

Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

- | | |
|-------------------------------------|--|
| n/a | Confirmed |
| ☐ | ☒ The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement |
| ☐ | ☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly |
| ☐ | ☒ The statistical test(s) used AND whether they are one- or two-sided
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ A description of all covariates tested |
| ☒ | ☐ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons |
| ☐ | ☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals) |
| ☐ | ☒ For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings |
| ☒ | ☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes |
| ☐ | ☒ Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated |

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection	No new data was produced in the present study.
Data analysis	LDlink 4.1 for linkage disequilibrium (LD), PhyML 3.3 for the maximum-likelihood phylogenies, tabix (HTSlib 1.10) for calling variants in the genomes. PLINK 1.90 for LD pruning. Mathematica 11.0 for creating maps. All software are publicly available and except Mathematica free of charge.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

GWAS results (round 3, ANA_B2_V2): <https://www.covid19hg.org/results/>
 Neandertal genomes (Altai, Vindija 33.19, Chagyrskaya): <http://cdna.eva.mpg.de/neandertal/>
 1000 genomes project (phase 3 release): <https://www.internationalgenome.org/>
 Ensembl (release 100): <http://www.ensembl.org/>

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	We used all available high-coverage Neandertal genomes (n=3). The sample size of the GWAS (3,199 cases and 897,488 controls) was limited by the data provided from the cohorts. We used all genomes in the phase 3 release (n=2504) of the 1000 genomes project.
Data exclusions	Sites which are not shared between any two individuals were excluded, since those positions in the genome are not informative for the phylogenetic relationship. This exclusion criterium was not pre-established.
Replication	The findings in our study are easily reproducible using publicly available genomes. The significance of the phylogenies was assessed using bootstrap: the identified haplotypes grouped with the Vindija Neandertal 100 times out of 100 bootstrap replicates. All eight cohorts contributing to the meta-analysis showed a positive correlation between the risk allele and hospitalization.
Randomization	We used all relevant public data at hand, hence we did not performed any randomization of a subsample or equivalent. The genetic association study is not the product of this manuscript, we have only interpreted the results in an evolutionary perspective. For the phylogenetic trees, however, we use the built-in random number generator of PhyML 3.3 to calculate the phylogenies. As stated above, all bootstrap replicates resulted in the same monophyletic group.
Blinding	We analysed publicly available meta statistics from a genetic association study of hospitalized COVID-19 patients. The nature of the underlying data (hospitalized COVID-19 patients) is such that blinding (of hospitalization and infection with SARS-CoV2) was not possible within ethical and practical constraints.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging