42 (0.0, 5297.95)	0.8575	539|0|0	508479|53|0	5.21E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT1*	M1	<0.1%	0.38 (0.0, 3004.31)	0.8315	539|0|0	508490|42|0	4.13E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT2*	M1	<0.1%	0.37 (0.0, 38.82)	0.6778	539|0|0	508405|127|0	1.25E-04
COVID19 positive severe vs COVID19 negative or unknown	*TBK1*	M1	<0.1%	0.38 (0.0, 211.44)	0.7619	539|0|0	508445|87|0	8.54E-05
COVID19 positive severe vs COVID19 negative or unknown	*TICAM1*	M1	<0.1%	0.89 (0.05, 15.25)	0.9349	539|0|0	508368|164|0	1.61E-04
COVID19 positive severe vs COVID19 negative or unknown	*TLR3*	M1	<0.1%	0.41 (0.01, 21.61)	0.6594	590|0|0	525950|277|0	2.63E-04
COVID19 positive severe vs COVID19 negative or unknown	*TLR7*	M1	<0.1%	42.12 (0.51, 3486.63)	0.0969	539|0|0	508503|25|4	3.24E-05
COVID19 positive severe vs COVID19 negative or unknown	*TRAF3*	M1	<0.1%	0.43 (0.0, 281622.0)	0.9011	539|0|0	508504|28|0	2.75E-05
COVID19 positive severe vs COVID19 negative or unknown	*UNC93B1*	M1	<0.1%	3.35 (0.18, 61.63)	0.4157	538|1|0	508128|404|0	3.98E-04
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR1*	M1	<1%	2.62 (0.18, 38.8)	0.4837	571|1|0	516685|342|0	3.31E-04

COVID19 positive severe vs COVID19 negative or unknown	*IFNAR2*	M1	<1%	1.97 (0.17, 22.68)	0.5855	589|1|0	525553|674|0	6.41E-04
COVID19 positive severe vs COVID19 negative or unknown	*IKBKG*	M1	<1%	14.74 (1.12, 193.22)	0.04042	539|0|0	508491|31|10	5.01E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF3*	M1	<1%	3.02 (0.6, 15.18)	0.1793	589|1|0	525854|373|0	3.55E-04
COVID19 positive severe vs COVID19 negative or unknown	*IRF7*	M1	<1%	2.68 (0.39, 18.58)	0.3189	588|2|0	525395|832|0	7.92E-04
COVID19 positive severe vs COVID19 negative or unknown	*IRF9*	M1	<1%	0.42 (0.0, 5297.95)	0.8575	539|0|0	508479|53|0	5.21E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT1*	M1	<1%	0.38 (0.0, 3004.31)	0.8315	539|0|0	508490|42|0	4.13E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT2*	M1	<1%	0.37 (0.0, 38.82)	0.6778	539|0|0	508405|127|0	1.25E-04
COVID19 positive severe vs COVID19 negative or unknown	*TBK1*	M1	<1%	0.38 (0.0, 211.44)	0.7619	539|0|0	508445|87|0	8.54E-05
COVID19 positive severe vs COVID19 negative or unknown	*TICAM1*	M1	<1%	0.89 (0.05, 15.25)	0.9349	539|0|0	508368|164|0	1.61E-04
COVID19 positive severe vs COVID19 negative or unknown	*TLR3*	M1	<1%	0.41 (0.01, 21.61)	0.6594	590|0|0	525950|277|0	2.63E-04
COVID19 positive severe vs COVID19 negative or unknown	*TLR7*	M1	<1%	42.12 (0.51, 3486.63)	0.0969	539|0|0	508503|25|4	3.24E-05
COVID19 positive severe vs COVID19 negative or unknown	*TRAF3*	M1	<1%	0.43 (0.0, 281622.0)	0.9011	539|0|0	508504|28|0	2.75E-05
COVID19 positive severe vs COVID19 negative or unknown	*UNC93B1*	M1	<1%	3.35 (0.18, 61.63)	0.4157	538|1|0	508128|404|0	3.98E-04
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR1*	M1	singleton	0.37 (0.0, 165.53)	0.7518	539|0|0	508477|55|0	5.40E-05
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR2*	M1	singleton	0.48 (0.0, 901579.0)	0.9216	539|0|0	508500|32|0	3.14E-05
COVID19 positive severe vs COVID19 negative or unknown	*IKBKG*	M1	singleton	0.58 (0.0, 711727.0)	0.939	490|0|0	399233|6|1	1.00E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF3*	M1	singleton	24.01 (0.35, 1669.95)	0.1419	539|0|0	508495|37|0	3.63E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF7*	M1	singleton	0.45 (0.0, 19828.4)	0.8843	539|0|0	508481|51|0	5.01E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF9*	M1	singleton	0.45 (0.0, 564343.0)	0.9115	539|0|0	508505|27|0	2.65E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT1*	M1	singleton	0.38 (0.0, 9818.87)	0.8505	539|0|0	508502|30|0	2.95E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT2*	M1	singleton	0.39 (0.0, 13826.4)	0.861	539|0|0	508487|45|0	4.42E-05
COVID19 positive severe vs COVID19 negative or unknown	*TBK1*	M1	singleton	0.38 (0.0, 28255.6)	0.8649	539|0|0	508501|31|0	3.04E-05
COVID19 positive severe vs COVID19 negative or unknown	*TICAM1*	M1	singleton	15.49 (0.28, 860.18)	0.1812	539|0|0	508489|43|0	4.22E-05
COVID19 positive severe vs COVID19 negative or unknown	*TLR3*	M1	singleton	0.38 (0.0, 18335.2)	0.8602	539|0|0	508509|23|0	2.26E-05
COVID19 positive severe vs COVID19 negative or unknown	*TLR7*	M1	singleton	0.4 (0.0, 3891300000.0)	0.9371	490|0|0	399229|9|2	1.63E-05
COVID19 positive severe vs COVID19 negative or unknown	*TRAF3*	M1	singleton	0.42 (0.0, 1871470.0)	0.9114	539|0|0	508514|18|0	1.77E-05
COVID19 positive severe vs COVID19 negative or unknown	*UNC93B1*	M1	singleton	0.42 (0.0, 20393.0)	0.8758	539|0|0	508489|43|0	4.22E-05
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR1*	M3	<0.1%	1.07 (0.15, 7.68)	0.9458	589|1|0	525500|727|0	6.91E-04
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR2*	M3	<0.1%	1.88 (0.17, 20.82)	0.6068	589|1|0	525529|698|0	6.63E-04
COVID19 positive severe vs COVID19 negative or unknown	*IKBKG*	M3	<0.1%	12.55 (0.99, 159.28)	0.051	539|0|0	508452|70|10	8.84E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF3*	M3	<0.1%	2.53 (0.54, 11.8)	0.2388	589|1|0	525713|514|0	4.89E-04
COVID19 positive severe vs COVID19 negative or unknown	*IRF7*	M3	<0.1%	3.07 (0.81, 11.64)	0.09817	587|3|0	524764|1463|0	1.39E-03
COVID19 positive severe vs COVID19 negative or unknown	*IRF9*	M3	<0.1%	0.42 (0.0, 5297.95)	0.8575	539|0|0	508479|53|0	5.21E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT1*	M3	<0.1%	0.38 (0.01, 14.6)	0.6027	590|0|0	526009|218|0	2.07E-04
COVID19 positive severe vs COVID19 negative or unknown	*STAT2*	M3	<0.1%	1.64 (0.36, 7.55)	0.5246	587|3|0	524718|1508|1	1.44E-03
COVID19 positive severe vs COVID19 negative or unknown	*TBK1*	M3	<0.1%	1.96 (0.33, 11.47)	0.456	588|2|0	525137|1089|1	1.04E-03
COVID19 positive severe vs COVID19 negative or unknown	*TICAM1*	M3	<0.1%	0.89 (0.05, 15.22)	0.9349	539|0|0	508365|167|0	1.64E-04
COVID19 positive severe vs COVID19 negative or unknown	*TLR3*	M3	<0.1%	0.74 (0.24, 2.26)	0.5951	588|2|0	523680|2546|1	2.42E-03
COVID19 positive severe vs COVID19 negative or unknown	*TLR7*	M3	<0.1%	1.22 (0.29, 5.15)	0.7855	557|0|0	517105|467|160	7.59E-04
COVID19 positive severe vs COVID19 negative or unknown	*TRAF3*	M3	<0.1%	14.61 (1.54, 138.27)	0.01935	571|1|0	516792|235|0	2.28E-04
COVID19 positive severe vs COVID19 negative or unknown	*UNC93B1*	M3	<0.1%	3.13 (1.26, 7.77)	0.01414	584|6|0	524612|1615|0	1.54E-03
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR1*	M3	<1%	1.07 (0.15, 7.68)	0.9458	589|1|0	525500|727|0	6.91E-04
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR2*	M3	<1%	1.88 (0.17, 20.82)	0.6068	589|1|0	525529|698|0	6.63E-04
COVID19 positive severe vs COVID19 negative or unknown	*IKBKG*	M3	<1%	1.41 (0.48, 4.17)	0.5303	556|0|1	516444|949|339	1.57E-03
COVID19 positive severe vs COVID19 negative or unknown	*IRF3*	M3	<1%	2.53 (0.54, 11.8)	0.2388	589|1|0	525713|514|0	4.89E-04
COVID19 positive severe vs COVID19 negative or unknown	*IRF7*	M3	<1%	3.07 (0.81, 11.64)	0.09817	587|3|0	524764|1463|0	1.39E-03
COVID19 positive severe vs COVID19 negative or unknown	*IRF9*	M3	<1%	0.42 (0.0, 5297.95)	0.8575	539|0|0	508479|53|0	5.21E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT1*	M3	<1%	0.38 (0.01, 14.6)	0.6027	590|0|0	526009|218|0	2.07E-04
COVID19 positive severe vs COVID19 negative or unknown	*STAT2*	M3	<1%	1.64 (0.36, 7.55)	0.5246	587|3|0	524718|1508|1	1.44E-03
COVID19 positive severe vs COVID19 negative or unknown	*TBK1*	M3	<1%	1.96 (0.33, 11.47)	0.456	588|2|0	525137|1089|1	1.04E-03
COVID19 positive severe vs COVID19 negative or unknown	*TICAM1*	M3	<1%	0.89 (0.05, 15.22)	0.9349	539|0|0	508365|167|0	1.64E-04

COVID19 positive severe vs COVID19 negative or unknown	*TLR3*	M3	<1%	0.97 (0.41, 2.26)	0.9396	585|5|0	521403|4822|2	4.59E-03
COVID19 positive severe vs COVID19 negative or unknown	*TLR7*	M3	<1%	1.22 (0.29, 5.15)	0.7855	557|0|0	517105|467|160	7.59E-04
COVID19 positive severe vs COVID19 negative or unknown	*TRAF3*	M3	<1%	1.27 (0.49, 3.25)	0.6217	587|3|0	523530|2693|4	2.57E-03
COVID19 positive severe vs COVID19 negative or unknown	*UNC93B1*	M3	<1%	3.13 (1.26, 7.77)	0.01414	584|6|0	524612|1615|0	1.54E-03
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR1*	M3	singleton	0.37 (0.0, 119.72)	0.738	539|0|0	508465|67|0	6.58E-05
COVID19 positive severe vs COVID19 negative or unknown	*IFNAR2*	M3	singleton	0.47 (0.0, 448932.0)	0.9144	539|0|0	508498|34|0	3.34E-05
COVID19 positive severe vs COVID19 negative or unknown	*IKBKG*	M3	singleton	0.57 (0.0, 614503.0)	0.9374	490|0|0	399232|7|1	1.13E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF3*	M3	singleton	20.95 (0.32, 1352.58)	0.1525	539|0|0	508480|52|0	5.11E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF7*	M3	singleton	0.42 (0.0, 600.62)	0.8166	557|0|0	517640|92|0	8.88E-05
COVID19 positive severe vs COVID19 negative or unknown	*IRF9*	M3	singleton	0.45 (0.0, 564343.0)	0.9115	539|0|0	508505|27|0	2.65E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT1*	M3	singleton	0.38 (0.0, 269.14)	0.7735	539|0|0	508458|74|0	7.27E-05
COVID19 positive severe vs COVID19 negative or unknown	*STAT2*	M3	singleton	0.4 (0.0, 128.93)	0.7543	572|0|0	516919|108|0	1.04E-04
COVID19 positive severe vs COVID19 negative or unknown	*TBK1*	M3	singleton	0.38 (0.0, 184.6)	0.7614	557|0|0	517628|104|0	1.00E-04
COVID19 positive severe vs COVID19 negative or unknown	*TICAM1*	M3	singleton	15.0 (0.27, 819.65)	0.1846	539|0|0	508486|46|0	4.52E-05
COVID19 positive severe vs COVID19 negative or unknown	*TLR3*	M3	singleton	0.41 (0.01, 15.67)	0.6287	590|0|0	526065|161|1	1.55E-04
COVID19 positive severe vs COVID19 negative or unknown	*TLR7*	M3	singleton	11.63 (0.84, 161.65)	0.06761	539|0|0	508468|49|15	7.76E-05
COVID19 positive severe vs COVID19 negative or unknown	*TRAF3*	M3	singleton	0.4 (0.0, 689.93)	0.8098	539|0|0	508461|71|0	6.97E-05
COVID19 positive severe vs COVID19 negative or unknown	*UNC93B1*	M3	singleton	0.42 (0.0, 250.75)	0.7916	572|0|0	516939|88|0	8.50E-05

* RR: individuals who have genotype Reference/Reference for all variants included in burden test. RA: individuals who have genotype Reference/Alternate for at least one variant. AA: individuals who have genotype Alternate/Alternate for at least one variant.

Supplementary Table 10. Results from burden association tests for 32 additional genes of biological or therapeutic interest.

Trait	Gene	Burden test	MAF	Odds Ratio [95% CI]	P-value	N cases with RR|RA|AA genotype*	N controls with RR|RA|AA genotype*	AAF
COVID19 positive hospitalized vs COVID19 negative or unknown	IL23R	M1	<1%	3.849[0.853;17.373]	8.00E-02	1871|2|0	508324|208|0	0.00021
COVID19 positive hospitalized vs COVID19 negative or unknown	IL1A	M3	<1%	2.350[0.835;6.611]	1.10E-01	2016|4|0	525349|415|1	0.0004
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNL3	M1	<1%	14.959[0.345;647.891]	1.60E-01	1872|1|0	508438|94|0	0.00009
COVID19 positive hospitalized vs COVID19 negative or unknown	IL1A	M1	<1%	4.218[0.574;31.008]	1.60E-01	2019|1|0	525641|124|0	0.00012
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNL1	M3	<1%	0.369[0.086;1.585]	1.80E-01	2085|0|0	534569|395|1	0.00037
COVID19 positive hospitalized vs COVID19 negative or unknown	TMPRSS2	M1	<1%	2.526[0.646,9.876]	1.80E-01	1936|4|0	516764|506|0	0.00049
COVID19 positive hospitalized vs COVID19 negative or unknown	C5	M1	<1%	2.077[0.702;6.144]	1.90E-01	2081|4|0	534324|640|1	0.0006
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNL1	M1	<1%	0.369[0.081;1.687]	2.00E-01	2085|0|0	534607|357|1	0.00033
COVID19 positive hospitalized vs COVID19 negative or unknown	IL17RC	M3	<1%	1.643[0.749;3.604]	2.20E-01	2080|5|0	533824|1140|1	0.00107
COVID19 positive hospitalized vs COVID19 negative or unknown	VEGFA	M3	<1%	0.558[0.219;1.418]	2.20E-01	2083|2|0	533873|1091|1	0.00102
COVID19 positive hospitalized vs COVID19 negative or unknown	IL7R	M1	<1%	1.668[0.692;4.019]	2.50E-01	2079|6|0	533848|1117|0	0.00105
COVID19 positive hospitalized vs COVID19 negative or unknown	IL12B	M3	<1%	2.200[0.438;11.048]	3.40E-01	2017|1|0	526033|194|0	0.00018
COVID19 positive hospitalized vs COVID19 negative or unknown	IL23A	M3	<1%	0.366[0.046;2.919]	3.40E-01	1938|0|0	517449|282|1	0.00027
COVID19 positive hospitalized vs COVID19 negative or unknown	IL17RA	M1	<1%	0.359[0.040;3.220]	3.60E-01	2020|0|0	525537|228|0	0.00022
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNLR1	M3	<1%	0.366[0.040;3.321]	3.70E-01	1938|0|0	517531|201|0	0.00019
COVID19 positive hospitalized vs COVID19 negative or unknown	IL1B	M3	<1%	0.369[0.039;3.491]	3.80E-01	2005|0|0	526208|262|0	0.00025
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNL3	M3	<1%	3.464[0.185;64.982]	4.10E-01	1939|1|0	517141|129|0	0.00013
COVID19 positive hospitalized vs COVID19 negative or unknown	JAK1	M1	<1%	1.942[0.398;9.474]	4.10E-01	1937|1|0	517541|189|2	0.00019
COVID19 positive hospitalized vs COVID19 negative or unknown	JAK1	M3	<1%	1.942[0.398;9.474]	4.10E-01	1937|1|0	517541|189|2	0.00019
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNLR1	M1	<1%	0.365[0.030;4.527]	4.30E-01	1938|0|0	517571|161|0	0.00015
COVID19 positive hospitalized vs COVID19 negative or unknown	IL1B	M1	<1%	0.368[0.030;4.481]	4.30E-01	1873|0|0	508320|212|0	0.00021
COVID19 positive hospitalized vs COVID19 negative or unknown	JAK2	M1	<1%	0.366[0.029;4.555]	4.30E-01	1938|0|0	517530|202|0	0.00019
COVID19 positive hospitalized vs COVID19 negative or unknown	IL23R	M3	<1%	0.847[0.554;1.296]	4.40E-01	2067|18|0	529085|5861|19	0.00551
COVID19 positive hospitalized vs COVID19 negative or unknown	VEGFA	M1	<1%	0.661[0.218;2.002]	4.60E-01	2083|2|0	534217|747|1	0.0007
COVID19 positive hospitalized vs COVID19 negative or unknown	IL1R1	M1	<1%	0.666[0.222;1.995]	4.70E-01	1936|2|0	517281|444|7	0.00044
COVID19 positive hospitalized vs COVID19 negative or unknown	IL7R	M3	<1%	1.269[0.666;2.419]	4.70E-01	2075|10|0	532768|2197|0	0.00205
COVID19 positive hospitalized vs COVID19 negative or unknown	TMPRSS2	M3	<1%	1.341[0.606,2.967]	4.70E-01	2077|8|0	533498|1467|0	0.00137
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNG	M3	<1%	0.366[0.020;6.537]	4.90E-01	1873|0|0	508402|130|0	0.00013
COVID19 positive hospitalized vs COVID19 negative or unknown	BTK	M3	<1%	0.497[0.061;4.077]	5.10E-01	2020|0|0	525622|114|29	0.00016
COVID19 positive hospitalized vs COVID19 negative or unknown	IL6	M3	<1%	0.369[0.019;7.067]	5.10E-01	1953|0|0	516905|122|0	0.00012
COVID19 positive hospitalized vs COVID19 negative or unknown	IL6R	M1	<1%	0.377[0.020;7.210]	5.20E-01	1940|0|0	517152|118|0	0.00011
COVID19 positive hospitalized vs COVID19 negative or unknown	IL12B	M1	<1%	0.365[0.016;8.562]	5.30E-01	1873|0|0	508442|90|0	0.00009
COVID19 positive hospitalized vs COVID19 negative or unknown	IL1R1	M3	<1%	0.739[0.283;1.931]	5.40E-01	2082|3|0	534274|684|7	0.00065
COVID19 positive hospitalized vs COVID19 negative or unknown	IL6	M1	<1%	0.367[0.014;9.615]	5.50E-01	1873|0|0	508423|109|0	0.00011
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNGR1	M3	<1%	0.651[0.149;2.841]	5.70E-01	2084|1|0	534532|433|0	0.0004
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNL2	M3	<1%	1.481[0.380;5.766]	5.70E-01	2082|3|0	534408|557|0	0.00052
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNB1	M3	<1%	0.828[0.423;1.623]	5.80E-01	2011|7|0	524038|2186|3	0.00208
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNG	M1	<1%	0.364[0.011;12.464]	5.80E-01	1873|0|0	508453|79|0	0.00008
COVID19 positive hospitalized vs COVID19 negative or unknown	JAK2	M3	<1%	0.850[0.481;1.503]	5.80E-01	2075|10|0	532245|2714|6	0.00255
COVID19 positive hospitalized vs COVID19 negative or unknown	IL4R	M1	<1%	1.931[0.154;24.219]	6.10E-01	1937|1|0	517553|179|0	0.00017
COVID19 positive hospitalized vs COVID19 negative or unknown	PDCD1	M3	<1%	0.367[0.005;29.373]	6.50E-01	1873|0|0	508473|59|0	0.00006
COVID19 positive hospitalized vs COVID19 negative or unknown	IL17A	M1	<1%	0.364[0.004;35.613]	6.70E-01	1873|0|0	508492|40|0	0.00004
COVID19 positive hospitalized vs COVID19 negative or unknown	IL23A	M1	<1%	0.365[0.002;57.511]	7.00E-01	1873|0|0	508494|38|0	0.00004
COVID19 positive hospitalized vs COVID19 negative or unknown	ACE2	M1	<1%	0.392[0.002;61.868]	7.20E-01	1873|0|0	508485|44|3	0.00005
COVID19 positive hospitalized vs COVID19 negative or unknown	IL1RAP	M3	<1%	1.272[0.349;4.641]	7.20E-01	2083|2|0	534386|579|0	0.00054
COVID19 positive hospitalized vs COVID19 negative or unknown	IL4R	M3	<1%	1.534[0.147;16.057]	7.20E-01	2017|1|0	526039|188|0	0.00018
COVID19 positive hospitalized vs COVID19 negative or unknown	PDCD1	M1	<1%	0.367[0.002;83.673]	7.20E-01	1873|0|0	508492|40|0	0.00004
COVID19 positive hospitalized vs COVID19 negative or unknown	CSF2	M3	<1%	0.368[0.001;136.635]	7.40E-01	1873|0|0	508491|41|0	0.00004
COVID19 positive hospitalized vs COVID19 negative or unknown	BTK	M1	<1%	0.363[0.001;230.098]	7.60E-01	1873|0|0	508505|27|0	0.00003
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNGR1	M1	<1%	0.807[0.145;4.481]	8.10E-01	2084|1|0	534629|336|0	0.00031

COVID19 positive hospitalized vs COVID19 negative or unknown	ACE2	M3	<1%	0.944[0.582;1.533]	8.20E-01	2079|2|4	532861|1626|478	0.00241
COVID19 positive hospitalized vs COVID19 negative or unknown	CCR5	M1	<1%	0.939[0.521;1.690]	8.30E-01	2077|8|0	532508|2453|4	0.0023
COVID19 positive hospitalized vs COVID19 negative or unknown	CCR5	M3	<1%	0.939[0.521;1.690]	8.30E-01	2077|8|0	532508|2453|4	0.0023
COVID19 positive hospitalized vs COVID19 negative or unknown	IL1RAP	M1	<1%	1.281[0.142;11.540]	8.30E-01	1872|1|0	508333|199|0	0.0002
COVID19 positive hospitalized vs COVID19 negative or unknown	CSF2	M1	<1%	0.370[0.000;6631.170]	8.40E-01	1873|0|0	508515|17|0	0.00002
COVID19 positive hospitalized vs COVID19 negative or unknown	IL17RC	M1	<1%	1.113[0.317;3.899]	8.70E-01	2083|2|0	534378|587|0	0.00055
COVID19 positive hospitalized vs COVID19 negative or unknown	IL17A	M3	<1%	0.885[0.140;5.608]	9.00E-01	1872|1|0	508249|283|0	0.00028
COVID19 positive hospitalized vs COVID19 negative or unknown	C5	M3	<1%	0.984[0.670;1.445]	9.30E-01	2059|26|0	529016|5928|21	0.00558
COVID19 positive hospitalized vs COVID19 negative or unknown	IL6R	M3	<1%	1.089[0.143;8.291]	9.30E-01	2084|1|0	534746|219|0	0.0002
COVID19 positive hospitalized vs COVID19 negative or unknown	IL17RA	M3	<1%	1.009[0.713;1.429]	9.60E-01	2052|33|0	527528|7417|20	0.00697
COVID19 positive hospitalized vs COVID19 negative or unknown	IL33	M3	<1%	0.988[0.649;1.505]	9.60E-01	2063|22|0	529239|5720|6	0.00536
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNB1	M1	<1%	0.987[0.470;2.070]	9.70E-01	1946|7|0	515284|1741|2	0.00169
COVID19 positive hospitalized vs COVID19 negative or unknown	IL33	M1	<1%	0.993[0.652;1.513]	9.70E-01	2063|22|0	529265|5694|6	0.00533
COVID19 positive hospitalized vs COVID19 negative or unknown	IFNL2	M1	<1%	0.992[0.240;4.100]	9.90E-01	2083|2|0	534469|496|0	0.00046

* RR: individuals who have genotype Reference/Reference for all variants included in burden test. RA: individuals who have genotype Reference/Alternate for at least one variant. AA: individuals who have genotype Alternate/Alternate for at least one variant.